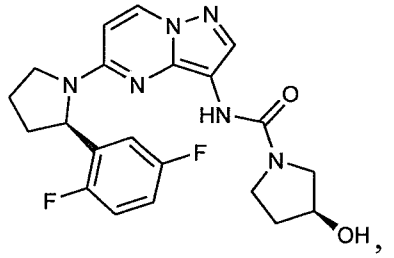
PCT Patent Publication Nos. WO 2010/033941, WO 2010/048314, WO 2011/006074, and WO 2011/146336 disclose compounds which exhibit Trk family protein tyrosine kinase inhibition, and which are useful in the treatment of pain, cancer, inflammation, neurodegenerative diseases and certain infectious diseases.

WO 2010/048314 discloses in Example 14A a hydrogen sulfate salt of (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide. WO 2010/048314 does not disclose the particular form of the hydrogen sulfate salt described herein when prepared according to the method of Example 14A in that document. In particular, WO 2010/048314 does not disclose crystalline form (I-HS) as described below.

All documents, including scientific articles, patent publications and applications, and the like, referenced in the present disclosure are hereby incorporated by reference in their entirety.

SUMMARY

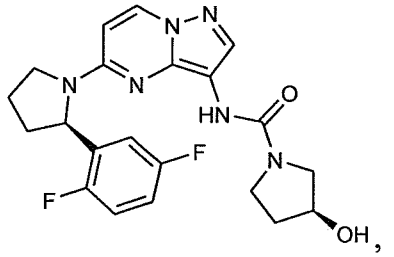
Provided herein are methods of treating a pediatric cancer in a subject in need thereof comprising administering to the subject a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or combinations thereof.

In one aspect, there is provided use of a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:



(I)

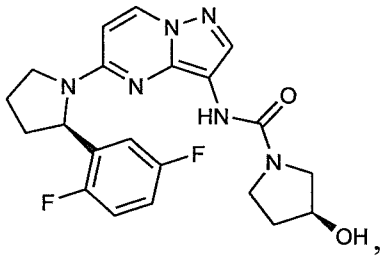
a pharmaceutically acceptable salt thereof, or combinations thereof, in the manufacture of a medicament for the treatment of a pediatric cancer in a subject in need thereof.

In some embodiments, the subject is an infant, child, or adolescent. For example, the subject is an infant.

In some embodiments, the pediatric cancer is a mesenchymal cancer. For example, the mesenchymal cancer can be selected from the group consisting of: pediatric nephroma, congenital fibrosarcoma (CFS), pediatric high-grade glioma (HGG), mesenchymal cancers (infant fibrosarcoma (IF), congenital mesoblastic nephroma, congenital infantile fibrosarcoma (CIFS); pilocytic astrocytoma, brain tumors, pediatic acute leukemia, Ph-like

hydroxypyrrolidine-1-carboxamide

having the formula **(I)**:

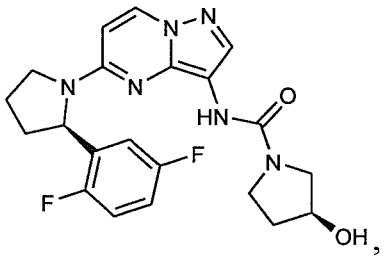


(I)

a pharmaceutically acceptable salt thereof, or a combination thereof.

In one aspect, there is provided use of a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide

having the formula **(I)**:

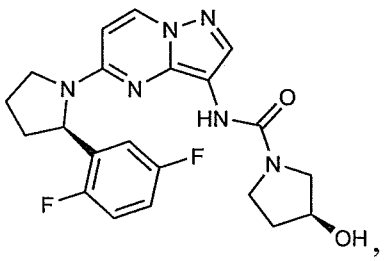


(I)

a pharmaceutically acceptable salt thereof, or a combination thereof, in the manufacture of a medicament for the treatment of an infantile fibrosarcoma.

Further provided herein is a method of treating a subject diagnosed or identified as having a Trk-associated pediatric cancer, the method comprising administering to the subject a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide

having the formula **(I)**:

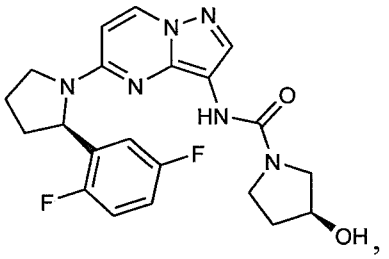


(I)

a pharmaceutically acceptable salt thereof, or a combination thereof.

In one aspect, there is provided use of a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide

having the formula **(I)**:



(I)

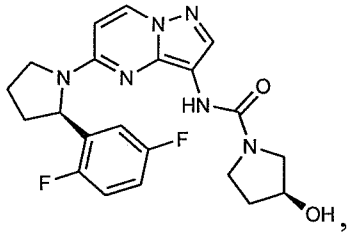
a pharmaceutically acceptable salt thereof, or a combination thereof, in the manufacture of a medicament for the treatment of a subject diagnosed or identified as having a Trk-associated pediatric cancer.

This disclosure also provides a method for treating a pediatric cancer in a subject in need thereof, the method comprising:

(a) determining if the cancer is associated with one or more of overexpression, activation, amplification, and mutation of a Trk kinase; and

(b) if the cancer is determined to be associated with one or more of overexpression, activation, amplification, and mutation of a Trk kinase, administering to the subject a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide

having the formula **(I)**:

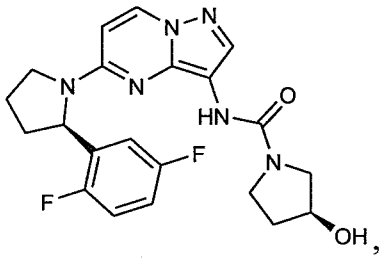


(I)

a pharmaceutically acceptable salt thereof, or a combination thereof.

In one aspect, there is provided use of a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide

having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or a combination thereof, in the manufacture of a medicament for the treatment of a pediatric cancer in a subject in need thereof,

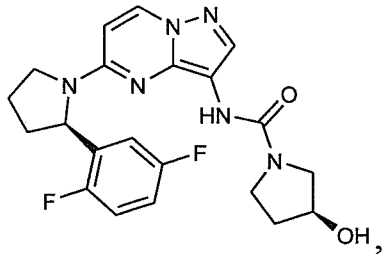
wherein the cancer is determined to be associated with one or more of overexpression, activation, amplification, and mutation of a Trk kinase.

This disclosure also provides a method for treating a pediatric cancer in a subject in need thereof, the method comprising:

(a) identifying the cancer as associated with one or more of overexpression, activation, amplification, and mutation of a Trk kinase; and

(b) administering to the subject a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide

having the formula **(I)**:



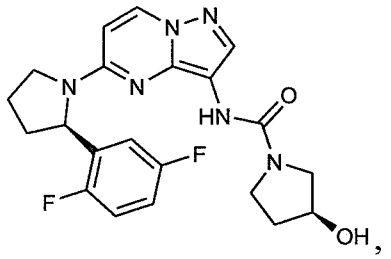
(I)

a pharmaceutically acceptable salt thereof, or a combination thereof.

Further provided herein are methods for treating a pediatric cancer in a subject in need thereof, the method comprising:

(a) determining if the cancer is mediated by a Trk kinase; and

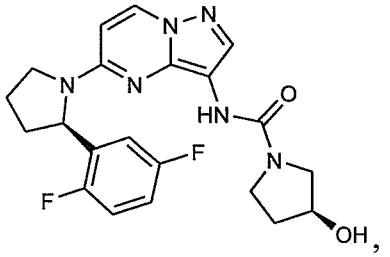
(b) if the cancer is determined to be mediated by a Trk kinase, administering to the subject a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or a combination thereof.

In one aspect, there is provided use of a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide
having the formula **(I)**:



(I)

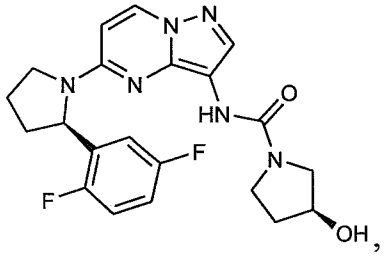
a pharmaceutically acceptable salt thereof, or a combination thereof, in the manufacture of a medicament for the treatment of a pediatric cancer in a subject in need thereof,

wherein the cancer is determined to be mediated by a Trk kinase.

Further provided herein are methods for treating a pediatric cancer in a subject in need thereof, the method comprising:

(a) identifying the cancer as mediated by a Trk kinase; and

(b) administering to the subject a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide
having the formula **(I)**:



(I)

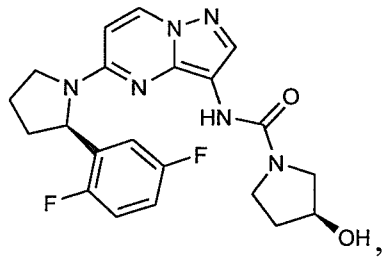
a pharmaceutically acceptable salt thereof, or a combination thereof.

Also provided herein are methods of treating a pediatric subject comprising:

(a) performing an assay on a sample obtained from the subject to determine whether the subject has dysregulation of a NTRK gene, a Trk protein, or expression or level of the same; and

(b) administering to a subject determined to have dysregulation of a NTRK gene, a Trk protein, or expression or activity, or level of the same a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide

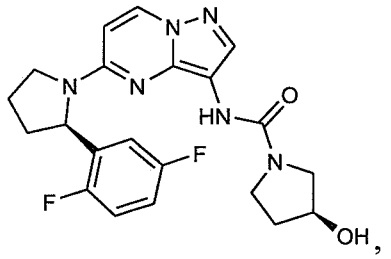
having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or a combination thereof.

In one aspect, there is provided use of a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide
having the formula **(I)**:



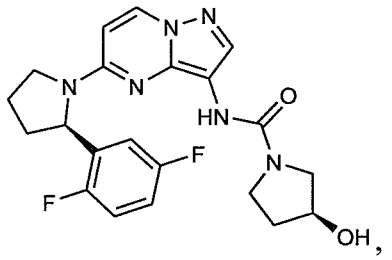
(I)

a pharmaceutically acceptable salt thereof, or a combination thereof, in the manufacture of a medicament for the treatment of a pediatric subject, wherein the subject is determined to have dysregulation of a NTRK gene, a Trk protein, or expression or activity, or level of the same, based on an assay performed on a sample obtained from the subject to determine whether the subject has dysregulation of a NTRK gene, a Trk protein, or expression or level of the same.

In some embodiments, the dysregulation of a NTRK gene, a Trk protein, or expression or level of the same is a chromosome translation that results in the translation of a Trk fusion protein. For example,

What is claimed:

1. Use of a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or combinations thereof, in the manufacture of a medicament for the treatment of a pediatric cancer in a subject in need thereof.

2. The use of claim 1, wherein the subject is an infant, child, or adolescent.

3. The use of claim 1, wherein the subject is an infant.

4. The use of any one of claims 1-3, wherein the pediatric cancer is a mesenchymal cancer.

5. The use of claim 4, wherein the mesenchymal cancer is selected from the group consisting of: pediatric nephroma, congenital fibrosarcoma (CFS), pediatric high-grade glioma (HGG), mesenchymal cancers (infant fibrosarcoma (IF), congenital mesoblastic nephroma, congenital infantile fibrosarcoma (CIFS); pilocytic astrocytoma, brain tumors, pediatic acute leukemia, Ph-like acute lymphoblastic leukemia, cellular congenital mesoblastic nephroma (CMN); infantile fibrosarcoma, pediatric high-grade glioma (HGG), diffuse intrinsic pontine gliomas (DIPGs), non-brainstem HGGs (NBS-HGGs), anaplastic large cell lymphoma (ALCL), non-Hodgkin's lymphoma (NHL), pediatric papillary thyroid carcinoma, soft tissue sarcoma, spitzoid melanoma, pediatric hemangiopericytoma-like sarcoma, spindle cell sarcoma, NOS with myo/haemangiopericytic growth pattern, lung cancer, advanced pediatric solid tumors, neuroectodermal-derived tumors, pediatric colorectal cancer, adrenal neuroblastoma, and central nervous system tumors.

6. The use of any one of claims 1-3, wherein the pediatric cancer is a fibrosarcoma.

7. The use of any one of claims 1-3, wherein the pediatric cancer is infantile fibrosarcoma.

8. The use of any one of claims 1-7, wherein the cancer is mediated by TrkA.

9. The use of any one of claims 1-7, wherein the cancer is mediated by TrkB.

10. The use of any one of claims 1-7, wherein the cancer is mediated by TrkC.

11. The use of any one of claims 1-6, wherein the cancer is mediated by TrkA, TrkB, TrkC, or combinations thereof.

12. The use of any one of claims 6-11, wherein surgical resection has failed to inhibit progression of the fibrosarcoma in the subject.

13. The use of any one of claims 1-12, wherein chemotherapy previously failed to inhibit tumor progression in the subject.

14. The use of claim 13, wherein the chemotherapy comprises administration at least one of vincristine, actinomycin-D, cyclophosphamide, ifosfamide, etoposide, or doxorubicin.

15. The use of any one of claims 1-14, wherein chemotherapy comprising administration of at least one of vincristine, actinomycin-D, and cyclophosphamide failed to inhibit tumor progression in the subject.

16. The use of any one of claims 1-14, wherein chemotherapy comprising administration of at least one of ifosfamide and doxorubicin failed to inhibit tumor progression in the subject.

17. The use of any one of claims 1-16, the subject is ETV6-NTRK3 fusion positive.

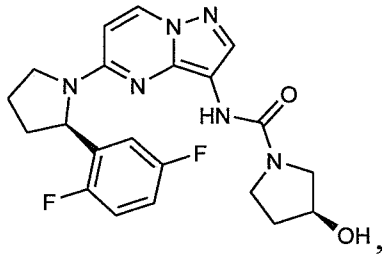
18. The use of any one of claims 1-17, further comprising performing a morphological diagnosis prior to administering the compound of formula **(I)**, a

pharmaceutically acceptable salt thereof, or a combination thereof.

19. The use of any one of claims 1-18, further comprising performing molecular testing prior to administering the compound of formula **(I)**, a pharmaceutically acceptable salt thereof, or a combination thereof.

20. The use of any one of claims 1-19, further comprising performing morphological diagnosis and molecular testing prior to administering the compound of formula **(I)**, a pharmaceutically acceptable salt thereof, or a combination thereof.

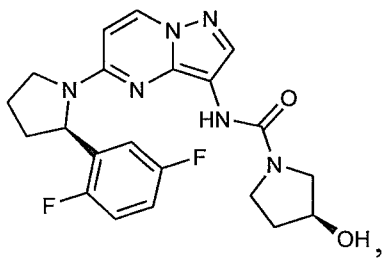
21. Use of a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide
having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or a combination thereof, in the manufacture of a medicament for the treatment of an infantile fibrosarcoma.

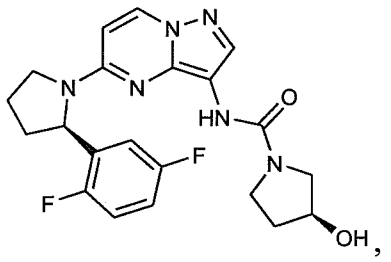
22. Use of a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide
having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or a combination thereof, in the manufacture of a medicament for the treatment of a subject diagnosed or identified as having a Trk-associated pediatric cancer.

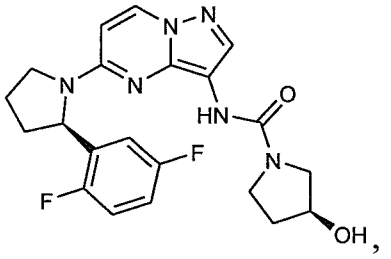
23. Use of a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide
having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or a combination thereof, in the manufacture of a medicament for the treatment of a pediatric cancer in a subject in need thereof,
wherein the cancer is determined to be associated with one or more of overexpression, activation, amplification, and mutation of a Trk kinase.

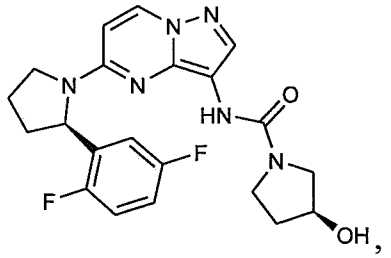
24. Use of a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide
having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or a combination thereof, in the manufacture of a medicament for the treatment of a pediatric cancer in a subject in need thereof,
wherein the cancer is determined to be mediated by a Trk kinase.

25. Use of a therapeutically effective amount of (S)-N-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide
having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or a combination thereof, in the manufacture of a medicament for the treatment of a pediatric subject, wherein the subject is determined to have dysregulation of a NTRK gene, a Trk protein, or expression or activity, or level of the same, based on an assay performed on a sample obtained from the subject to determine whether the subject has dysregulation of a NTRK gene, a Trk protein, or expression or level of the same.

26. The use of claim 25, wherein the dysregulation of a NTRK gene, a Trk protein, or expression or level of the same is a chromosome translation that results in the translation of a Trk fusion protein.

27. The use of claim 25, wherein the Trk fusion protein is NTRK3-ETV6.

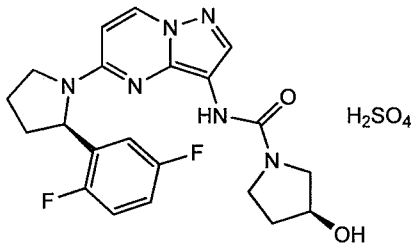
28. The use of claim 25, wherein the dyregulation of a NTRK gene, a Trk protein, or expression or activity of the same is one or more point mutations in the gene.

29. The use of any one of claims 1-28, wherein the compound of formula **(I)** is a pharmaceutically acceptable salt.

30. The use of any one of claims 1-29, wherein the compound of formula **(I)** is a hydrogen sulfate salt.

31. The use of any one of claims 1-30, wherein the compound of formula **(I)** is provided as a crystalline form.

32. The use of claim 31, wherein the crystalline form has the formula **(I-HS)**:



I-HS.

33. The use of any one of claims 1-32, wherein the compound of formula **(I)**, a pharmaceutically acceptable salt thereof, or a combination thereof, is provided as a liquid formulation.

34. The use of claim 33, wherein the liquid further comprises a solubilizing agent.

35. The use of any one of claims 33 to 34, wherein the compound of formula **(I)**, a pharmaceutically acceptable salt thereof, or a combination thereof, is present in an amount from about 0.5 wt.% to about 7 wt. %.

36. The use of any one of claims 33 to 35, wherein the compound of formula **(I)**, a pharmaceutically acceptable salt thereof, or a combination thereof is present in an amount of about 1.5 wt.% to about 2.5 wt.%.

37. The use of any one of claims 33 to 36, wherein the compound of formula **(I)** has a concentration of about 5 mg/mL to about 50 mg/mL in the liquid formulation.

38. The use of any one of claims 33 to 37, wherein the compound of formula **(I)** has a concentration of about 15 mg/mL to about 35 mg/mL in the liquid formulation.

39. The use of any one of claims 33 to 38, wherein the compound of formula **(I)** has a concentration of about 20 mg/mL in the liquid formulation.

40. The use of any one of claims 33 to 39, wherein the solubilizing agent is selected from the group consisting a cyclodextrin, a glycol, a glycerol, and combinations thereof.

41. The use of any one of claims 33 to 40, wherein the solubilizing agent comprises a cyclodextrin.

42. The use of any one of claims 33 to 41, wherein the solubilizing agent is selected from the group consisting of a β-cyclodextrin derivative, a γ-cyclodextrin, and combinations thereof.

43. The use of any one of claims 33 to 42, wherein the solubilizing agent comprises a hydroxy alkyl-γ-cyclodextrin

44. The use of any one of claims 33 to 41, wherein the solubilizing agent comprises a β-cyclodextrin selected from the group consisting of a hydroxy alkyl-β-cyclodextrin, a sulfoalkyl ether-β-cyclodextrin, and combinations thereof.

45. The use of any one of claims 33 to 41, wherein the solubilizing agent comprises hydroxypropyl-β-cyclodextrin.

46. The use of any one of claims 33 to 42, wherein the solubilizing agent is present in an amount of about 5 wt.% to about 35 wt.%.

47. The use of any one of claims 33 to 46, wherein the solubilizing agent is present in an amount of about 13 wt.% to about 17 wt.%.

48. The use of any one of claims 33 to 47, wherein the formulation further comprises a base.

49. The use of any one of claim 48, wherein the base comprises at least one of a citrate, a lactate, a phosphate, a maleate, a tartrate, a succinate, an acetate, a carbonate, or a hydroxide.

50. The use of claim 48, wherein the base comprises at least one of lithium lactate, sodium lactate, potassium lactate, calcium lactate, lithium phosphate, sodium phosphate, potassium phosphate, calcium phosphate, lithium maleate, sodium maleate, potassium

maleate, calcium maleate, lithium tartrate, sodium tartrate, potassium tartrate, calcium tartrate, lithium succinate, sodium succinate, potassium succinate, calcium succinate, lithium acetate, sodium acetate, potassium acetate, calcium acetate, sodium carbonate, potassium carbonate, calcium carbonate, sodium bicarbonate, potassium bicarbonate, calcium bicarbonate, sodium hydroxide, potassium hydroxide, or calcium hydroxide.

51. The use of claim 48, wherein the base is a citrate.

52. The use of claim 51, wherein the citrate comprises at least one of lithium citrate monohydrate, sodium citrate monohydrate, potassium citrate monohydrate, calcium citrate monohydrate, lithium citrate dihydrate, sodium citrate dihydrate, potassium citrate dihydrate, calcium citrate dihydrate, lithium citrate trihydrate, sodium citrate trihydrate, potassium citrate trihydrate, calcium citrate trihydrate, lithium citrate tetrahydrate, sodium citrate tetrahydrate, potassium citrate tetrahydrate, calcium citrate tetrahydrate, lithium citrate pentahydrate, sodium citrate pentahydrate, potassium citrate pentahydrate, calcium citrate pentahydrate, lithium citrate hexahydrate, sodium citrate hexahydrate, potassium citrate hexahydrate, calcium citrate hexahydrate, lithium citrate heptahydrate, sodium citrate heptahydrate, potassium citrate heptahydrate, or calcium citrate heptahydrate.

53. The use of claim 51, wherein the base comprises at least one of sodium citrate monohydrate, potassium citrate monohydrate, calcium citrate monohydrate, sodium citrate dihydrate, potassium citrate dihydrate, calcium citrate dihydrate, sodium citrate trihydrate, potassium citrate trihydrate, calcium citrate trihydrate, sodium citrate tetrahydrate, potassium citrate tetrahydrate, calcium citrate tetrahydrate, sodium citrate pentahydrate, potassium citrate pentahydrate, calcium citrate pentahydrate, sodium citrate hexahydrate, potassium citrate hexahydrate, calcium citrate hexahydrate, sodium citrate heptahydrate, potassium citrate heptahydrate, or calcium citrate heptahydrate.

54. The use of claim 51, wherein the base comprises sodium citrate dihydrate.

55. The use of any one of claims 48 to 54, wherein the base is present in the liquid formulation in an amount of about 0.1 wt.% to about 5 wt.%.

56. The use of any one of claims 33 to 55, wherein the formulation has a pH of about

2 to about 7.

57. The use of any one of claims 33 to 56, wherein the formulation has a pH of about 3 to about 4.

58. The use of any one of claims 33 to 57, wherein the formulation has a pH of about 3.5.

59. The use of any one of claims 33 to 58, wherein the liquid formulation further comprises a sweetener.

60. The use of any one of claim 59, wherein the sweetener comprises a sugar.

61. The use of claim 60, wherein the sugar comprises sucrose.

62. The use of claim 59, wherein the sweetener comprises an intense sweetener.

63. The use of claim 62, wherein the intense sweetener comprises sucralose.

64. The use of any one of claims 59 to 63, wherein the sweetener is present in an amount of about 30 wt.% to about 70 wt.%.

65. The use of any one of claims 59 to 64, wherein the sweetener is present in an amount of about 45 wt.% to about 55 wt.%.

66. The use of any one of claims 33 to 65, wherein the liquid formulation further comprises a bitterness masking agent.

67. The use of claim 66, wherein the bitterness masking agent is present in an amount of about 0.01 wt.% to about 2 wt.%.

68. The use of any one of claims 66 to 67, wherein the bitterness masking agent is present in an amount of about 0.2 wt.% to about 0.5 wt.%.

69. The use of any one of claims 33 to 68, wherein the formulation further comprises a flavoring agent.

70. The use of claim 69, wherein the flavoring agent comprises at least one of a natural flavoring agent, a natural fruit flavoring agent, an artificial flavoring agent, an artificial fruit flavoring agent, or a flavor enhancer.

71. The use of claim 69 or 70, wherein the flavoring agent is present in an amount of about 0.01 wt.% to about 2 wt.%.

72. The use of any one of claims 69 to 71, wherein the flavoring agent is present in an amount of about 0.01 wt.% to about 0.1 wt.%.

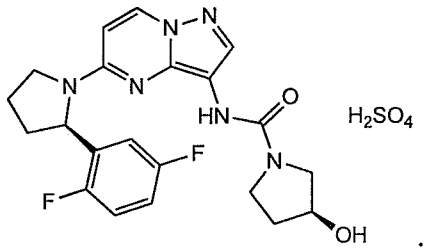
73. The use of any one of claims 33 to 72, wherein the formulation further comprises a coloring agent.

74. The use of any one of claims 33 to 73, wherein the liquid formulation is prepared from a pharmaceutically acceptable salt of the compound of formula **(I)**.

75. The use of any one of claims 33 to 74, wherein the liquid formulation is prepared from the hydrogen sulfate salt of the compound of formula **(I)**.

76. The use of any one of claims 33 to 75, wherein the liquid formulation is prepared from a crystalline form of the compound of formula **(I)**.

77. The use of claim 76, wherein the crystalline form has the formula **(I-HS)**:



I-HS

78. The use of claim 33, wherein the liquid formulation further comprises:

a solubilizing agent; and

a base;

wherein:

the formulation has a pH of about 2.5 to about 5.5; and

the compound of formula (I) has a concentration of about 15 mg/mL to about 35 mg/mL in the liquid formulation.

79. The use of claim 78, wherein the formulation has a pH of about 3 to about 4.

80. The use of any one of claims 78 to 79, wherein the base comprises sodium citrate dihydrate.

81. The use of claim 33, wherein the liquid formulation further comprises:

a solubilizing agent;

a base;

a sweetener;

a bitterness masking agent; and

a flavoring agent,

wherein:

the formulation has a pH of about 3 to about 4; and

the compound of formula (I) has a concentration of about 15 mg/mL to about 35 mg/mL in the liquid formulation.

82. The use of claim 48, wherein the base comprises sodium citrate dihydrate.

83. The use of any one of claims 81 to 82, wherein the sweetener comprises sucrose.

84. The use of claim 33, wherein the liquid formulation further comprises:

a solubilizing agent present in an amount of about 5 wt.% to about 35 wt.%;

a base present in an amount of about 0.1 wt.% to about 5 wt.% ;

wherein:

the formulation has a pH of about 2.5 to about 5.5; and

the compound of formula (I) has a concentration of about 20 mg/mL to about 30 mg/mL in the liquid formulation.

85. The use of claim 33, wherein the liquid formulation further comprises:

a solubilizing agent present in an amount of about 5 wt.% to about 35 wt.%;

a base present in an amount of about 0.1 wt.% to about 5 wt.% ;

a sweetener present in an amount of about 30 wt.% to about 70 wt.%;

a bitterness masking agent present in an amount of about 0.2 wt.% to about 0.5 wt.%; and

a flavoring agent present in an amount of about 0.01 wt.% to about 2 wt.%,

wherein:

the formulation has a pH of about 2.5 to about 5.5; and

the compound of formula (I) has a concentration of about 20 mg/mL to about 30 mg/mL in the liquid formulation.

86. The use of claim 33, wherein the liquid formulation further comprises:

a solubilizing agent present in an amount of about 5 wt.% to about 35 wt.%;

a base comprising sodium citrate dihydrate present in an amount of about 0.1 wt.% to about 5 wt.%;

a sweetener comprising sucrose present in an amount of about 30 wt.% to about 70 wt.%;

a bitterness masking agent is present in an amount of about 0.2 wt.% to about 0.5 wt.%; and

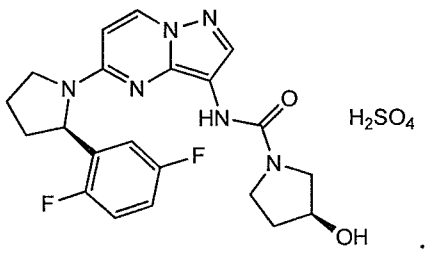
a flavoring agent present in an amount of about 0.01 wt.% to about 2 wt.%,

wherein:

the formulation has a pH of about 3 to about 4; and

the compound of formula (I) has a concentration of about 20 mg/mL to about 30 mg/mL in the liquid formulation.

87. The use of any one of claims 33 to 86, wherein the liquid formulation is prepared from a crystalline form of the compound of formula **(I)** having the formula (I-HS):



88. The use of claim 87, wherein the crystalline form is characterized by having XRPD diffraction peaks (2θ degrees) at 18.4±0.2, 20.7±0.2, 23.1±0.2, and 24.0±0.2.

89. The use of claim 87, wherein the crystalline form is characterized by having XRPD diffraction peaks (2θ degrees) at 10.7±0.2, 18.4±0.2, 20.7±0.2, 23.1±0.2, and 24.0±0.2.

90. The use of claim 87, wherein the crystalline form is characterized by having XRPD diffraction peaks (2θ degrees) at 10.7±0.2, 18.4±0.2, 19.2±0.2, 20.2±0.2, 20.7±0.2, 21.5±0.2, 23.1±0.2, and 24.0±0.2.

91. The use of claim 87, wherein the crystalline form is characterized by having XRPD diffraction peaks (2θ degrees) at 10.7±0.2, 15.3±0.2, 16.5±0.2, 18.4±0.2, 19.2±0.2, 19.9±0.2, 20.2±0.2, 20.7±0.2, 21.5±0.2, 22.1±0.2, 23.1±0.2, 24.0±0.2. 24.4±0.2, 25.6±0.2, 26.5±0.2, 27.6±0.2, 28.2±0.2, 28.7±0.2, 30.8±0.2, and 38.5±0.2.

92. The use of any one of claims 33 to 91, wherein the liquid formulation is an oral liquid formulation.

93. The use of any one of claims 1-92, wherein the compound of formula **(I)**, a pharmaceutically acceptable salt thereof, or a combination thereof, is to be administered in 28-day cycles.

94. The use of any one of claims 1-93, wherein the compound is to be administered in a dosage calculated to be the equal to the exposure of an adult taking the compound of formula **(I)**, a pharmaceutically acceptable salt thereof, or a combination thereof, at a dose of 100 mg twice a day.