[0001b] In another aspect, the present disclosure refers to a therapeutic or prophylactic composition comprising a crystalline salt or co-crystal disclosed herein.

[0001c] In yet another aspect, the present disclosure refers to a use of a crystalline salt or co-crystal or a composition disclosed herein, in the manufacture of a medicament for treating a condition or a disorder in a subject in need thereof, wherein the condition or disorder is selected from: pain, anxiety, epilepsies, muscle spasms, pruritus, itch, cognitive impairment, alcohol dependence, drug addition, schizophrenia, depression, autism, panic disorder, and generalized anxiety disorder.

[0001d] In a further aspect, the present disclosure refers to a crystalline salt or co-crystal or a composition disclosed herein, for use in therapy.

[0001e] In another aspect, the present disclosure refers to a method for preparing a crystalline salt or co-crystal of 2',6-difluoro-5'-[3-(1-hydroxy-1-methylethyl)-imidazo[1,2-b][1,2,4]triazin-7-yl]biphenyl-2-carbonitrile with phosphoric acid, the method comprising

crystallizing 2',6-difluoro-5'-[3-(1-hydroxy-1-methylethyl)-imidazo[1,2-b][1,2,4]triazin-7-yl]biphenyl-2-carbonitrile phosphate from a solution comprising one or more of: ethyl acetate, methyl ethyl ketone, 2-methyl butanone, dimethyl sulfoxide, dimethylformamide, dimethyl acetamide, acetone, water, tetrahydrofuran (THF), 2-methyl-THF, isopropyl acetate (IPAC), acetonitrile, and dichloromethane,

wherein the crystalline salt or co-crystal provides an X-ray Powder Diffraction (XRPD) pattern having characteristic peak locations of at least three values selected from the following: about 6.4, 7.5, 10.2, 12.7, 13.3, 14.5, 16.0, 17.1, 17.4,

CLAIMS

WHAT IS CLAIMED IS:

1. A crystalline salt or co-crystal of 2',6-difluoro-5'-[3-(1-hydroxy-1-methylethyl)-imidazo[1,2-b][1,2,4]triazin-7-yl]biphenyl-2-carbonitrile with phosphoric acid, wherein the crystalline salt or co-crystal has at least one of the following properties:
   (a) an X-ray powder diffraction (XRPD) pattern substantially the same as shown in FIG. 19, when measured using the parameters described in Table 1;
   (b) an XRPD pattern substantially the same as shown in FIG. 1, when measured using the parameters described in Table 1;
   (c) an XRPD pattern having characteristic peak locations of at least three values selected from the following: about 6.4, 7.5, 10.2, 12.7, 13.3, 14.5, 16.0, 17.1, 17.4, 17.9, 18.5, 19.1, 19.7, 20.3, 20.9, 21.5, 22.6, 23.7, 26.2, 26.7, 26.9, 27.5, 28.4, 30.2, and 32.1 ± 0.2 degrees, 2-theta, when measured using the parameters described in Table 1;
   (d) an XRPD pattern having characteristic peak locations of at least three values selected from the following: about 6.4, 7.5, 12.7, 13.3, 17.1, 17.4, 18.5, 19.1, 19.7, 26.7, 30.2, and 32.1 ± 0.2 degrees, 2-Theta, when measured using the parameters described in Table 1;
   (e) a differential scanning calorimetry (DSC) thermogram substantially the same as shown in FIG. 2A;
   (f) a DSC thermogram with an endothermic peak at about 205°C;
   (g) stable for at least a week at about 40° C; and
   (h) stable for at least a week at about 25° C.
2. The crystalline salt or co-crystal of claim 1, wherein the crystalline salt or co-crystal provides an XRPD pattern substantially the same as shown in FIG. 19, when measured using the parameters described in Table 1.
3. The crystalline salt or co-crystal of claim 1, wherein the crystalline salt or co-crystal provides an XRPD pattern substantially the same as shown in FIG. 1, when measured using the parameters described in Table 1.
4. The crystalline salt or co-crystal of claim 1, wherein the crystalline salt or co-crystal provides an XRPD pattern having characteristic peak locations of at least three values selected from the following: about 6.4, 7.5, 10.2, 12.7, 13.3, 14.5, 16.0, 17.1, 17.4, 17.9,

18.5, 19.1, 19.7, 20.3, 20.9, 21.5, 22.6, 23.7, 26.2, 26.7, 26.9, 27.5, 28.4, 30.2, and 32.1 ± 0.2 degrees, 2-theta, when measured using the parameters described in Table 1.

5. The crystalline salt or co-crystal of claim 1, wherein the crystalline salt or co-crystal provides an XRPD pattern having characteristic peak locations of at least six values selected from the following: about 6.4, 7.5, 10.2, 12.7, 13.3, 14.5, 16.0, 17.1, 17.4, 17.9, 18.5, 19.1, 19.7, 20.3, 20.9, 21.5, 22.6, 23.7, 26.2, 26.7, 26.9, 27.5, 28.4, 30.2, and 32.1 ± 0.2 degrees, 2-theta, when measured using the parameters described in Table 1.

6. The crystalline salt or co-crystal of claim 1, wherein the crystalline salt or co-crystal provides an XRPD pattern having characteristic peak locations of at least three values selected from the following: about 6.4, 7.5, 12.7, 13.3, 17.1, 17.4, 18.5, 19.1, 19.7, 26.7, 30.2, and 32.1 ± 0.2 degrees, 2-Theta, when measured using the parameters described in Table 1.

7. The crystalline salt or co-crystal of claim 1, wherein the crystalline salt or co-crystal provides a DSC thermogram substantially the same as shown in FIG. 2A.

8. The crystalline salt or co-crystal of claim 1, wherein the crystalline salt or co-crystal provides a DSC thermogram with an endothermic peak at about 205°C.

9. The crystalline salt or co-crystal of claim 1, wherein the crystalline salt or co-crystal is stable for at least a month at about 40° C.

10. The crystalline salt or co-crystal of claim 1, wherein the crystalline salt or co-crystal is stable for at least a month at about 25° C.

11. The crystalline salt or co-crystal of claim 1, wherein the crystalline salt or co-crystal provides substantially the same XRPD pattern post-storage at 40° C and 75% RH for at least a week.

12. The crystalline salt or co-crystal of claim 1, wherein the crystalline salt or co-crystal provides substantially the same XRPD pattern post-storage at 40° C and 75% RH for at least two weeks.

13. The crystalline salt or co-crystal of claim 1, wherein the crystalline salt or co-crystal is a salt.

14. The crystalline salt or co-crystal of claim 1, wherein the crystalline salt or co-crystal is a co-crystal.

15. A therapeutic or prophylactic composition comprising a crystalline salt or co-crystal according to any one of claims 1-14.

16. Use of a crystalline salt or co-crystal according to any one of claims 1-14 or a composition according to claim 15, in the manufacture of a medicament for treating a condition or a disorder in a subject in need thereof, wherein the condition or disorder is

selected from: pain, anxiety, epilepsies, muscle spasms, pruritus, itch, cognitive impairment, alcohol dependence, drug addition, schizophrenia, depression, autism, panic disorder, and generalized anxiety disorder.

17. The use of claim 16, wherein the condition or disorder is pain.

18. The use of claim 17, wherein the pain is Fibromyalgia, Inflammatory pain, Neuropathic pain, Peripheral Diabetic Neuropathy, Chemotherapy induced pain, HIV associated Neuropathy, Post-herpetic neuralgia, Musculoskeletal pain, Rheumatoid arthritis, Osteoarthritis, Post-operative pain, Burn pain, Sunburn pain, or Phantom limb pain.

19. The use of claim 16, wherein the condition or disorder is itch.

20. The use of claim 19, wherein the itch is Chronic Itch, Neurogenic itch, Uremic Pruritus, Neurodermatitis, Notalgia Paresthetica, Atopic Dermatitis, Prurigo Nodularis, Psoriasis, Psychogenic itch or Aquagenic Itch.

21. The use of claim 16, wherein the condition or disorder is epilepsy.

22. The use of claim 21, wherein the epilepsy is Focal epilepsy, Generalized epilepsy, Dravet Syndrome, Childhood absence epilepsy (CAE), Juvenile absence epilepsy, Juvenile myoclonic epilepsy (JME), West Syndrome, Lennox-Gastaut syndrome (LGS), Sunflower Syndrome, Staticus epilepticus, Nerve agent induced seizures, Tremors from alcohol withdrawl, Traumatic Brain Injury, Tuberous Sclerosis Complex, Doose Syndrome, Rasmussen's Syndrome, Early myoclonic encephalopathy, Malignant migrating partial seizures of infancy, Epilepsy with continuous spike and waves during slow wave sleep, Landau-Kleffner syndrome, Benign epilepsy with centrotemporal spikes, Benign familial neonatal infantile seizures, Cortical dysplasia focal epilepsy syndrome, Generalized epilepsy with febrile seizure plus (GEFS+), Myoclonic atonic epilepsy, Malignant migrating partial seizures of infancy, Ohtahara syndrome (a.k.a. early infantile epileptic encephalopathy), or Partial epilepsy and febrile seizures plus.

23. The use of claim 16, wherein the condition or disorder is autism.

24. The use of claim 23, wherein the autism is an autism resulting from SCN2a mutation, fragile X syndrome, or autism related to ion-channel dysfunction.

25. A crystalline salt or co-crystal according to any one of claims 1-14 or a composition according to claim 15, for use in therapy.

26. A method for preparing a crystalline salt or co-crystal of 2',6-difluoro-5'-[3-(1-hydroxy-1-methylethyl)-imidazo[1,2-b][1,2,4]triazin-7-yl]biphenyl-2-carbonitrile with phosphoric acid, the method comprising

crystallizing 2',6-difluoro-5'-[3-(1-hydroxy-1-methylethyl)-imidazo[1,2-b][1,2,4]triazin-7-yl]biphenyl-2-carbonitrile phosphate from a solution comprising one

or more of: ethyl acetate, methyl ethyl ketone, 2-methyl butanone, dimethyl sulfoxide, dimethylformamide, dimethyl acetamide, acetone, water, tetrahydrofuran (THF), 2-methyl-THF, isopropyl acetate (IPAC), acetonitrile, and dichloromethane,

wherein the crystalline salt or co-crystal provides an X-ray Powder Diffraction (XRPD) pattern having characteristic peak locations of at least three values selected from the following: about 6.4, 7.5, 10.2, 12.7, 13.3, 14.5, 16.0, 17.1, 17.4, 17.9, 18.5, 19.1, 19.7, 20.3, 20.9, 21.5, 22.6, 23.7, 26.2, 26.7, 26.9, 27.5, 28.4, 30.2, and 32.1 ± 0.2 degrees, 2-theta, when measured using the parameters described in Table 1.

27. The method of claim 26, wherein the crystalline salt or co-crystal provides an XRPD pattern having characteristic peak locations of at least three values selected from the following: about 6.4, 7.5, 12.7, 13.3, 17.1, 17.4, 18.5, 19.1, 19.7, 26.7, 30.2, and 32.1 ± 0.2 degrees, 2-Theta, when measured using the parameters described in Table 1.

28. The method of claim 26 or 27, wherein the crystalline salt or co-crystal provides an XRPD pattern substantially the same as shown in FIG. 19, when measured using the parameters described in Table 1.