[0041] In another aspect, the present disclosure provides a pharmaceutical composition including ivosidenib and a second molecule, the second molecule being selected from among 3-amino-5-fluoropyridine, 2-chloro-4-cyanopyridine, (*S*)-*N*-((*S*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide, 2-(2-Chlorophenyl)-*N*-(3,3-difluorocyclobutyl)-2-((5-fluoropyridin-3-yl)amino)acetamide, (*S*)-5-(((*S*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)(5-fluoropyridin-3-yl)amino)-4-((4-cyanopyridin-2-yl)amino)-5-oxopentanoic acid, (*S*)-4-(bis(4-cyanopyridin-2-yl)amino)-5-(((*S*)-1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)(5-fluoropyridin-3-yl)amino)-5-oxopentanoic acid, (*S*)-2-(2-Chlorophenyl)-2-((5-((4-cyanopyridin-2-yl)amino)-2-oxo-3,4-dihydro-2*H*-pyran-6-yl)(5-fluoropyridin-3-yl)amino)-*N*-(3,3-difluorocyclobutyl)acetamide, (2*S*)-*N*-((1*S*)-2-((2-chloro-3,3-difluorocyclobutyl)amino)-1-(2-chlorophenyl)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide, (*S*)-1-(4-Cyanopyridin-2-yl)-*N*-((S)-1-(2,4-dichlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide, (*S*)-1-(4-Cyanopyridin-2-yl)-*N*-((*S*)-1-(2,3-dichlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide, (*S*)-*N*-((*S*)-1-(4-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide, 3-((2*S*)-1-(4-carbamoylpyridin-2-yl)-*N*-(1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-5-oxopyrrolidine-2-carboxamido)-5-fluoropyridine 1-oxide, and 4-carbamoyl-2-((2*S*)-2-((1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)(5-fluoropyridin-3-yl)carbamoyl)-5-oxopyrrolidin-1-yl)pyridine 1-oxide, wherein the second molecule is present at a quantity of 0.15% area% or less as determined by HPLC analysis.

[0041a] In one aspect, there is provided a pharmaceutical composition comprising ivosidenib and one or more pharmaceutically acceptable excipients, wherein the composition contains no more than 0.10% (area % by HPLC) of one or more of 3-amino-5-fluoropyridine; 2-chloro-4-cyanopyridine; (*S*)-*N*-((*S*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide; 2-(2-Chlorophenyl)-*N*-(3,3-difluorocyclobutyl)-2-((5-fluoropyridin-3-yl)amino)acetamide; (*S*)-5-(((*S*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)(5-fluoropyridin-3-yl)amino)-4-((4-cyanopyridin-2-yl)amino)-5-oxopentanoic acid; (*S*)-4-(bis(4-cyanopyridin-2-yl)amino)-5-(((*S*)-1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)(5-fluoropyridin-3-yl)amino)-5-

oxopentanoic acid; (*S*)-2-(2-Chlorophenyl)-2-((5-((4-cyanopyridin-2-yl)amino)-2-oxo-3,4-dihydro-2*H*-pyran-6-yl)(5-fluoropyridin-3-yl)amino)-*N*-(3,3-difluorocyclobutyl)acetamide; (2*S*)-*N*-((1*S*)-2-((2-chloro-3,3-difluorocyclobutyl)amino)-1-(2-chlorophenyl)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide; (*S*)-1-(4-Cyanopyridin-2-yl)-*N*-((S)-1-(2,4-dichlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide; (*S*)-1-(4-Cyanopyridin-2-yl)-*N*-((*S*)-1-(2,3-dichlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide; (*S*)-*N*-((*S*)-1-(4-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide; 3-((2*S*)-1-(4-carbamoylpyridin-2-yl)-*N*-(1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-5-oxopyrrolidine-2-carboxamido)-5-fluoropyridine 1-oxide;4-carbamoyl-2-((2*S*)-2-((1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)(5-fluoropyridin-3-yl)carbamoyl)-5-oxopyrrolidin-1-yl)pyridine 1-oxide; and (*S*)-1-(4-Cyanopyridin-2-yl)-*N*-((*S*)-1-(3,3-difluorocyclobutyl)-2-oxoindolin-3-yl)-N-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide, or salts, hydrates, or solvates thereof.

[0042] In another aspect, the present disclosure provides a pharmaceutical composition including ivosidenib and a second molecule, the second molecule being selected from among benzaldehyde, benzyl chloride, 2-chlorobenzyl chloride, 1-chloro-2-(chloromethyl)benzene, 1-chloro-2-(dichloromethyl)benzene, phenol, and benzene, wherein the second molecule is present at a quantity of 2 ppm or less.

[0043] In another aspect, the present disclosure provides a pharmaceutical composition comprising ivosidenib and one or more pharmaceutically acceptable excipients, wherein the composition contains no more than trace palladium, molybdenum, cadmium, lead, arsenic, mercury, cobalt, vanadium, and nickel.

[0043a] In one aspect, the present disclosure provides a pharmaceutical composition comprising ivosidenib and one or more pharmaceutically acceptable excipients, wherein the composition contains no more than 10 ppm of palladium.

[0043b] In another aspect, there is provided a pharmaceutical composition comprising ivosidenib and one or more pharmaceutically acceptable excipients, wherein the composition contains no more than 300 ppm of molybdenum.

[0044] In another aspect, the present disclosure provides a pharmaceutical composition comprising ivosidenib and one or more pharmaceutically acceptable excipients, wherein the composition contains no more than each of: 5000 ppm of isopropyl acetate, 5000 ppm *n*-heptane, 600 ppm dichloromethane, and 2 ppm benzene.

[0044a] In another aspect, there is provided a method for testing the suitability of an ivosidenib composition for use in therapy wherein the composition comprises less than a total of 2% of process contaminants, heavy metal impurities, and residual solvents.

[0045] In another aspect, the present disclosure provides a process for making ivosidenib comprising testing at one or more stage of the process for one or more of:

2-((2*S*)-2-((1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)(5-fluoropyridin-3-yl)carbamoyl)-5-oxopyrrolidin-1-yl)isonicotinamide; (*S*)-*N*-((S)-1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-5-oxo-*N*-(pyridin-3-yl)pyrrolidine-2-carboxamide; (*S*)-*N*-((*R*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide; (*R*)-*N*-((*S*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide; and (*R*)-*N*-((*R*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide,

or a salt, hydrate, or solvate thereof.

[0046] In another aspect, the present disclosure provides a process for making ivosidenib comprising testing at one or more stage of the process for one or more of:

3-amino-5-fluoropyridine;

2-chloro-4-cyanopyridine;

(*S*)-*N*-((*S*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide;

2-(2-Chlorophenyl)-*N*-(3,3-difluorocyclobutyl)-2-((5-fluoropyridin-3-yl)amino)acetamide;

(*S*)-5-(((*S*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)(5-fluoropyridin-3-yl)amino)-4-((4-cyanopyridin-2-yl)amino)-5-oxopentanoic acid;

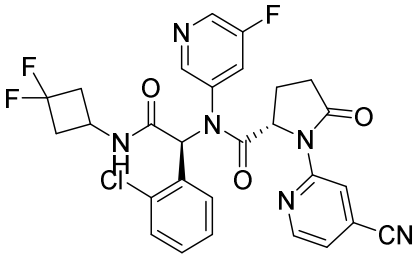
(*S*)-4-(bis(4-cyanopyridin-2-yl)amino)-5-(((*S*)-1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)(5-fluoropyridin-3-yl)amino)-5-oxopentanoic acid;

(*S*)-2-(2-Chlorophenyl)-2-((5-((4-cyanopyridin-2-yl)amino)-2-oxo-3,4-dihydro-2*H*-pyran-6-yl)(5-fluoropyridin-3-yl)amino)-*N*-(3,3-difluorocyclobutyl)acetamide;

CLAIMS

What is claimed is:

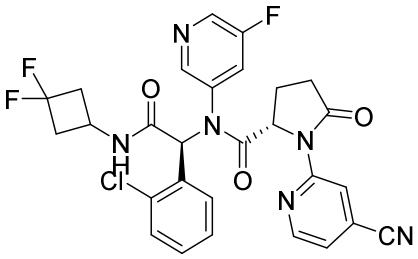
1. Solid state Form E of a compound of formula (I):



(I).

or a hydrate or solvate thereof.

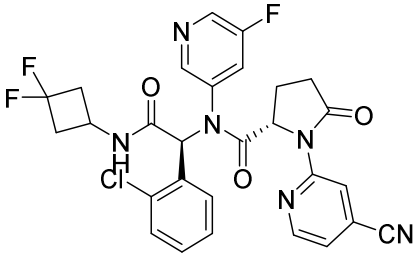
2. The compound of claim 1, wherein the Form E is a solvated form.
3. The compound of claim 2, wherein the compound is Form E isopropyl acetate solvate.
4. Solid state Form G of a compound of formula (I):



(I).

or a hydrate or solvate thereof.

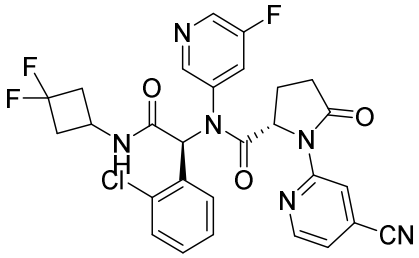
5. The compound of claim 4, wherein the Form G is a solvated or hydrated form.
6. Solid state Form M of a compound of formula (I):



(I).

or a hydrate or solvate thereof.

7. The compound of claim 6, wherein the Form M is anhydrous.
8. Solid state Form N of a compound of formula (I):



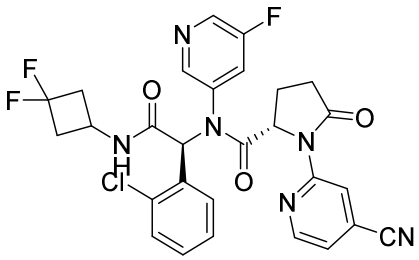
(I).

or a hydrate or solvate thereof.

9. The compound of claim 8, wherein the Form N is anhydrous.

10. A pharmaceutical composition comprising one or more compounds of any one of claims 1 – 9.

11. A solid state form of the compound of Formula I



(I).

or a hydrate or solvate thereof that is chosen from A, C, D, E, F, G, H, I, J, K, M, or N.

12. The solid state form of claim 11, wherein the form is partially crystalline.

13. The solid state form of claim 12, selected from Form A.

14. The solid state form of claim 12, selected from Form I.

15. The solid state form of claim 12, selected from Form K.

16. The solid state form of claim 11, or a hydrate or solvate thereof, selected from Form A.

17. The solid state form of claim 11, or a hydrate or solvate thereof, selected from Form I.

18. The solid state form of claim 11, or a hydrate or solvate thereof, selected from Form K.

19. The solid state form of claim 11, wherein the form includes 10%, 20%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, or 99.9% crystalline form B.

20. The solid state form of claim 11, wherein the form includes 10%, 20%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, or 99.9% crystalline form L.

21. A process for making Form L of ivosidenib comprising making one or more meta-stable form of ivosidenib in anhydrous, hydrated, or solvated form, and allowing such one or more meta-stable form of ivosidenib to convert to Form L.

22. The process of claim 21, wherein the one or meta-stable form is selected from C, D, E, F, H, J, M, or N, each individually in anhydrous, hydrated, or solvated form.

23. A pharmaceutical composition comprising ivosidenib in a mixture of two or more of Form L, Form B, Form A, Form C, Form D, Form E, Form F, Form G, Form H, Form I, Form J, Form K, Form M, and Form N, each individually in anhydrous, hydrated, or solvated form.

24. The pharmaceutical composition of claim 23, further comprising no more than 0.15% (area% by HPLC) of a compound selected from:
2-((2*S*)-2-((1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)(5-fluoropyridin-3-yl)carbamoyl)-5-oxopyrrolidin-1-yl)isonicotinamide;
(*S*)-*N*-((S)-1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-5-oxo-*N*-(pyridin-3-yl)pyrrolidine-2-carboxamide;
(*S*)-*N*-((*R*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide;
(*R*)-*N*-((*S*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide; and
(*R*)-*N*-((*R*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide.

25. The pharmaceutical composition of claim 23, comprising at least one of Form A, Form C, Form D, Form E, Form F, Form G, Form H, Form I, Form J, Form K, Form M, and Form N; and about 10% or less of Form B.

26. The pharmaceutical composition of claim 23, comprising at least one of Form A, Form C, Form D, Form E, Form F, Form G, Form H, Form I, Form J, Form K, Form M, and Form N; and about 10% or less of Form L.

27. The pharmaceutical composition of claim 23, further comprising an amorphous form of the compound of Formula I.

28. The pharmaceutical composition of claim 23, wherein the mixture comprises Form L and one or more of Form B, Form A, Form C, Form D, Form E, Form F,

Form G, Form H, Form I, Form J, Form K, Form M, and Form N, each individually in anhydrous, hydrated, or solvated form.

29. The pharmaceutical composition of claim 28, where the Form B, Form A, Form C, Form D, Form E, Form F, Form G, Form H, Form I, Form J, Form K, Form M, or Form N, each individually in anhydrous, hydrated, or solvated form converts to Form L.

30. A solid dosage form comprising a substantially amorphous drug product intermediate and further comprising any one or more of Form A, Form C, Form D, Form E, Form F, Form G, Form H, Form I, Form J, Form K, Form M, or Form N, each individually in an anhydrous, hydrated, or solvated form.

31. A solid dosage form comprising ivosidenib in a substantially amorphous form and further comprising any one or more of crystalline Form L, Form B, Form A, Form C, Form D, Form E, Form F, Form G, Form H, Form I, Form J, Form K, Form M, or Form N, each individually in anhydrous, hydrated, or solvated form, and one or more pharmaceutically acceptable excipients.

32. The solid dosage form of claim 31, further comprising no more than 0.15% (area% by HPLC) of a compound selected from:
2-((2*S*)-2-((1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)(5-fluoropyridin-3-yl)carbamoyl)-5-oxopyrrolidin-1-yl)isonicotinamide;
(*S*)-*N*-((S)-1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-5-oxo-*N*-(pyridin-3-yl)pyrrolidine-2-carboxamide;
(*S*)-*N*-((*R*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide;
(*R*)-*N*-((*S*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide; and
(*R*)-*N*-((*R*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide.

33. The solid dosage form of claim 31, further comprising a polymer chosen from hydroxypropylmethylcellulose (HPMC), hydroxypropylmethylcellulose phthalate (HPMCP), hydroxypropylmethylcellulose acetate succinate (HPMCAS), hydroxypropylcellulose (HPC), ethylcellulose, or cellulose acetate phthalate; polyvinylpyrrolidones (PVP); polyethylene glycols (PEG); polyvinyl alcohols (PVA), Polyvinyl Acetate Phthalate (PVAP); acrylates, polyvinylpyrollidone-vinyl acetate (PVP-VA), polyvinyl caprolactam-polyvinyl, and acetate-

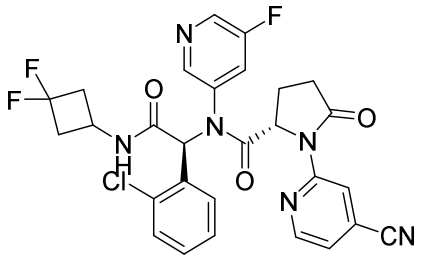
polyethyleneglycol copolymer, Methylacrylate/methacrylic acid copolymer; Soluplus; Copovidone; and mixtures thereof.

34. The solid dosage form of claim 33, wherein the polymer is chosen from HPMC, HPMCP, HPMCAS, PVAP and copovidone

35. A pharmaceutical composition comprising Form L drug product, where the Form L drug product is created via any one or more of Form B, Form A, Form C, Form D, Form E, Form F, Form G, Form H, Form I, Form J, Form K, Form M, or Form N each individually in anhydrous, hydrated, or solvated form.

36. The pharmaceutical composition of claim 35, wherein the Form L drug product contains Form L and one or more of Form B, Form A, Form C, Form D, Form E, Form F, Form G, Form H, Form I, Form J, Form K, Form M, or Form N each individually in anhydrous, hydrated, or solvated form.

37. A compound selected from one of forms E, G, M, or N, of a compound of formula (I)



(I).

, each individually in anhydrous, hydrated, or solvated form that is substantially free of any other solid state forms of the compound of formula (I).

38. A solid form of ivosidenib having an x-ray powder diffraction pattern comprising a peak at 6.3± 0.2 °2θ and one or more of the following peaks 11.6± 0.2 °2θ, 12.0 ± 0.2 °2θ , 17.1 ± 0.2 °2θ, and 21.0 ± 0.2 °2θ. (Form E).

39. A solid form of ivosidenib having an x-ray powder diffraction pattern comprising one or two or three or four or five peaks chosen from 11.4 ± 0.2 °2θ, 17.7 ± 0.2 °2θ, 17.8 ± 0.2 °2θ, 19.7 ± 0.2 °2θ, and 21.4 ± 0.2 °2θ. (Form M).

40. A solid form of ivosidenib having an x-ray powder diffraction pattern comprising one or two or three or four or five peaks chosen from 8.6 ± 0.2 °2θ, 14.4 ± 0.2 °2θ, 18.6 ± 0.2 °2θ, 20.3 ± 0.2 °2θ and 22.9± 0.2 °2θ. (Form N).

41. A pharmaceutical composition comprising ivosidenib and one or more pharmaceutically acceptable excipients wherein the composition contains no more than 0.15% (area% by HPLC) of a compound selected from:

2-((2*S*)-2-((1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)(5-fluoropyridin-3-yl)carbamoyl)-5-oxopyrrolidin-1-yl)isonicotinamide;
(*S*)-*N*-((S)-1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-5-oxo-*N*-(pyridin-3-yl)pyrrolidine-2-carboxamide;
(*S*)-*N*-((*R*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide;
(*R*)-*N*-((*S*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide; and
(*R*)-*N*-((*R*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide.

42. A pharmaceutical composition comprising ivosidenib and one or more pharmaceutically acceptable excipients, wherein the composition contains no more than 0.10% (area % by HPLC) of one or more of:
3-amino-5-fluoropyridine;
2-chloro-4-cyanopyridine;
(*S*)-*N*-((*S*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide;
2-(2-Chlorophenyl)-*N*-(3,3-difluorocyclobutyl)-2-((5-fluoropyridin-3-yl)amino)acetamide;
(*S*)-5-(((*S*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)(5-fluoropyridin-3-yl)amino)-4-((4-cyanopyridin-2-yl)amino)-5-oxopentanoic acid;
(*S*)-4-(bis(4-cyanopyridin-2-yl)amino)-5-(((*S*)-1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)(5-fluoropyridin-3-yl)amino)-5-oxopentanoic acid;
(*S*)-2-(2-Chlorophenyl)-2-((5-((4-cyanopyridin-2-yl)amino)-2-oxo-3,4-dihydro-2*H*-pyran-6-yl)(5-fluoropyridin-3-yl)amino)-*N*-(3,3-difluorocyclobutyl)acetamide;
(2*S*)-*N*-((1*S*)-2-((2-chloro-3,3-difluorocyclobutyl)amino)-1-(2-chlorophenyl)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide;
(*S*)-1-(4-Cyanopyridin-2-yl)-*N*-((S)-1-(2,4-dichlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide;
(*S*)-1-(4-Cyanopyridin-2-yl)-*N*-((*S*)-1-(2,3-dichlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide;

(*S*)-*N*-((*S*)-1-(4-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide;
3-((2*S*)-1-(4-carbamoylpyridin-2-yl)-*N*-(1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-5-oxopyrrolidine-2-carboxamido)-5-fluoropyridine 1-oxide;
4-carbamoyl-2-((2*S*)-2-((1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)(5-fluoropyridin-3-yl)carbamoyl)-5-oxopyrrolidin-1-yl)pyridine 1-oxide; and
(*S*)-1-(4-Cyanopyridin-2-yl)-*N*-((*S*)-1-(3,3-difluorocyclobutyl)-2-oxoindolin-3-yl)-N-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide, or salts, hydrates, or solvates thereof.

43. A pharmaceutical composition comprising ivosidenib and one or more pharmaceutically acceptable excipients, wherein the composition contains no more than 2 ppm of one or more of benzaldehyde, benzyl chloride, 2-chlorobenzyl chloride, 1-chloro-2-(chloromethyl)benzene, 1-chloro-2-(dichloromethyl)benzene, phenol, and benzene.

44. A pharmaceutical composition comprising ivosidenib and one or more pharmaceutically acceptable excipients, wherein the composition contains no more than 10 ppm of palladium.

45. A pharmaceutical composition comprising ivosidenib and one or more pharmaceutically acceptable excipients, wherein the composition contains no more than 300 ppm of molybdenum.

46. A pharmaceutical composition comprising ivosidenib and one or more pharmaceutically acceptable excipients, wherein the composition contains no more than:
5000 ppm of isopropyl acetate;
600 ppm *n*-heptane;
600 ppm dichloromethane; or
2 ppm benzene.

47. A method for testing the suitability of an ivosidenib composition for use in therapy wherein the composition comprises less than a total of 2% of process contaminants, heavy metal impurities, and residual solvents.

48. The method of claim 47, wherein the process contaminant is one or more of: 2-((2*S*)-2-((1-(2-chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)(5-fluoropyridin-3-yl)carbamoyl)-5-oxopyrrolidin-1-yl)isonicotinamide; (*S*)-*N*-((S)-1-(2-

chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-5-oxo-*N*-(pyridin-3-yl)pyrrolidine-2-carboxamide; (*S*)-*N*-((*R*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide; (*R*)-*N*-((*S*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide; and (*R*)-*N*-((*R*)-1-(2-Chlorophenyl)-2-((3,3-difluorocyclobutyl)amino)-2-oxoethyl)-1-(4-cyanopyridin-2-yl)-*N*-(5-fluoropyridin-3-yl)-5-oxopyrrolidine-2-carboxamide.

49. The method of claim 47, wherein the residual solvent is one or more of: benzaldehyde, benzyl chloride, 2-chlorobenzyl chloride, 1-chloro-2-(chloromethyl)benzene, 1-chloro-2-(dichloromethyl)benzene, phenol, or benzene.

50. The method of claim 47, wherein the heavy metal impurity is one or more of palladium and molybdenum.