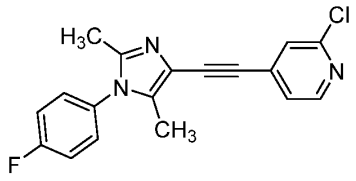
CLAIMS

1. A method of treating a medical condition associated with tuberous sclerosis complex (TSC), comprising administering to a subject in need thereof a composition comprising a therapeutically effective amount of a compound or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula I:



(I).

2. The method of claim 1, wherein administering comprises administering the compound of Formula I in its free base form.

3. The method of claim 1, wherein administering comprises administering the compound of Formula I in the form of a pharmaceutically acceptable salt thereof.

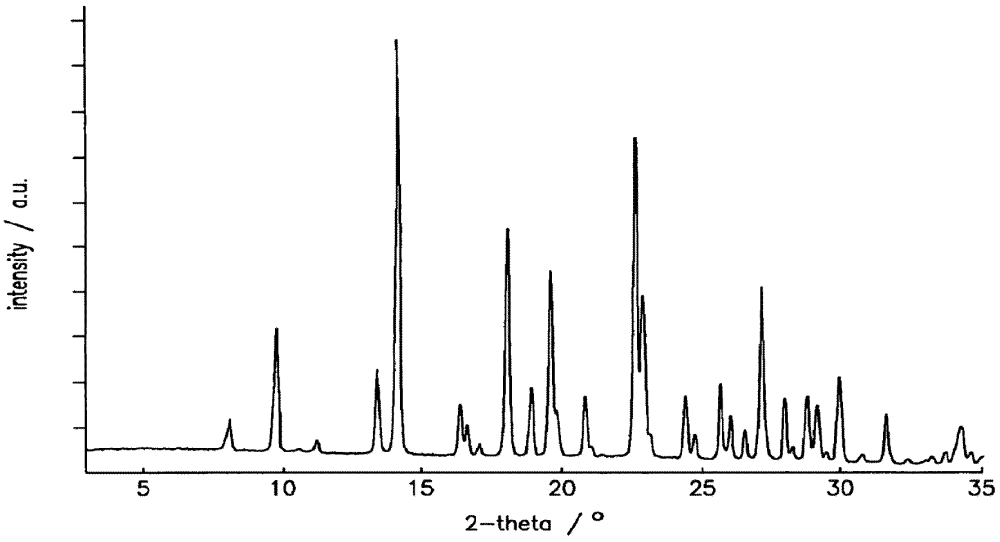
4. The method of claim 3, wherein the pharmaceutically acceptable salt is a monosulfate salt or a hemisulfate salt.

5. The method of claim 4, wherein the pharmaceutically acceptable salt is in a crystalline form or an amorphous form.

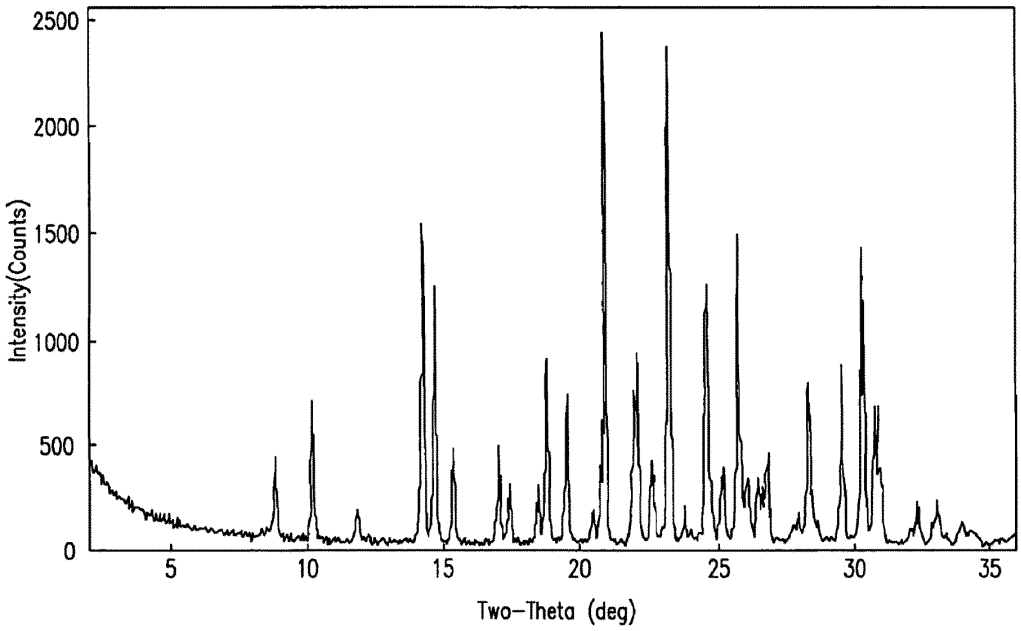
6. The method of claim 5, wherein the pharmaceutically acceptable salt comprises a crystalline anhydrate form (Form A) of a monosulfate salt of the compound of Formula I, wherein Form A is characterized by at least three peaks selected from the following X-ray powder diffraction peaks obtained with a $Cu_{K\alpha}$ radiation at 2θ (2 Theta): 9.8±0.2°, 13.4±0.2°, 14.2±0.2°, 18.1±0.2°, 18.9±0.2°, 19.6±0.2°, 22.6±0.2°, 22.9±0.2°, 25.7±0.2°, 27.1±0.2°, and 29.9±0.2°.

7. The method of claim 6, wherein Form A is characterized by the following X-ray powder diffraction peaks obtained with a $Cu_{K\alpha}$ radiation at 2θ (2 Theta): 9.8±0.2°, 13.4±0.2°, 14.2±0.2°, 18.1±0.2°, 18.9±0.2°, 19.6±0.2°, 22.6±0.2°, 22.9±0.2°, 25.7±0.2°, 27.1±0.2°, and 29.9±0.2°.

8. The method of claim 6 or 7, wherein Form A has an X-ray powder diffraction (XRPD) pattern as substantially shown below:

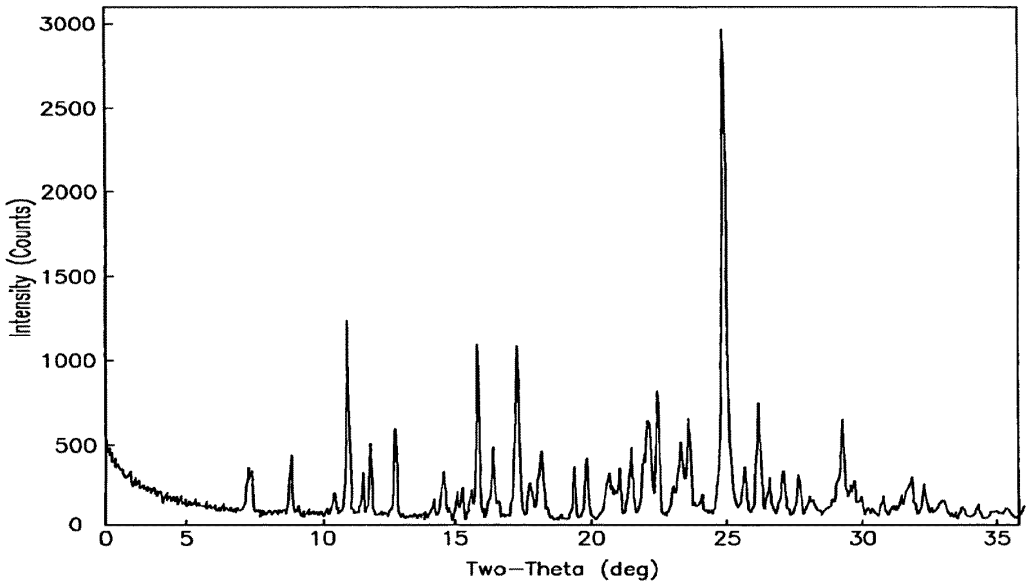


9. The method of claim 5, wherein the pharmaceutically acceptable salt comprises a crystalline monohydrate form (Form B) of a monosulfate salt of the compound of Formula I, wherein Form B has an XRPD pattern as substantially shown below:



10. The method of claim 5, wherein the pharmaceutically acceptable salt comprises an amorphous form of a monosulfate salt of the compound of Formula I, characterized by an infrared spectrum having bands at 2730, 2592, 2219, 1633, 1586, 1570, 1513, 1375, 1343, 1293, 1226, 1157, 1130, 1084, 1040, 986, 903, 848, 788, 712 and 670 cm^{-1} (±3 cm^{-1}).

11. The method of claim 5, wherein the pharmaceutically acceptable salt comprises a crystalline hemihydrate form (Form C) of a hemisulfate salt of the compound of Formula I, wherein Form C has an XRPD pattern as substantially shown below:



12. The method of any one of claims 1-11, wherein the composition is an immediate release formulation encapsulated in a capsule, a modified release tablet formulation, or a modified release pellet formulation encapsulated in a capsule.

13. The method of claim 12, wherein the composition is a modified release pellet formulation encapsulated in a capsule, and the compound of Formula I, or a pharmaceutically acceptable salt thereof, is present in an amount from about 0.05 mg to about 20 mg.

14. The method of any one of claims 1-13, wherein the compound of Formula I, or a pharmaceutically acceptable salt thereof, is present in the composition in an amount from about 0.01% to about 20% by weight, based on the total weight of the composition.

15. The method of claim 14, wherein the compound of Formula I, or a pharmaceutically acceptable salt thereof, is present in the composition in an amount from about 0.05% to about 15% by weight, based on the total weight of the composition.

16. The method of claim 12, wherein the composition is a modified release pellet formulation encapsulated in a capsule, and a Form A monosulfate salt of the compound of Formula I is present in the composition in an amount from about 0.05 mg to about 20 mg.

17. The method of claim 16, wherein the Form A monosulfate salt is present in the composition in an amount from about 0.01% to about 20% by weight, based on the total weight of the composition.

18. The method of claim 17, wherein the Form A monosulfate salt is present in the composition in an amount from about 0.05% to about 15% by weight, based on the total weight of the composition.

19. The method of any one of claims 1-18, wherein the composition is an immediate release formulation encapsulated in a capsule, comprising the following formulation:

	mg/capsule
Form A of monosulfate salt	0.065
Lactose Monohydrate	108.934
Starch Maize Partially Pregelatinized (type 1500)	60.00
Croscarmellose Sodium	8.00
Povidone 30	15.00
Sodium lauryl sulfate	1.00
Talc	6.00
Magnesium Stearate	1.00
Total	200.00

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20. The method of any one of claims 1-18, wherein the composition is an immediate release formulation encapsulated in a capsule, comprising the following formulation:

	mg/capsule
Form A of monosulfate salt	0.650
Lactose Monohydrate	109.349
Starch Maize Partially Pregelatinized (type 1500)	60.00
Croscarmellose Sodium	8.00
Povidone 30	15.00
Sodium lauryl sulfate	—
Talc	6.00
Magnesium Stearate	1.00
Total	200.00

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21. The method of any one of claims 1-18, wherein the composition is an immediate release formulation encapsulated in a capsule, comprising the following formulation:

	mg/capsule
Form A of monosulfate salt	2.602
Lactose Monohydrate	107.398
Starch Maize Partially Pregelatinized (type 1500)	60.00
Croscarmellose Sodium	8.00
Povidone 30	15.00
Sodium lauryl sulfate	—
Talc	6.00
Magnesium Stearate	1.00
Total	200.00

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22. The method of any one of claims 1-18, wherein the composition is an immediate release formulation encapsulated in a capsule, comprising the following formulation:

	mg/capsule
Form A of monosulfate salt	26.02
Lactose Monohydrate	83.98
Starch Maize Partially Pregelatinized (type 1500)	60.00
Croscarmellose Sodium	8.00
Povidone 30	15.00
Sodium lauryl sulfate	—
Talc	6.00
Magnesium Stearate	1.00
Total	200.00

23. The method of any one of claims 1-18, wherein the composition is a modified release pellet formulation encapsulated in a capsule, and the composition comprises a formulation selected from the group consisting of Formulation 1, Formulation 2, Formulation 3, and Formulation 4, as shown in the table below.

Group	Formulation 1	Formulation 2	Formulation 3	Formulation 4
Ingredient	Quantity (mg/capsule)			
Form A monosulfate	0.13	0.26	0.65	1.30
Microcrystalline cellulose	64.62	129.24	64.10	128.20
Methacrylic acid copolymer	30.00	60.00	30.00	60.00
Hypromellose	5.00	10.00	5.00	10.00
Talc	0.25	0.50	0.25	0.50
Total	100.00	200.00	100.00	200.00

24. The method of claim 6, wherein the pharmaceutically acceptable salt is 90% by weight or more of the crystalline Form A based on the total weight of the salt present in the composition.

25. The method of claim 24, wherein the pharmaceutically acceptable salt is 95% by weight or more of the crystalline Form A based on the total weight of the salt present in the composition.

26. The method of claim 25, wherein the pharmaceutically acceptable salt is 99% by weight or more of the crystalline Form A based on the total weight of the salt present in the composition.

27. The method of any one of claims 1-26, wherein administering comprises administering once daily the compound of Formula I, or a pharmaceutically acceptable salt thereof.

28. The method of any one of claims 1-27, wherein administering comprises administering the compound of Formula I, or a pharmaceutically acceptable salt thereof, in an amount of about 0.1 mg to about 3.5 mg once daily.

29. The method of any one of claims 1-28, wherein administering comprises administering the compound of Formula I, or a pharmaceutically acceptable salt thereof, in an amount of about 0.1 mg to about 3 mg once daily.

30. The method of any one of claims 1-29, wherein administering comprises administering the compound of Formula I, or a pharmaceutically acceptable salt thereof, in an amount of about 1.5 mg to about 3.5 mg once daily.

31. The method of any one of claims 1-30, wherein administering comprises administering the compound of Formula I, or a pharmaceutically acceptable salt thereof, in an amount of about 1 mg to about 3 mg once daily.

32. The method of any one of claims 1-31, wherein administering comprises administering the compound of Formula I, or a pharmaceutically acceptable salt thereof, in an amount of about 3.5 mg, about 3.0 mg, about 2.5 mg, about 2.0 mg, about 1.5 mg, or about 1.0 mg once daily.

33. The method of any one of claims 1-32, wherein administering comprises administering the compound of Formula I, or a pharmaceutically acceptable salt thereof, in an amount of about 3.5 mg once daily.

34. The method of any one of claims 1-33, wherein administering comprises administering the compound of Formula I, or a pharmaceutically acceptable salt thereof, in an amount of about 3 mg once daily.

35. The method of any one of claims 1-34, wherein administering comprises administering orally the compound of Formula I, or a pharmaceutically acceptable salt thereof.

36. The method of any one of claims 1-35, wherein administering comprises administering the compound of Formula I, or a pharmaceutically acceptable salt thereof, as a unit dose.

37. The method of any one of claims 1-36, wherein the subject has a weight of at least 40 kg.

38. The method of any one of claims 1-36, wherein the subject has a weight of less than 40 kg.

39. The method of any one of claims 1-38, wherein the medical condition associated with TSC is a TSC-associated neuropsychiatric disorder, a TSC-associated tumor, or a heart arrhythmia.

40. The method of claim 39, wherein the medical condition associated with TSC is a TSC-associated neuropsychiatric disorder selected from the group consisting of autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), anxiety disorder, and depressive disorder.

41. The method of claim 39, wherein the medical condition associated with TSC is a TSC-associated tumor selected from the group consisting of subependymal giant cell astrocytomas (SEGAs), angiomyolipomas (ALM), renal cell carcinoma, oncocytomas, lymphangioleiomyomatosis (LAM), cardiac rhabdomyomas, ungual fibromas, intraoral fibromas, retinal lesions, retinal hamartomas, and pancreatic neuroendocrine kidney diseases.

42. The method of any one of claims 1-41, wherein the medical condition associated with TSC is selected from the group consisting of seizures, intellectual disability, developmental delay, behavioral problems, skin abnormalities, lung diseases, kidney diseases, and heart diseases.

43. The method of any one of claims 1-42, wherein the therapeutic effect of the treatment is determined by:

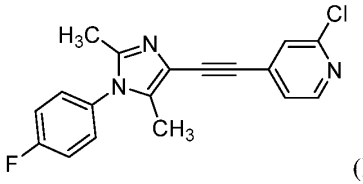
a) reduction of seizure occurrence or frequency;

b) reduction of the size of a tumor in the brain, eyes, heart, kidney, skin, or lungs;

c) suppression of tumor growth in the brain, eyes, heart, kidney, skin, or lungs; or

d) improvement of cognitive function.

44. A solid pharmaceutical composition, comprising a pharmaceutical excipient; and a solid form of a compound of Formula I:



(I),

wherein the solid form is a crystalline anhydrate form (Form A) of a monosulfate salt of the compound of Formula I, characterized by at least three peaks selected from the following XRPD peaks obtained with a $Cu_{K\alpha}$ radiation at 2θ (2 Theta): 9.8±0.2°, 13.4±0.2°, 14.2±0.2°, 18.1±0.2°, 18.9±0.2°, 19.6±0.2°, 22.6±0.2°, 22.9±0.2°, 25.7±0.2°, 27.1±0.2°, and 29.9±0.2°; and

has a particle size (Dv50) of less than or equal to about 100 µm; wherein the solid pharmaceutical composition is the form of a matrix pellet.

45. The pharmaceutical composition of claim 44, wherein the solid form has a particle size of less than 47 µm.

46. The pharmaceutical composition of claim 44, wherein the solid form has a particle size of less than or equal to about 25 µm.

47. The pharmaceutical composition of claim 44, wherein the solid form has a particle size of less than or equal to about 10 µm.

48. The pharmaceutical composition of any one of claims 44-47, wherein the Form A monosulfate salt is present in the composition in an amount of 1% by weight or less, based on the total weight of the composition.

49. The pharmaceutical composition of claim 48, wherein the Form A monosulfate salt is present in the composition in an amount of 0.5% by weight or less, based on the total weight of the composition.

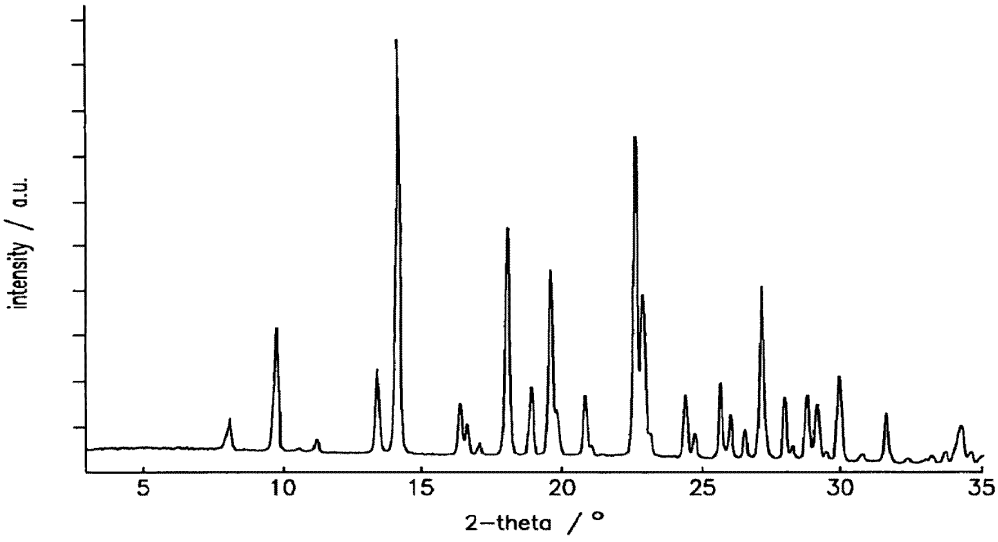
50. The pharmaceutical composition of any one of claims 44-49, wherein the pharmaceutical excipient comprises one or more of a polymer, a binder, a disintegrant, a lubricant, and a glidant.

51. The pharmaceutical composition of claim 50, the polymer is one or more polymers selected from the group consisting of a cellulose, methacrylic acid copolymer, and hypromellose.

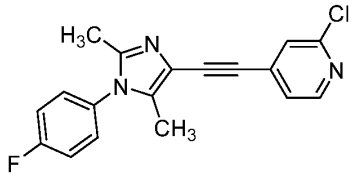
52. The pharmaceutical composition of any one of claims 44-51, wherein the Form A monosulfate salt is characterized by the following XRPD peaks obtained with a $Cu_{K\alpha}$ radiation at

2θ (2 Theta): 9.8±0.2°, 13.4±0.2°, 14.2±0.2°, 18.1±0.2°, 18.9±0.2°, 19.6±0.2°, 22.6±0.2°, 22.9±0.2°, 25.7±0.2°, 27.1±0.2°, and 29.9±0.2°.

53. The pharmaceutical composition of any one of claims 44-52, wherein the Form A monosulfate salt has an XRPD pattern as substantially shown below:



54. A method of preparing a matrix pellet comprising a crystalline anhydrate form (Form A) of a monosulfate salt of a compound of Formula I:



(I),

the method comprising:

granulating the Form A monosulfate salt and one or more polymers with purified water to form a mixture;

extruding, spheronizing, drying, and sieving the mixture to afford a solid material; and

blending the solid material with another pharmaceutical excipient to afford a matrix pellet.

55. The method of claim 54, further comprising filling the matrix pellet into a capsule to form a matrix pellet capsule.

56. The method of claim 54 or 55, wherein the Form A monosulfate salt has a particle size (Dv50) of less than about 100 µm.

57. The method of any one of claims 54-56, wherein the Form A monosulfate salt has a particle size (Dv50) of less than 47 µm.

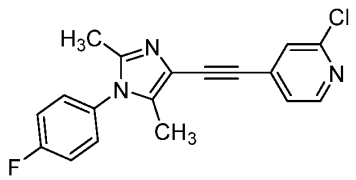
58. The method of any one of claims 54-56, wherein the Form A monosulfate salt has a particle size (Dv50) of about 10 µm or less.

59. The method of any one of claims 54-58, wherein the one or more polymers are selected from the group consisting of a cellulose, methacrylic acid copolymer, and hypromellose.

60. The method of any one of claims 54-59, wherein the other pharmaceutical excipient comprises talc.

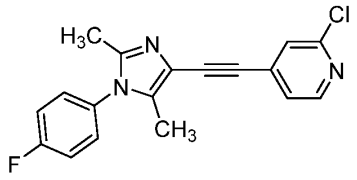
61. A method of treating tuberous sclerosis complex, comprising administering to a subject in need thereof a pharmaceutical composition of any one of claims 44-53.

62. A method of treating tuberous sclerosis complex, comprising administering to a subject in need thereof a composition comprising a therapeutically effective amount of an mGlu5 negative allosteric modulator (NAM), or a pharmaceutically acceptable salt thereof, wherein the mGlu5 NAM is a compound of Formula I:



(I).

63. A method of treating tuberous sclerosis complex, comprising administering to a subject in need thereof a composition comprising a therapeutically effective amount of an mGlu5 negative allosteric modulator (NAM), or a pharmaceutically acceptable salt thereof, wherein the mGlu5 NAM is a compound of Formula I:

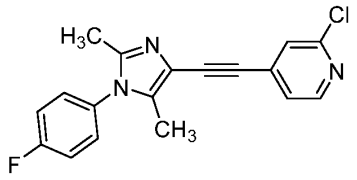


(I),

wherein administering comprises administering the compound of Formula I, or a pharmaceutically acceptable salt thereof, in an amount of about 1.5 mg to about 3.5 mg once daily.

64. The method of claim 63, wherein the subject has a weight of at least 40 kg.

65. A method of treating tuberous sclerosis complex, comprising administering to a subject in need thereof a composition comprising a therapeutically effective amount of an mGlu5 negative allosteric modulator (NAM), or a pharmaceutically acceptable salt thereof, wherein the mGlu5 NAM is a compound of Formula I:



(I),

wherein administering comprises administering the compound of Formula I, or a pharmaceutically acceptable salt thereof, in an amount of about 1.0 mg to about 3.0 mg once daily.

66. The method of claim 65, wherein the subject has a weight of less than 40 kg.