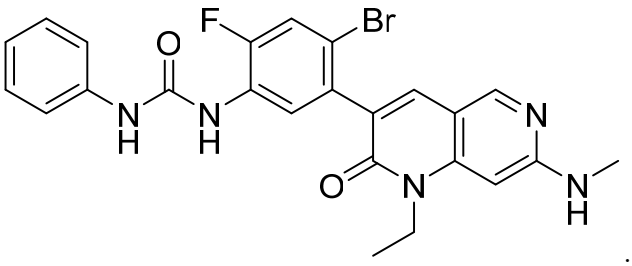
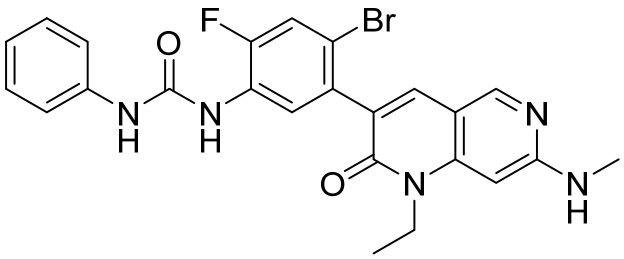
compound of Formula (I) as described herein has the following structure:



Formula (I)

[0005a] In one aspect of the present disclosure, there is provided a pharmaceutical composition comprising:

a) a solid dispersion comprising: a compound represented by Formula (I) or pharmaceutically acceptable salt thereof,



Formula (I)

and hydroxypropylmethyl cellulose acetate succinate; and

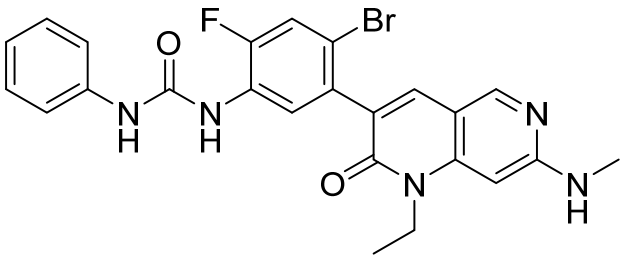
b) one or more pharmaceutically acceptable carriers, and

c) one or more anilinic substances;

wherein the one or more single anilinic substances is present in an amount equal to or less than 3.0% by weight.

[0005b] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising:

a) a solid dispersion comprising: an amorphous form of a compound represented by Formula (I)

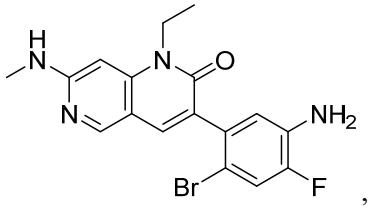


Formula (I)

and hydroxypropylmethyl cellulose acetate succinate; and

b) one or more pharmaceutically acceptable carriers;

wherein each of: a compound represented by Formula (II):

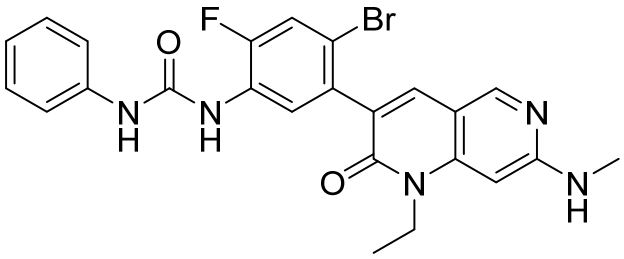


Formula (II)

aniline and diphenyl urea are present in amount equal to or less than 1.5% by weight based on the total weight of the composition.

[0005c] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising:

a) a solid dispersion comprising: an amorphous form of a compound represented by Formula (I)



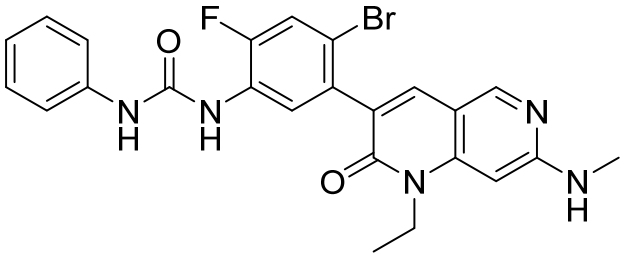
Formula (I)

and hydroxypropylmethyl cellulose acetate succinate; and

b) one or more pharmaceutically acceptable carriers;

wherein diphenyl urea is present in amount equal to or less than 0.5% by weight based on the total weight of the composition.

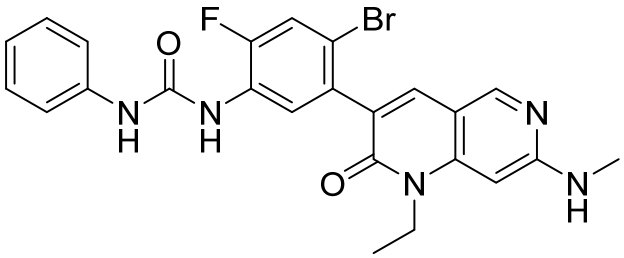
[0005d] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a solid dispersion comprising the compound represented by Formula (I)



Formula (I)

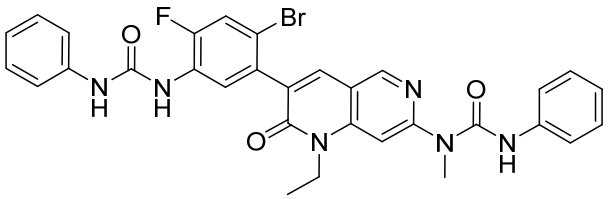
hydroxypropylmethyl cellulose acetate succinate, and one or more pharmaceutically acceptable carriers, excipients or diluents, wherein the composition comprises one or more anilinic substances each in an amount equal to or less than 3.0% by weight based on the weight of the compound of Formula (I).

[0005e] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising a solid dispersion comprising the compound represented by Formula (I)



Formula (I)

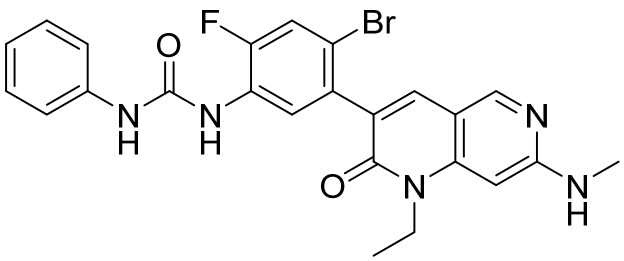
hydroxypropylmethyl cellulose acetate succinate, and one or more pharmaceutically acceptable carriers, excipients or diluents, wherein the pharmaceutical composition comprises one or more anilinic substances and a compound represented by Formula (III):



Formula (III)

each in an amount equal to or less than 3.0% by weight based on the weight of the compound of Formula (I).

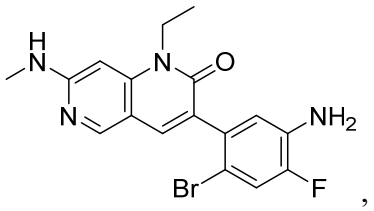
[0005f] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a solid dispersion comprising a compound represented by Formula (I)



Formula (I)

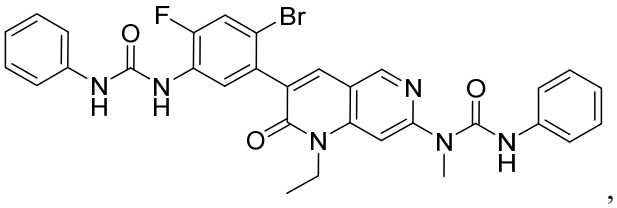
and hydroxypropylmethyl cellulose acetate succinate, and a pharmaceutically acceptable carrier, wherein the composition has less than 3% w/w of

each of: a compound represented by Formula (II):



Formula (II)

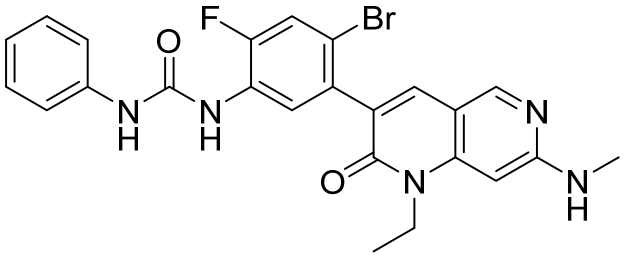
a compound represented by Formula (III):



Formula (III)

aniline, and diphenyl urea.

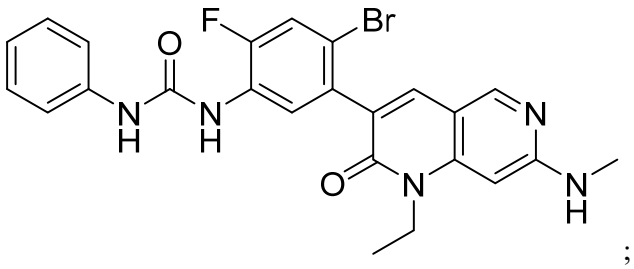
[0005g] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising a solid dispersion comprising a compound represented by Formula (I):



Formula (I)

and hydroxypropylmethyl cellulose acetate succinate, and a pharmaceutically acceptable carriers, wherein the composition has less than 3% w/w of each of: 3-(5-amino-2-bromo-4-fluorophenyl)-1-ethyl-7-(methylamino)-1,6-naphthyridin-2(1H)-one, aniline and diphenyl urea.

[0005h] In another aspect of the present disclosure, there is provided a pharmaceutically acceptable composition for a 50 mg single dosage unit of a compound represented by:



;

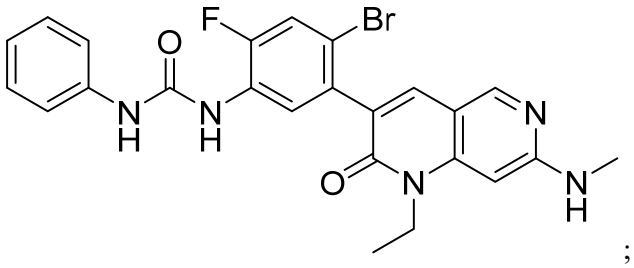
comprising:

an intragranular blend, wherein the intragranular blend comprises:

a solid dispersion having 50 mg of the compound wherein the compound is present in amorphous form, hydroxypropyl methyl cellulose acetate succinate; a bulking agent and/or filler; and a lubricant and/or a glidant; and

an extragranular blend comprising a glidant and/or a lubricant; wherein diphenyl urea is present in amount equal to or less than 0.5% by weight based on the total weight of the composition.

[0005i] In a further aspect of the present disclosure, there is provided a pharmaceutically acceptable composition for orally delivering to a patient 50 mg of a compound represented by:



;

comprising:

a solid dispersion having:

50 mg of the compound wherein the compound is present in amorphous form;

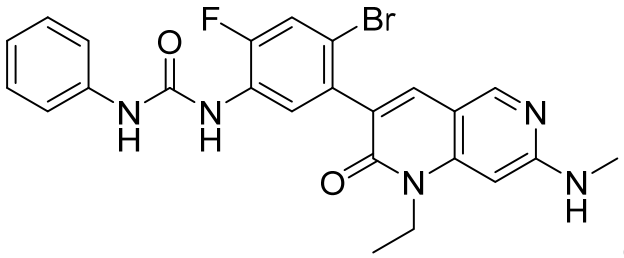
hydroxypropyl methyl cellulose acetate succinate;

a bulking agent,

a filler, and

a lubricant and/or a glidant; wherein diphenyl urea is present in amount equal to or less than 0.5% by weight based on the total weight of the composition.

[0005j] In another aspect of the present disclosure, there is provided a pharmaceutically acceptable composition for orally delivering 50 mg of a compound represented by:



comprising:

comprises:

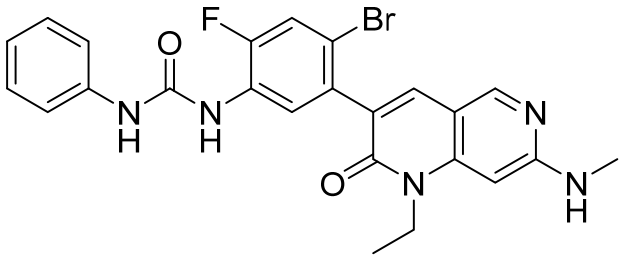
a solid dispersion having 50 mg of the compound wherein the compound is present in amorphous form, and hydroxypropylmethyl cellulose acetate succinate;

25-45% by weight of a bulking agent based on the total amount of the pharmaceutical composition;

25-45% by weight of a filler based on the total amount of the pharmaceutical composition; and

a glidant and/or a lubricant; wherein the composition has not more than 1.5% (w/w) of 3-(5-amino-2-bromo-4-fluorophenyl)-1-ethyl-7-(methylamino)-1,6-naphthyridin-2(1H)-one, when exposed to 60% relative humidity at 25 ºC for 1 month, 3 months or 6 months.

[0005k] In a further aspect of the present disclosure, there is provided a pharmaceutically acceptable tablet having 50 mg of a compound represented by:



;

wherein the tablet comprises:

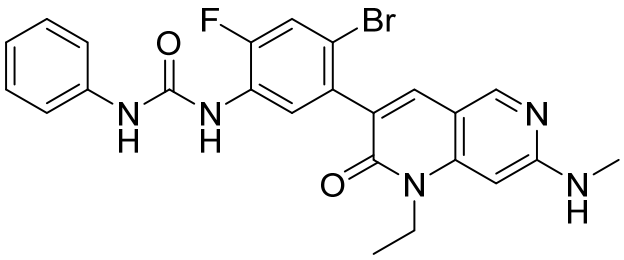
a solid dispersion having 50 mg of the compound wherein the compound is present in amorphous form, and hydroxypropyl methyl cellulose acetate succinate;

25-35% by weight microcrystalline cellulose based on the total weight of the tablet; and

25-35% by weight of lactose or a hydrate thereof based on the total amount of the pharmaceutical composition; wherein diphenyl urea is present in amount equal to or less than 0.5% by weight based on the total weight of the composition.

[0005l] In another aspect of the present disclosure, there is provided a use of the composition disclosed herein, or the pharmaceutically acceptable tablet disclosed herein, in the preparation of a medicament for the treatment of a disease selected from the group consisting of gastrointestinal stromal tumors (GIST), NF-1-deficient gastrointestinal stromal tumors, succinate dehydrogenase (SDH)-deficient gastrointestinal stromal tumors, KIT driven gastrointestinal stromal tumors, PDGFRA driven gastrointestinal stromal tumors, melanoma, acute myeloid leukemia, germ cell tumors of the seminoma or dysgerminoma, mastocytosis, mast cell leukemia, lung adenocarcinoma, squamous cell lung cancer, glioblastoma, glioma, pediatric glioma, astrocytomas, sarcomas, malignant peripheral nerve sheath sarcoma, intimal sarcomas, hypereosinophilic syndrome, idiopathic hypereosinophilic syndrome, chronic eosinophilic leukemia, eosinophilia-associated acute myeloid leukemia, lymphoblastic T-cell lymphoma, and non-small cell lung cancer.

[0005m] In a further aspect of the present disclosure, there is provided a solid dispersion comprising the compound represented by Formula (I)



Formula (I)

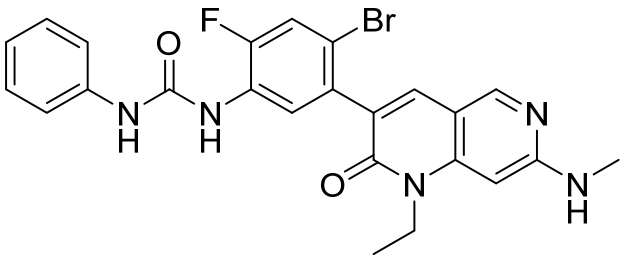
and hydroxypropylmethyl cellulose acetate succinate, wherein the solid dispersion comprises one or more anilinic substances each in an amount equal to or less than 3.0% by weight based on the weight of the compound of Formula (I).

[0005n] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising the solid dispersion disclosed herein and one or more pharmaceutically acceptable carriers, excipients or diluents.

[0005o] In a further aspect of the present disclosure, there is provided a use of the composition disclosed herein in the manufacture of a medicament for treating a disease selected from the group consisting of gastrointestinal stromal tumors (GIST), NF-1-deficient

gastrointestinal stromal tumors, succinate dehydrogenase (SDH)-deficient gastrointestinal stromal tumors, KIT driven gastrointestinal stromal tumors, PDGFRA driven gastrointestinal stromal tumors, melanoma, acute myeloid leukemia, germ cell tumors of the seminoma or dysgerminoma, mastocytosis, mast cell leukemia, lung adenocarcinoma, squamous cell lung cancer, glioblastoma, glioma, pediatric glioma, astrocytomas, sarcomas, malignant peripheral nerve sheath sarcoma, intimal sarcomas, hypereosinophilic syndrome, idiopathic hypereosinophilic syndrome, chronic eosinophilic leukemia, eosinophilia-associated acute myeloid leukemia, lymphoblastic T-cell lymphoma, and non-small cell lung cancer.

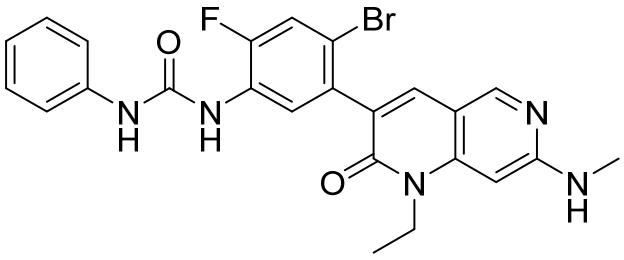
[0005p] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound represented by Formula (I)



Formula (I)

and one or more pharmaceutically acceptable carriers, excipients or diluents, wherein the pharmaceutical composition has less than 0.05% of diphenyl urea.

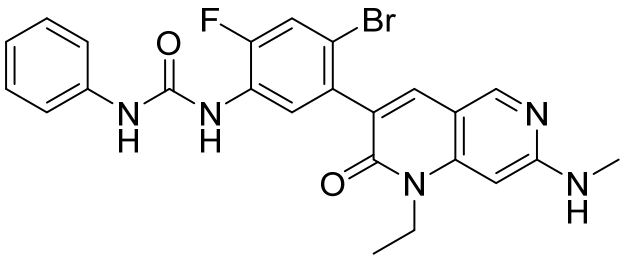
[0005q] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound represented by Formula (I)



Formula (I)

and one or more pharmaceutically acceptable carriers, excipients or diluents, wherein the pharmaceutical composition has less than 0.05% of diphenyl urea as detected by HPLC.

[0005r] In another aspect of the present disclosure, there is provided a solid dispersion comprising the compound represented by Formula (I)



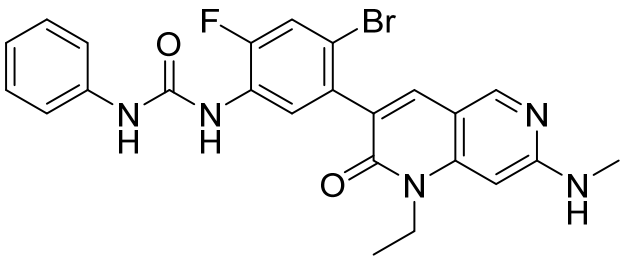
Formula (I)

and hydroxypropylmethyl cellulose acetate succinate, wherein the compound has a purity by HPLC of greater than 90%.

[0005s] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising the solid dispersion disclosed herein and one or more pharmaceutically acceptable carriers, excipients or diluents.

[0005t] In another aspect of the present disclosure, there is provided a use of the composition disclosed herein, in the manufacture of a medicament for treating a disease selected from the group consisting of gastrointestinal stromal tumors (GIST), NF-1-deficient gastrointestinal stromal tumors, succinate dehydrogenase (SDH)-deficient gastrointestinal stromal tumors, KIT driven gastrointestinal stromal tumors, PDGFRA driven gastrointestinal stromal tumors, melanoma, acute myeloid leukemia, germ cell tumors of the seminoma or dysgerminoma, mastocytosis, mast cell leukemia, lung adenocarcinoma, squamous cell lung cancer, glioblastoma, glioma, pediatric glioma, astrocytomas, sarcomas, malignant peripheral nerve sheath sarcoma, intimal sarcomas, hypereosinophilic syndrome, idiopathic hypereosinophilic syndrome, chronic eosinophilic leukemia, eosinophilia-associated acute myeloid leukemia, lymphoblastic T-cell lymphoma, and non-small cell lung cancer.

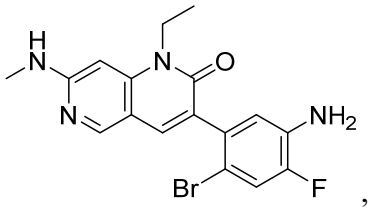
[0005u] In a further aspect of the present disclosure, there is provided a substantially purified compound represented by Formula (I)



Formula (I)

having less than 3.0% by weight of an impurity selected from the group consisting of a

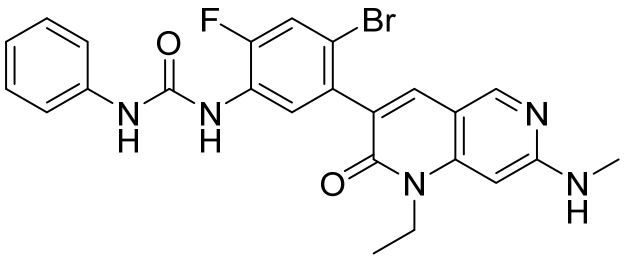
compound represented by Formula (II):



Formula (II)

aniline, and combinations thereof.

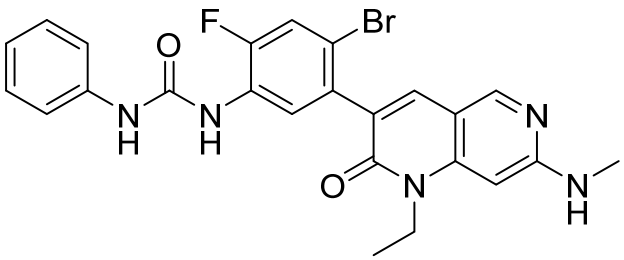
[0005v] In another aspect of the present disclosure, there is provided a high purity compound represented by Formula (I)



Formula (I)

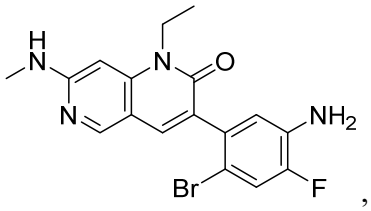
having less than 3.0% of anilinic substance impurities.

[0005w] In a further aspect of the present disclosure, there is provided a substantially purified compound represented by Formula (I)



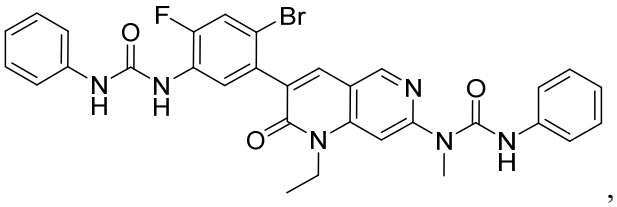
Formula (I)

having less than 3.0% by weight of an impurity selected from the group consisting of a compound represented by Formula (II):



Formula (II)

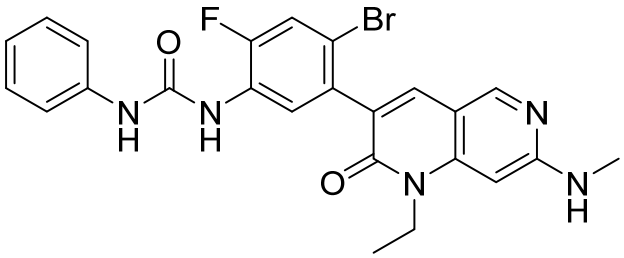
a compound represented by Formula (III):



Formula (III)

and combinations thereof.

[0005x] In another aspect of the present disclosure, there is provided a high purity compound represented by Formula (I)



Formula (I)

having less than 0.05% of a diphenyl urea impurity.

[0005y] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising any one of the compounds disclosed herein and one or more pharmaceutically acceptable excipients, carriers or diluents.

[0005z] In another aspect of the present disclosure, there is provided a use of the composition disclosed herein in the manufacture of a medicament for treating a disease selected from the group consisting of gastrointestinal stromal tumors (GIST), NF-1-deficient gastrointestinal stromal tumors, succinate dehydrogenase (SDH)-deficient gastrointestinal stromal tumors, KIT driven gastrointestinal stromal tumors, PDGFRA driven gastrointestinal

stromal tumors, melanoma, acute myeloid leukemia, germ cell tumors of the seminoma or dysgerminoma, mastocytosis, mast cell leukemia, lung adenocarcinoma, squamous cell lung cancer, glioblastoma, glioma, pediatric glioma, astrocytomas, sarcomas, malignant peripheral nerve sheath sarcoma, intimal sarcomas, hypereosinophilic syndrome, idiopathic hypereosinophilic syndrome, chronic eosinophilic leukemia, eosinophilia-associated acute myeloid leukemia, lymphoblastic T-cell lymphoma, and non-small cell lung cancer.

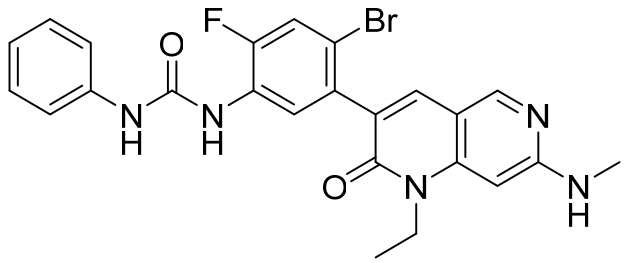
[0005aa] In a further aspect of the present disclosure, there is provided a use of the composition or one or more of the tablets disclosed herein in the manufacture of a medicament for treating a disease selected from the group consisting of gastrointestinal stromal tumors (GIST), NF-1-deficient gastrointestinal stromal tumors, succinate dehydrogenase (SDH)-deficient gastrointestinal stromal tumors, KIT driven gastrointestinal stromal tumors, PDGFRA driven gastrointestinal stromal tumors, lung cancer, glioblastoma, a glioma, malignant peripheral nerve sheath sarcoma, and hypereosinophilic syndrome.

[0005ab] In another aspect of the present disclosure, there is provided a use of the composition or one or more of the tablets disclosed herein in the manufacture of a medicament for treating a disease selected from the group consisting of KIT driven germ cell tumor, KIT driven skin cancer, or KIT driven renal cell carcinoma.

[0005ac] In a further aspect of the present disclosure, there is provided a use of the composition or one or more of the tablets disclosed herein in the manufacture of a medicament for treating a disease selected from the group consisting of penile cancer, PDGFRA driven penile cancer, prostate cancer, PDGFRA driven prostate cancer, PDGFRA driven non-melanoma skin cancer, PDGFRA driven glioma, PDGFRA driven sarcoma, PDGFRA driven glioblastoma, or PDGFRA driven pancreatic cancer.

[0005ad] In another aspect of the present disclosure, there is provided a use of the composition or one or more of the tablets disclosed herein in the manufacture of a medicament for treating a disease selected from the group consisting of vaginal cancer, prostate cancer, penile cancer, non-melanoma skin cancer, melanoma, or breast sarcoma, wherein the disease comprises a PDGFRAB mutation.

[0005ae] In a further aspect of the present disclosure, there is provided a process for the preparation of the solid dispersion comprising a compound of Formula (I)



Formula (I)

disclosed herein, the process comprising:

(a) mixing the compound of Formula (I), a solvent, the hydroxypropylmethyl cellulose acetate succinate and water to obtain a suspension;

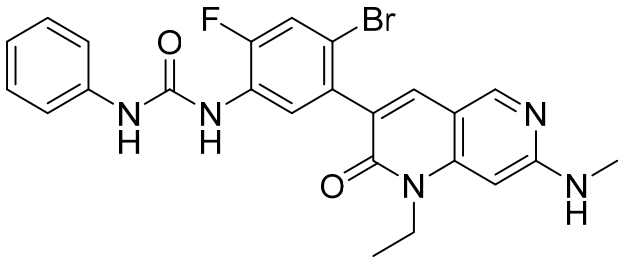
(b) optionally agitating and/or mixing the suspension while maintaining a temperature of 10 to 25 ºC;

(c) heating the suspension to dissolve the suspended particles prior to introduction into a spray-dryer; and

(d) spray-drying the suspension to obtain a spray-dried dispersion;

(e) drying the spray-dried dispersion; thereby obtaining the solid dispersion.

[0005af] In another aspect of the present disclosure, there is provided a solid dispersion comprising a compound of Formula (I)



Formula (I)

produced by the process disclosed herein.

[0005ag] In a further aspect of the present disclosure, there is provided a composition or one or more of the tablets disclosed herein, for use in therapy.

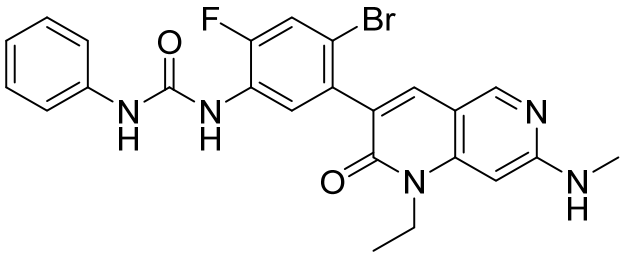
[0006] Provided herein, in part, are pharmaceutical compositions comprising a compound of Formula (I):

CLAIMS

What is claimed is:

1. A pharmaceutical composition comprising:

a) a solid dispersion comprising: a compound represented by Formula (I) or pharmaceutically acceptable salt thereof,



Formula (I)

and hydroxypropylmethyl cellulose acetate succinate; and

b) one or more pharmaceutically acceptable carriers, and

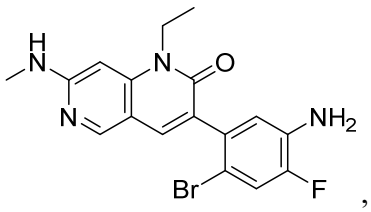
c) one or more anilinic substances;

wherein the one or more single anilinic substances is present in an amount equal to or less than 3.0% by weight.

2. The pharmaceutical composition of claim 1, wherein the anilinic substance is present in amount equal to or less than 0.5% by weight based on the total weight of the compound of Formula (I) present in the composition.

3. The pharmaceutical composition of claim 1 or 2, wherein the anilinic substance is present in an amount equal to or less than 0.3% by weight based on the total weight of the compound of Formula (I) present in the composition.

4. The pharmaceutical composition of any one of claims 1-3, wherein the anilinic substance is one of : the compound of Formula (II)



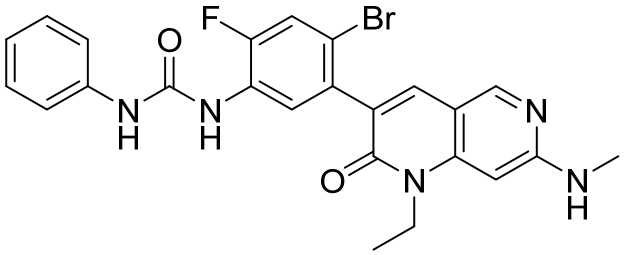
Formula (II)

aniline, or a combination thereof.

5. The pharmaceutical composition of any one of claims 1-4, wherein the compound is present in the solid dispersion as a free base in substantially amorphous form.

6. A pharmaceutical composition comprising:

a) a solid dispersion comprising: an amorphous form of a compound represented by Formula (I)

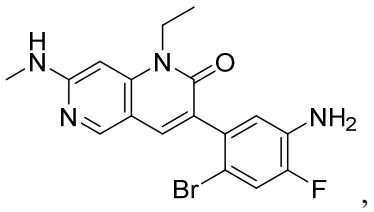


Formula (I)

and hydroxypropylmethyl cellulose acetate succinate; and

b) one or more pharmaceutically acceptable carriers;

wherein each of: a compound represented by Formula (II):

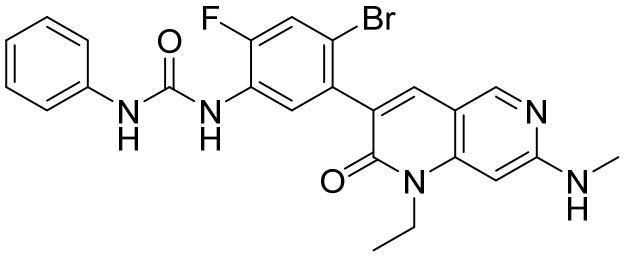


Formula (II)

aniline and diphenyl urea are present in amount equal to or less than 1.5% by weight based on the total weight of the composition.

7. A pharmaceutical composition comprising:

a) a solid dispersion comprising: an amorphous form of a compound represented by Formula (I)



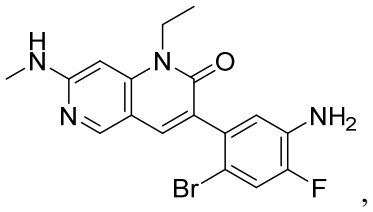
Formula (I)

and hydroxypropylmethyl cellulose acetate succinate; and

b) one or more pharmaceutically acceptable carriers;

wherein diphenyl urea is present in amount equal to or less than 0.5% by weight based on the total weight of the composition.

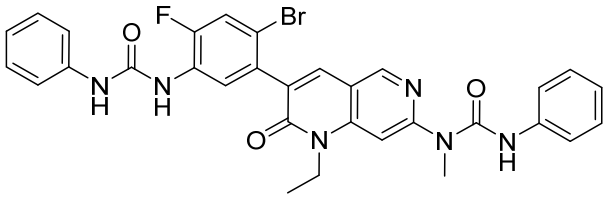
8. The pharmaceutical composition of any one of claims claim 1-6, wherein each of: a compound represented by Formula (II)



Formula (II)

aniline and diphenyl urea are present in amount equal to or less than 0.5% by weight based on the total weight of the compound of Formula (I).

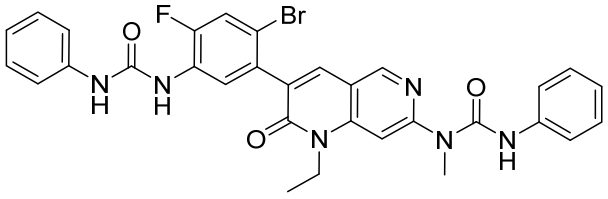
9. The pharmaceutically acceptable composition of any one of claims 1-8, further comprising less than 10% by weight of a compound represented by Formula (III):



Formula (III)

based on the weight of the compound of Formula (I).

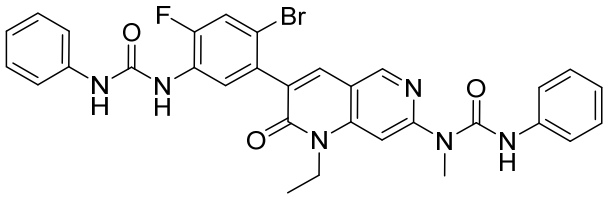
10. The pharmaceutically acceptable composition of any one of claims 1-9, further comprising less than 3% by weight of a compound represented by Formula (III):



Formula (III)

based on the weight of the compound of Formula (I).

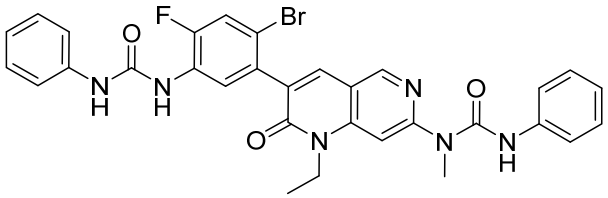
11. The pharmaceutically acceptable composition of any one of claims 1-10, further comprising less than 1% by weight of a compound represented by Formula (III):



Formula (III)

based on the weight of the compound of Formula (I).

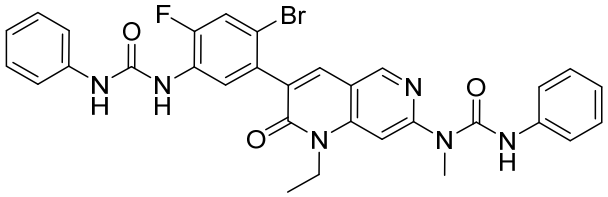
12. The pharmaceutically acceptable composition of any one of claims 1-11, further comprising 0.1 % by weight to 0.5% by weight of a compound represented by Formula (III):



Formula (III)

based on the weight of the compound of Formula (I).

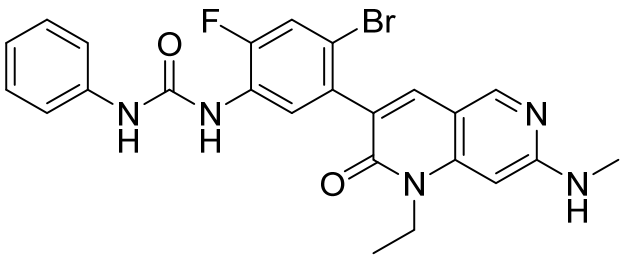
13. The pharmaceutically acceptable composition of any one of claims 1-12, further comprising 0.01 % by weight to 0.1% by weight of a compound represented by Formula (III):



Formula (III)

based on the weight of the compound of Formula (I).

14. A pharmaceutical composition comprising a solid dispersion comprising the compound represented by Formula (I)



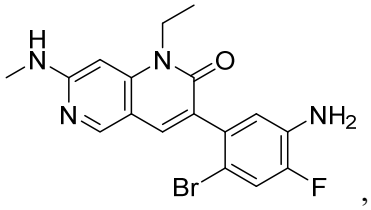
Formula (I)

hydroxypropylmethyl cellulose acetate succinate, and one or more pharmaceutically acceptable carriers, excipients or diluents, wherein the composition comprises one or more anilinic substances each in an amount equal to or less than 3.0% by weight based on the weight of the compound of Formula (I).

15. The composition of claim 14, wherein the composition has equal to or less than 0.5% by weight one or more anilinic substances based on the weight of the compound of Formula (I).

16. The composition of claim 14 or 15, wherein the composition equal to or less than 0.3% by weight anilinic substances based on the weight of the compound of Formula (I).

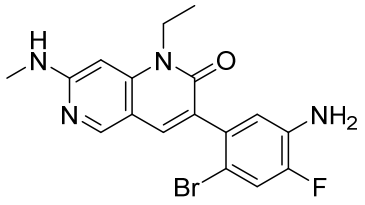
17. The composition of any one of claims 1-16, wherein the one or more anilinic substances is selected from the group consisting of a compound represented by Formula (II):



Formula (II)

aniline, and a combination thereof.

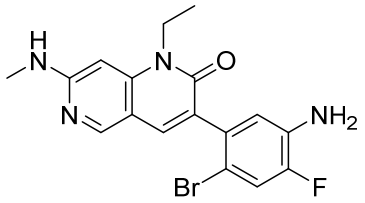
18. The pharmaceutically acceptable composition of any one of claims 1-17, wherein the one or more anilinic substances is a compound represented by Formula (II):



Formula (II)

and is present in the composition in an amount of less than 1 % by weight based on the weight of the compound of Formula (I).

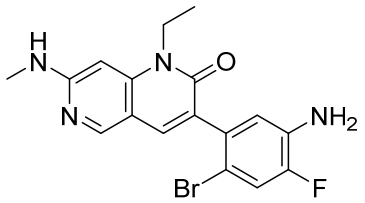
19. The pharmaceutically acceptable composition of any one of claims 1-18, wherein the one or more anilinic substances is a compound represented by Formula (II):



Formula (II)

and is present in the composition in an amount of less than 0.1 % by weight to 0.5% by weight based on the weight of the compound of Formula (I).

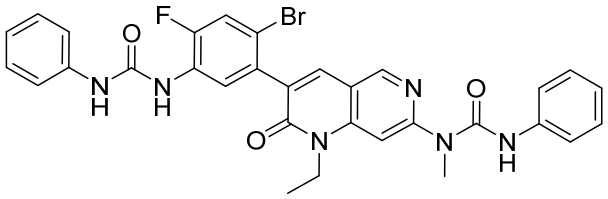
20. The pharmaceutically acceptable composition of any one of claims 1-19, wherein the one or more anilinic substances is a compound represented by Formula (II):



Formula (II)

and is present in the composition in an amount of less than 0.01 % by weight to 0.1% by weight based on the weight of the compound of Formula (I).

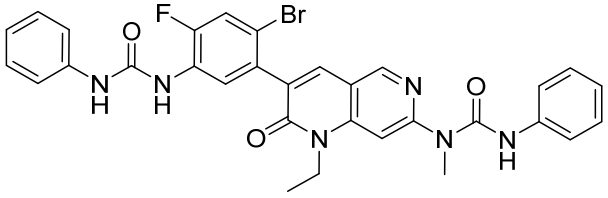
21. The pharmaceutically acceptable composition of any one of claims 1-20, further comprising less than 10% by weight of a compound represented by Formula (III):



Formula (III)

based on the weight of the compound of Formula (I).

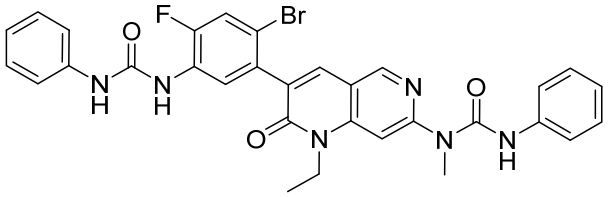
22. The pharmaceutically acceptable composition of any one of claims 1-21, further comprising less than 3% by weight of a compound represented by Formula (III):



Formula (III)

based on the weight of the compound of Formula (I).

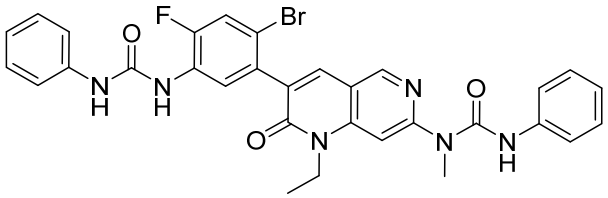
23. The pharmaceutically acceptable composition of any one of claims 1-22, further comprising less than 1% by weight of a compound represented by Formula (III):



Formula (III)

based on the weight of the compound of Formula (I).

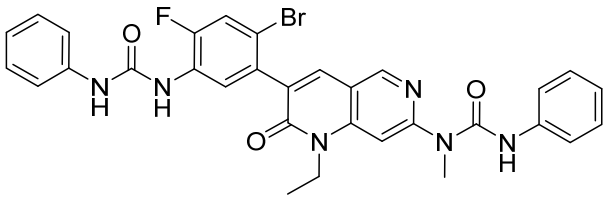
24. The pharmaceutically acceptable composition of any one of claims 1-23, further comprising 0.1 % by weight to 0.5% by weight of a compound represented by Formula (III):



Formula (III)

based on the weight of the compound of Formula (I).

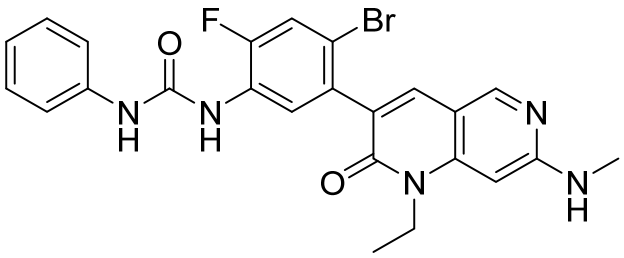
25. The pharmaceutically acceptable composition of any one of claims 1-24, further comprising 0.01 % by weight to 0.1% by weight of a compound represented by Formula (III):



Formula (III)

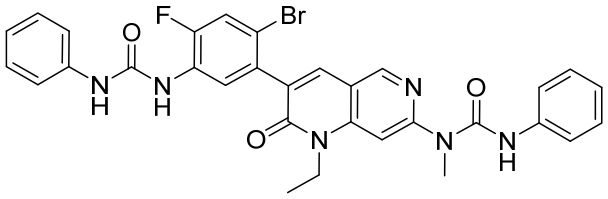
based on the weight of the compound of Formula (I).

26. A pharmaceutical composition comprising a solid dispersion comprising the compound represented by Formula (I)



Formula (I)

and hydroxypropylmethyl cellulose acetate succinate, and one or more pharmaceutically acceptable carriers, excipients or diluents, wherein the pharmaceutical composition comprises one or more anilinic substances and a compound represented by Formula (III):



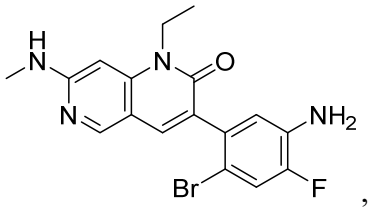
Formula (III)

each in an amount equal to or less than 3.0% by weight based on the weight of the compound of Formula (I).

27. The composition of claim 26, wherein the composition has equal to or less than 0.5% by weight one or more anilinic substances based on the weight of the compound of Formula (I).

28. The composition of claim 26 or 27, wherein the composition equal to or less than 0.3% by weight anilinic substances based on the weight of the compound of Formula (I).

29. The composition of any one of claims 26-28, wherein the one or more anilinic substances is selected from the group consisting of a compound represented by Formula (II):

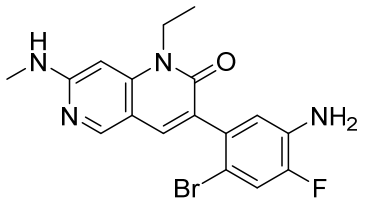


Formula (II)

aniline, and a combination thereof.

30. The pharmaceutically acceptable composition of any one of claims 26-29, wherein the

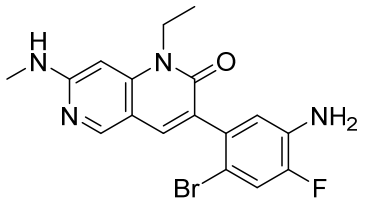
one or more anilinic substances is a compound represented by Formula (II):



Formula (II)

and is present in the composition in an amount of less than 1 % by weight based on the weight of the compound of Formula (I).

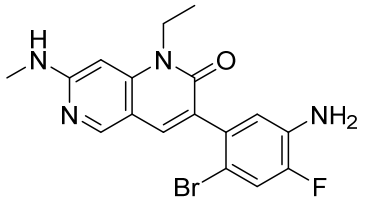
31. The pharmaceutically acceptable composition of any one of claims 26-30, wherein the one or more anilinic substances is a compound represented by Formula (II):



Formula (II)

and is present in the composition in an amount of less than 0.1 % by weight to 0.5% by weight based on the weight of the compound of Formula (I).

32. The pharmaceutically acceptable composition of any one of claims 26-31, wherein the one or more anilinic substances is a compound represented by Formula (II):



Formula (II)

and is present in the composition in an amount of less than 0.01 % by weight to 0.1% by weight based on the weight of the compound of Formula (I).

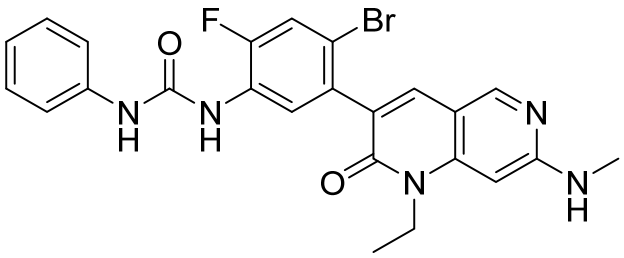
33. The pharmaceutically acceptable composition of any one of claims 26-32, wherein the compound of Formula (III) is present in the composition in an amount of less than 1% by weight based on the weight of the compound of Formula (I).

34. The pharmaceutically acceptable composition of any one of claims 26-33, wherein the

compound of Formula (III) is present in the composition in an amount of less than 0.1 % by weight to 0.5% by weight by weight based on the weight of the compound of Formula (I).

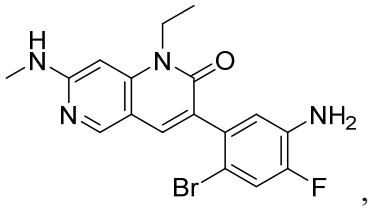
35. The pharmaceutically acceptable composition of any one of claims 26-34, wherein the compound of Formula (III) is present in the composition in an amount of less than 0.01 % by weight to 0.1 % by weight by weight based on the weight of the compound of Formula (I).

36. A pharmaceutical composition comprising a solid dispersion comprising a compound represented by Formula (I)



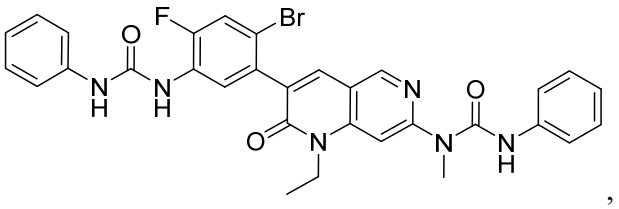
Formula (I)

and hydroxypropylmethyl cellulose acetate succinate, and a pharmaceutically acceptable carrier, wherein the composition has less than 3% w/w of each of: a compound represented by Formula (II):



Formula (II)

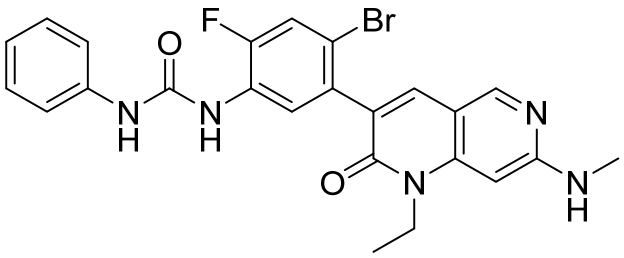
a compound represented by Formula (III):



Formula (III)

aniline, and diphenyl urea.

37. A pharmaceutical composition comprising a solid dispersion comprising a compound represented by Formula (I):



Formula (I)

and hydroxypropylmethyl cellulose acetate succinate, and a pharmaceutically acceptable carriers, wherein the composition has less than 3% w/w of each of: 3-(5-amino-2-bromo-4-fluorophenyl)-1-ethyl-7-(methylamino)-1,6-naphthyridin-2(1H)-one, aniline and diphenyl urea.

38. The composition of any one of claims 1-37, wherein the composition comprises 10% to 50% by weight of the compound based on the total weight of the composition.

39. The composition of any one of claims 1-38, wherein the composition comprises 10% to 30% by weight of the compound, based on the total weight of the composition

40. The composition of any one of claims 1-39, wherein the composition comprises 20% to 30% by weight of the compound based on the total weight of the composition.

41. The composition of any one of claims 1-40, wherein the composition comprises 25% by weight of the compound based on the total weight of the composition.

42. The composition of any one of claims 1-41, wherein the compound has a purity of at least 98% as determined by HPLC.

43. The composition of any one of claims 1-42, wherein the compound is substantially in amorphous form.

44. The composition of any one of claims 1-43, wherein the ratio of the compound represented by Formula (I) and the one or more pharmaceutically acceptable carrier is from 40:60 to 10:90.

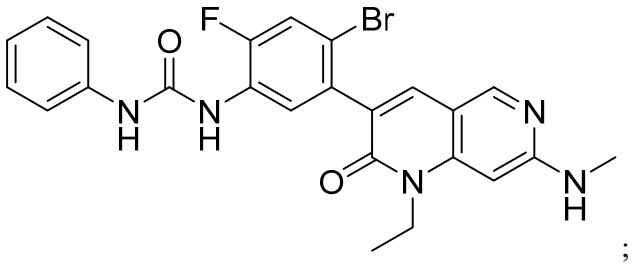
45. The composition of any one of claims 1-44, wherein the ratio of the compound represented by Formula (I) and one or more pharmaceutically acceptable carrier is from 30:70 to 20:80.

46. The composition of any one of claims 1-45, wherein the ratio of the compound represented by Formula (I) and one or more pharmaceutically acceptable carrier is 25:75.

47. The composition of any one of claims 1-46, wherein the composition is a solid oral formulation.

48. The composition of claim 47, wherein the solid oral formulation is a tablet.

49. A pharmaceutically acceptable composition for a 50 mg single dosage unit of a compound represented by:



;

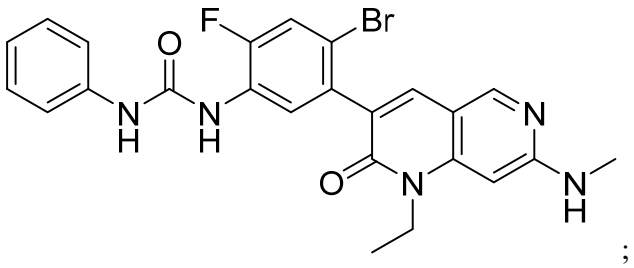
comprising:

an intragranular blend, wherein the intragranular blend comprises:

a solid dispersion having 50 mg of the compound wherein the compound is present in amorphous form, hydroxypropyl methyl cellulose acetate succinate; a bulking agent and/or filler; and a lubricant and/or a glidant; and

an extragranular blend comprising a glidant and/or a lubricant; wherein diphenyl urea is present in amount equal to or less than 0.5% by weight based on the total weight of the composition.

50. A pharmaceutically acceptable composition for orally delivering to a patient 50 mg of a compound represented by:



;

comprising:

a solid dispersion having:

50 mg of the compound wherein the compound is present in amorphous form;

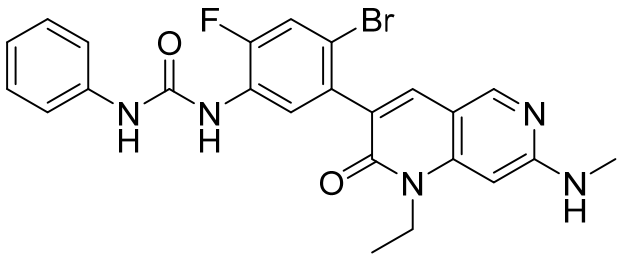
hydroxypropyl methyl cellulose acetate succinate;

a bulking agent,

a filler, and

a lubricant and/or a glidant; wherein diphenyl urea is present in amount equal to or less than 0.5% by weight based on the total weight of the composition.

51. A pharmaceutically acceptable composition for orally delivering 50 mg of a compound represented by:



comprising:

comprises:

a solid dispersion having 50 mg of the compound wherein the compound is present in amorphous form, and hydroxypropylmethyl cellulose acetate succinate;

25-45% by weight of a bulking agent based on the total amount of the pharmaceutical composition;

25-45% by weight of a filler based on the total amount of the pharmaceutical composition; and

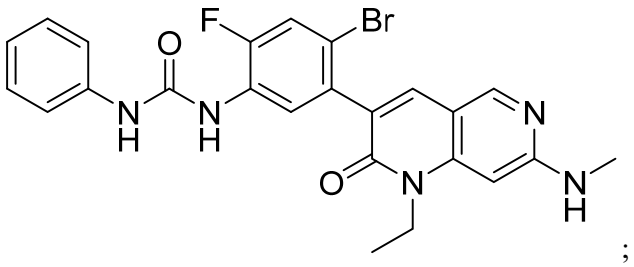
a glidant and/or a lubricant; wherein the composition has not more than 1.5% (w/w) of 3-(5-amino-2-bromo-4-fluorophenyl)-1-ethyl-7-(methylamino)-1,6-naphthyridin-2(1H)-one, when exposed to 60% relative humidity at 25 ºC for 1 month, 3 months or 6 months.

52. The pharmaceutically acceptable composition of claim 51, wherein the bulking agent is microcrystalline cellulose.

53. The pharmaceutically acceptable composition of any one of claims 51-52, wherein the filler is lactose or a hydrate thereof.

54. The pharmaceutically acceptable composition of any one of claims 51-53, wherein the composition is in the form of a tablet.

55. A pharmaceutically acceptable tablet having 50 mg of a compound represented by:



;

wherein the tablet comprises:

a solid dispersion having 50 mg of the compound wherein the compound is present in amorphous form, and hydroxypropyl methyl cellulose acetate succinate;

25-35% by weight microcrystalline cellulose based on the total weight of the tablet; and

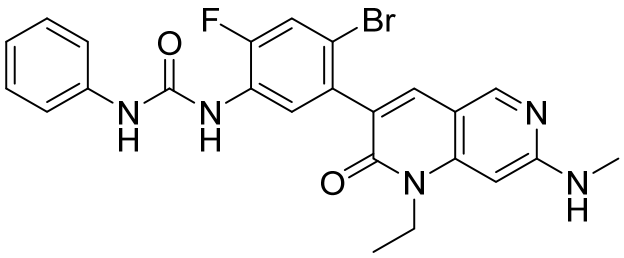
25-35% by weight of lactose or a hydrate thereof based on the total amount of the pharmaceutical composition; wherein diphenyl urea is present in amount equal to or less than 0.5% by weight based on the total weight of the composition.

56. The pharmaceutically acceptable tablet of claim 55, further comprising at least one of: magnesium stearate, crospovidone and silicon dioxide.

57. Use of the composition of any one of claims 1-54, or the pharmaceutically acceptable tablet of claims 59-60, in the preparation of a medicament for the treatment of a disease selected from the group consisting of gastrointestinal stromal tumors (GIST), NF-1-deficient gastrointestinal stromal tumors, succinate dehydrogenase (SDH)-deficient gastrointestinal stromal tumors, KIT driven gastrointestinal stromal tumors, PDGFRA driven gastrointestinal stromal tumors, melanoma, acute myeloid leukemia, germ cell tumors of the seminoma or dysgerminoma, mastocytosis, mast cell leukemia, lung adenocarcinoma, squamous cell lung cancer, glioblastoma, glioma, pediatric glioma, astrocytomas, sarcomas, malignant peripheral nerve sheath sarcoma, intimal sarcomas, hypereosinophilic syndrome, idiopathic hypereosinophilic syndrome, chronic eosinophilic leukemia, eosinophilia-associated acute myeloid leukemia, lymphoblastic T-cell lymphoma, and non-small cell lung cancer.

58. The use of claim 57, wherein the disease is gastrointestinal stromal tumors (GIST).

59. A solid dispersion comprising the compound represented by Formula (I)

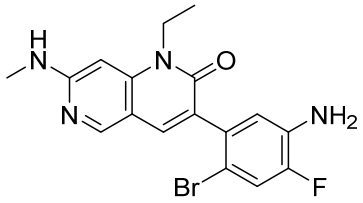


Formula (I)

and hydroxypropylmethyl cellulose acetate succinate, wherein the solid dispersion comprises one or more anilinic substances each in an amount equal to or less than 3.0% by weight based on the weight of the compound of Formula (I).

60. A pharmaceutical composition comprising the solid dispersion of claim 59 and one or more pharmaceutically acceptable carriers, excipients or diluents.

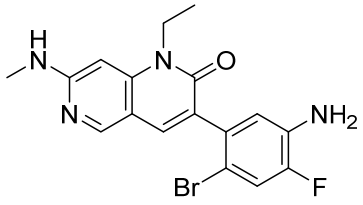
61. The solid dispersion of claim 59 or the pharmaceutically acceptable composition of claim 60, wherein the one or more anilinic substances is a compound represented by Formula (II):



Formula (II)

and is present in the composition in an amount of less than 1 % by weight based on the weight of the compound of Formula (I).

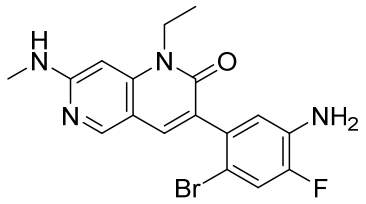
62. The solid dispersion of claim 59 and 61 or the pharmaceutically acceptable composition of claim 60 or 61, wherein the one or more anilinic substances is a compound represented by Formula (II):



Formula (II)

and is present in the composition in an amount of less than 0.1 % by weight to 0.5% by weight based on the weight of the compound of Formula (I).

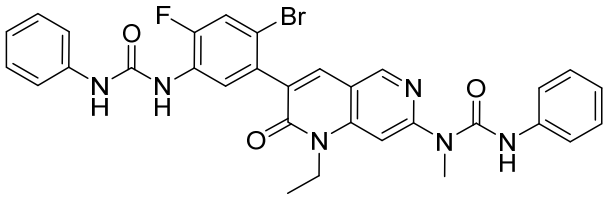
61. The solid dispersion of claim 59 and 61-62 or the pharmaceutically acceptable composition of any one of claims 60-62, wherein the one or more anilinic substances is a compound represented by Formula (II):



Formula (II)

and is present in the composition in an amount of less than 0.01 % by weight to 0.1% by weight based on the weight of the compound of Formula (I).

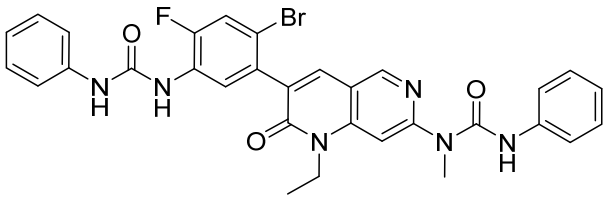
64. The solid dispersion of claim 59 and 61-63 or the pharmaceutically acceptable composition of any one of claims 61-63, further comprising less than 10% by weight of a compound represented by Formula (III):



Formula (III)

based on the weight of the compound of Formula (I).

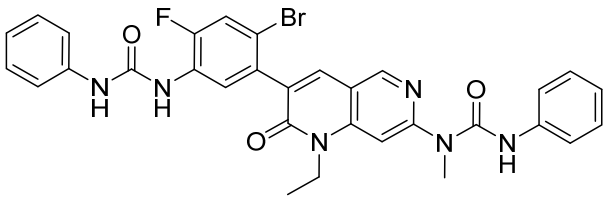
65. The solid dispersion of claim 59 and 61-64 or the pharmaceutically acceptable composition of any one of claims 61-64, further comprising less than 3% by weight of a compound represented by Formula (III):



Formula (III)

based on the weight of the compound of Formula (I).

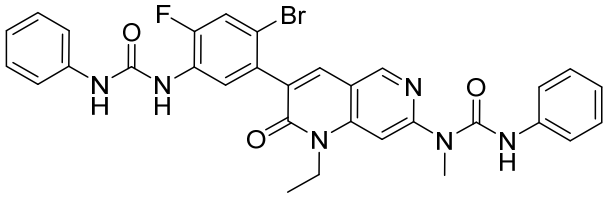
66. The solid dispersion of claim 59 and 61-65 or the pharmaceutically acceptable composition of any one of claims 61-65, further comprising less than 1% by weight of a compound represented by Formula (III):



Formula (III)

based on the weight of the compound of Formula (I).

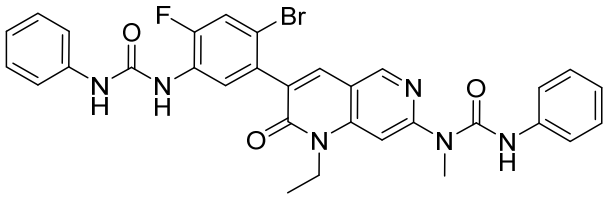
67. The solid dispersion of claim 59 and 61-66 or the pharmaceutically acceptable composition of any one of claims 61-66, further comprising 0.1 % by weight to 0.5% by weight of a compound represented by Formula (III):



Formula (III)

based on the weight of the compound of Formula (I).

68. The solid dispersion of claim 59 and 61-67 or the pharmaceutically acceptable composition of any one of claims 61-67, further comprising 0.01 % by weight to 0.1% by weight of a compound represented by Formula (III):



Formula (III)

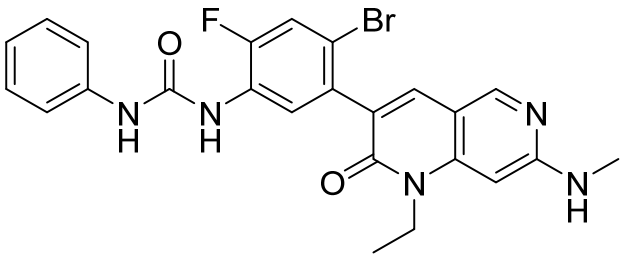
based on the weight of the compound of Formula (I).

69. Use of the composition of any one of claims 61-68 in the manufacture of a medicament for treating a disease selected from the group consisting of gastrointestinal stromal tumors (GIST), NF-1-deficient gastrointestinal stromal tumors, succinate

dehydrogenase (SDH)-deficient gastrointestinal stromal tumors, KIT driven gastrointestinal stromal tumors, PDGFRA driven gastrointestinal stromal tumors, melanoma, acute myeloid leukemia, germ cell tumors of the seminoma or dysgerminoma, mastocytosis, mast cell leukemia, lung adenocarcinoma, squamous cell lung cancer, glioblastoma, glioma, pediatric glioma, astrocytomas, sarcomas, malignant peripheral nerve sheath sarcoma, intimal sarcomas, hypereosinophilic syndrome, idiopathic hypereosinophilic syndrome, chronic eosinophilic leukemia, eosinophilia-associated acute myeloid leukemia, lymphoblastic T-cell lymphoma, and non-small cell lung cancer.

70. The use of claim 69, wherein the disease is gastrointestinal stromal tumors (GIST).

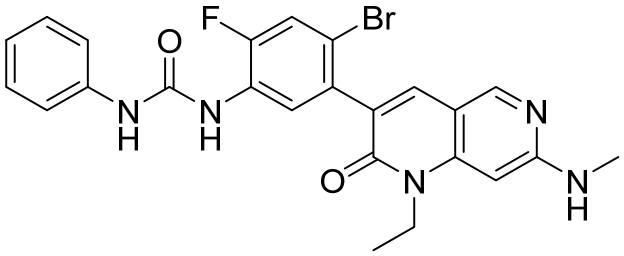
71. A pharmaceutical composition comprising a compound represented by Formula (I)



Formula (I)

and one or more pharmaceutically acceptable carriers, excipients or diluents, wherein the pharmaceutical composition has less than 0.05% of diphenyl urea.

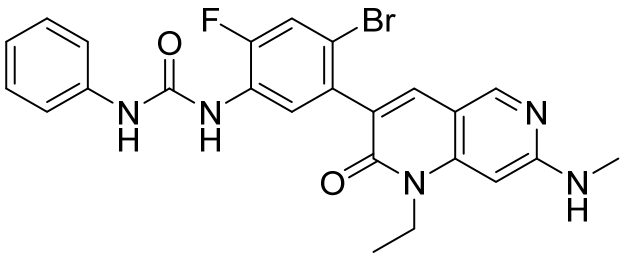
72. A pharmaceutical composition comprising a compound represented by Formula (I)



Formula (I)

and one or more pharmaceutically acceptable carriers, excipients or diluents, wherein the pharmaceutical composition has less than 0.05% of diphenyl urea as detected by HPLC.

73. A solid dispersion comprising the compound represented by Formula (I)



Formula (I)

and hydroxypropylmethyl cellulose acetate succinate, wherein the compound has a purity by HPLC of greater than 90%.

74. The solid dispersion of claim 73, having a purity by HPLC of greater than 95%.

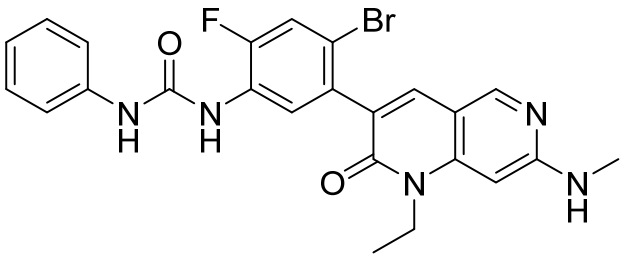
75. A pharmaceutical composition comprising the solid dispersion of claim 73 and one or more pharmaceutically acceptable carriers, excipients or diluents.

76. A pharmaceutical composition comprising the solid dispersion of claim 74 and one or more pharmaceutically acceptable carriers, excipients or diluents.

77. Use of the composition of claim 75 or 76, in the manufacture of a medicament for treating a disease selected from the group consisting of gastrointestinal stromal tumors (GIST), NF-1-deficient gastrointestinal stromal tumors, succinate dehydrogenase (SDH)-deficient gastrointestinal stromal tumors, KIT driven gastrointestinal stromal tumors, PDGFRA driven gastrointestinal stromal tumors, melanoma, acute myeloid leukemia, germ cell tumors of the seminoma or dysgerminoma, mastocytosis, mast cell leukemia, lung adenocarcinoma, squamous cell lung cancer, glioblastoma, glioma, pediatric glioma, astrocytomas, sarcomas, malignant peripheral nerve sheath sarcoma, intimal sarcomas, hypereosinophilic syndrome, idiopathic hypereosinophilic syndrome, chronic eosinophilic leukemia, eosinophilia-associated acute myeloid leukemia, lymphoblastic T-cell lymphoma, and non-small cell lung cancer.

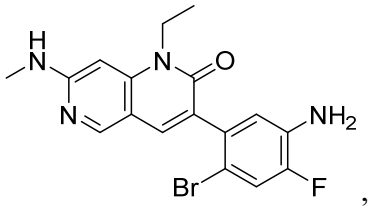
78. The use of claim 77, wherein the disease is gastrointestinal stromal tumors (GIST).

79. A substantially purified compound represented by Formula (I)



Formula (I)

having less than 3.0% by weight of an impurity selected from the group consisting of a compound represented by Formula (II):

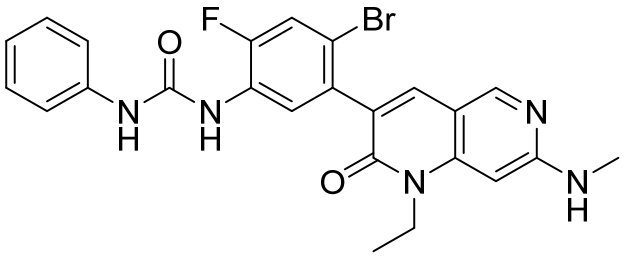


Formula (II)

aniline, and combinations thereof.

80. The compound of claim 79, wherein each of the impurities is in an amount equal to or less than 0.5% by weight based on the weight of the compound of Formula (I).

81. A high purity compound represented by Formula (I)



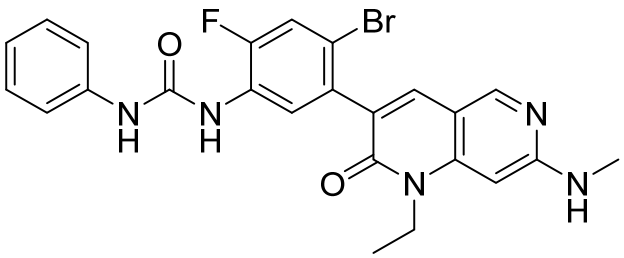
Formula (I)

having less than 3.0% of anilinic substance impurities.

82. The compound of claim 82, wherein the compound comprises less than 0.5% of each of one or more anilinic substances.

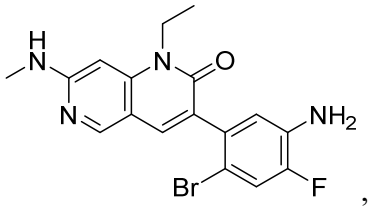
83. The compound of claim 82, wherein each of the impurities is in an amount equal to or less than 0.5% by weight based on the weight of the compound of Formula (I).

84. A substantially purified compound represented by Formula (I)



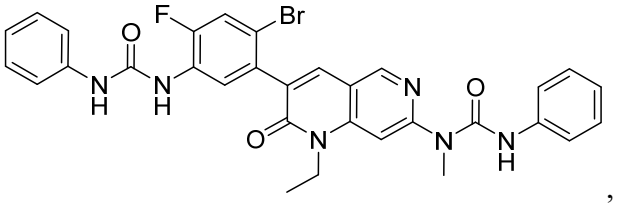
Formula (I)

having less than 3.0% by weight of an impurity selected from the group consisting of a compound represented by Formula (II):



Formula (II)

a compound represented by Formula (III):

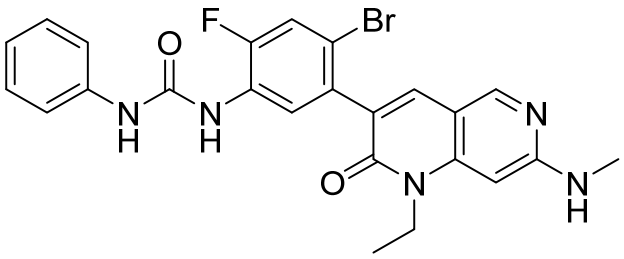


Formula (III)

and combinations thereof.

85. The compound of claim 84, wherein the impurity is in an amount equal to or less than 0.5% by weight based on the weight of the compound of Formula (I).

86. A high purity compound represented by Formula (I)



Formula (I)

having less than 0.05% of a diphenyl urea impurity.

87. The compound of claim 86, wherein the compound comprises less than 0.5% of each of one or more anilinic substances.

88. A pharmaceutical composition comprising any one of the compounds of claims 79-87 and one or more pharmaceutically acceptable excipients, carriers or diluents.

89. Use of the composition of claim 88 in the manufacture of a medicament for treating a disease selected from the group consisting of gastrointestinal stromal tumors (GIST), NF-1-deficient gastrointestinal stromal tumors, succinate dehydrogenase (SDH)-deficient gastrointestinal stromal tumors, KIT driven gastrointestinal stromal tumors, PDGFRA driven gastrointestinal stromal tumors, melanoma, acute myeloid leukemia, germ cell tumors of the seminoma or dysgerminoma, mastocytosis, mast cell leukemia, lung adenocarcinoma, squamous cell lung cancer, glioblastoma, glioma, pediatric glioma, astrocytomas, sarcomas, malignant peripheral nerve sheath sarcoma, intimal sarcomas, hypereosinophilic syndrome, idiopathic hypereosinophilic syndrome, chronic eosinophilic leukemia, eosinophilia-associated acute myeloid leukemia, lymphoblastic T-cell lymphoma, and non-small cell lung cancer.

90. Use of the composition or one or more of the tablets of any one of claims 1-56, 60-68, 71-72, 75-76, and 88 in the manufacture of a medicament for treating a disease selected from the group consisting of gastrointestinal stromal tumors (GIST), NF-1-deficient gastrointestinal stromal tumors, succinate dehydrogenase (SDH)-deficient gastrointestinal stromal tumors, KIT driven gastrointestinal stromal tumors, PDGFRA driven gastrointestinal stromal tumors, lung cancer, glioblastoma, a glioma, malignant peripheral nerve sheath sarcoma, and hypereosinophilic syndrome.

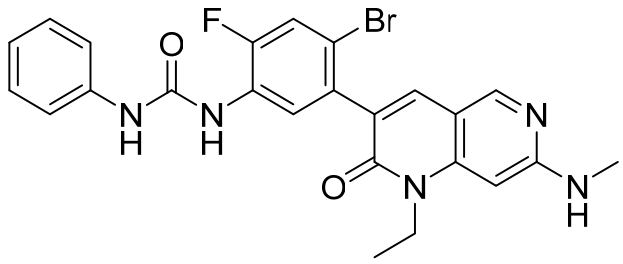
91. Use of the composition or one or more of the tablets of any one of claims 1-56, 60-68, 71-72, 75-76, and 88 in the manufacture of a medicament for treating a disease selected from the group consisting of KIT driven germ cell tumor, KIT driven skin cancer, or KIT driven renal cell carcinoma.

92. Use of the composition or one or more of the tablets of any one of claims 1-56, 60-68, 71-72, 75-76, and 88 in the manufacture of a medicament for treating a disease selected from the group consisting of penile cancer, PDGFRA driven penile cancer, prostate cancer, PDGFRA driven prostate cancer, PDGFRA driven non-melanoma skin cancer, PDGFRA driven glioma, PDGFRA driven sarcoma, PDGFRA driven glioblastoma, or PDGFRA driven pancreatic cancer.

93. Use of the composition or one or more of the tablets of any one of claims 1-56, 60-68, 71-72, 75-76, and 88 in the manufacture of a medicament for treating a disease selected from the group consisting of vaginal cancer, prostate cancer, penile cancer, non-melanoma skin cancer, melanoma, or breast sarcoma, wherein the disease comprises a PDGFRAB mutation.

94. The use of claim 93, wherein the disease is gastrointestinal stromal tumors (GIST).

95. A process for the preparation of the solid dispersion comprising a compound of Formula (I)



Formula (I)

according to any one of claims 59, 61-68, and 73-74, the process comprising:

(a) mixing the compound of Formula (I), a solvent, the hydroxypropylmethyl cellulose acetate succinate and water to obtain a suspension;

(b) optionally agitating and/or mixing the suspension while maintaining a temperature of 10 to 25 ºC;

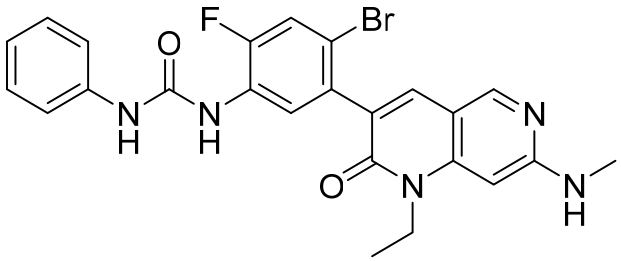
(c) heating the suspension to dissolve the suspended particles prior to introduction into a spray-dryer; and

(d) spray-drying the suspension to obtain a spray-dried dispersion;

(e) drying the spray-dried dispersion; thereby obtaining the solid dispersion.

96. The process of claim 95, wherein heating comprises passing the suspension through an in-line heat exchanger.

97. A solid dispersion comprising a compound of Formula (I)



Formula (I)

produced by the process of claim 95 or 96.

98. The composition or one or more of the tablets of any one of claims 1-56, 60-68, 71-72, 75-76, and 88, for use in therapy.