

FORMS OF UREA DERIVATIVES AND RELATED USES**RELATED APPLICATION**

[001] This application claims priority to, and the benefit of, U.S. Provisional Patent Application No. 63/600,104 filed November 17, 2023, the entire content of which is hereby incorporated by reference.

BACKGROUND

[002] Autoimmune diseases are associated with the overproduction of proinflammatory factors. One of them is interleukin-1 (IL-1), produced by activated macrophages, monocytes, fibroblasts, and other components of the innate immune system like dendritic cells. IL-1 is involved in a variety of cellular activities, including cell proliferation, differentiation and apoptosis (Masters, S. L., et. al., Annu. Rev. Immunol. 2009. 27:621–68).

[003] In humans, 22 NLR proteins are divided into four NLR subfamilies according to their N-terminal domains. NLRA contains a CARD-AT domain, NLRB (NAIP) contains a BIR domain, NLRC (including NOD1 and NOD2) contains a CARD domain, and NLRP contains a pyrin domain. Multiple NLR family members are associated with inflammasome formation.

[004] Although inflammasome activation appears to have evolved as an important component of host immunity to pathogens, the NLRP3 inflammasome is unique in its ability to activate in response to endogenous sterile danger signals. Many such sterile signals have been elucidated, and their formation is associated with specific disease states. For example, uric acid crystals found in gout patients are effective triggers of NLRP3 activation. Similarly, cholesterol crystals found in atherosclerotic patients can also promote NLRP3 activation. Recognition of the role of sterile danger signals as NLRP3 activators led to IL-1 and IL-18 being implicated in a diverse range of pathophysiological indications including metabolic, physiologic, inflammatory, hematologic, and immunologic disorders.

[005] The disclosure arises from a need to provide further compounds for the specific modulation of NLRP3-dependent cellular processes. In particular, compounds with improved physicochemical, pharmacological, and pharmaceutical properties to existing compounds are desirable.

SUMMARY

[006] In some aspects, the present disclosure provides a morphic form of Compound A.

[007] In some aspects, the morphic form of Compound A is amorphous.

- [008] In some aspects, the morphic form of Compound A is a crystalline form.
- [009] In some aspects, the morphic form of Compound A is an anhydrous form.
- [010] In some aspects, the morphic form of Compound A is a dihydrate.
- [011] In some aspects, the morphic form of Compound A is a monohydrate.
- [012] In some aspects, the morphic form of Compound A is solvated.
- [013] In some aspects, the morphic form of Compound A is non-solvated.
- [014] In some aspects, the morphic form of Compound A is an anhydrous Form 1.
- [015] In some aspects, the morphic form of Compound A is a dihydrate Form 2.
- [016] In some aspects, the morphic form of Compound A is a monohydrate Form 3.
- [017] In some aspects, the morphic form of Compound A is crystalline having Form 4.
- [018] In some aspects, the morphic form of Compound A is crystalline having Form 5.
- [019] In some aspects, the morphic form of Compound A is crystalline having Form 6.
- [020] In some aspects, the morphic form of Compound A is crystalline having Form 7.
- [021] In some aspects, the morphic form of Compound A is crystalline having Form 8.
- [022] In some aspects, the morphic form of Compound A is an anhydrous Form 9.
- [023] In some aspects, the morphic form of Compound A is an anhydrous Form 10.
- [024] In some aspects, the morphic form of Compound A is an anhydrous Form 12.
- [025] In some aspects, the present disclosure provides a method of preparing a morphic form of Compound A described herein.
- [026] In some aspects, the present disclosure provides a pharmaceutical composition comprising a morphic form of Compound A as described herein, and one or more pharmaceutically acceptable carriers or excipients.
- [027] In some aspects, the present disclosure provides a method of inhibiting inflammasome (e.g., the NLRP3 inflammasome) activity (e.g., *in vitro* or *in vivo*), comprising contacting a cell with an effective amount of a morphic form of Compound A.
- [028] In some aspects, the present disclosure provides a method of treating or preventing a disease or disorder disclosed herein in a subject in need thereof, comprising administering to the subject an effective amount of a morphic form of Compound A.
- [029] In some aspects, the present disclosure provides a morphic form of Compound A for use in inhibiting inflammasome (e.g., the NLRP3 inflammasome) activity (e.g., *in vitro* or *in vivo*).
- [030] In some aspects, the present disclosure provides a morphic form of Compound A for use in treating or preventing a disease or disorder disclosed herein.

[031] In some aspects, the present disclosure provides use of a morphic form of Compound A in the manufacture of a medicament for inhibiting inflammasome (e.g., the NLRP3 inflammasome) activity (e.g., *in vitro* or *in vivo*).

[032] In some aspects, the present disclosure provides use of a morphic form of Compound A in the manufacture of a medicament for treating or preventing a disease or disorder disclosed herein.

[033] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. In the specification, the singular forms also include the plural unless the context clearly dictates otherwise. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present disclosure, suitable methods and materials are described below. All publications, patent applications, patents and other references mentioned herein are incorporated by reference. The references cited herein are not admitted to be prior art to the claimed invention. In the case of conflict, the present specification, including definitions, will control. In addition, the materials, methods and examples are illustrative only and are not intended to be limiting. In the case of conflict between the chemical structures and names of the compounds disclosed herein, the chemical structures will control.

[034] Other features and advantages of the disclosure will be apparent from the following detailed description and claims.

BRIEF DESCRIPTION OF THE FIGURES

[035] FIG. 1 is the solid form diagram of solid forms of Compound A.

[036] FIG. 2 depicts the XRPD diffractogram for Form 1.

[037] FIG. 3 depicts the DSC thermogram for Form 1.

[038] FIG. 4 depicts the XRPD diffractogram for Form 2 dihydrate.

[039] FIG. 5 depicts the ¹H-NMR spectrum for Form 2 dihydrate.

[040] FIG. 6 depicts the TGA and DSC overlay for Form 2 dihydrate.

[041] FIG. 7 depicts the GVS isotherm plot for Form 2 dihydrate.

[042] FIG. 8 depicts the GVS kinetic plot for Form 2 dihydrate.

[043] FIG. 9 depicts the SEM image for Form 2 dihydrate.

[044] FIG. 10 depicts the XRPD diffractogram for Form 3 monohydrate.

[045] FIG. 11 depicts the ¹H-NMR spectrum for Form 3 monohydrate.

[046] FIG. 12 depicts the TGA and DSC overlay for Form 3 monohydrate.

- [047] FIG. 13 depicts the GVS isotherm plot for Form 3 monohydrate.
- [048] FIG. 14 depicts the GVS kinetic plot for Form 3 monohydrate.
- [049] FIG. 15 depicts the SEM image for Form 3 monohydrate.
- [050] FIG. 16 depicts the ^1H -NMR spectrum for Form 4.
- [051] FIG. 17 depicts the DSC thermogram for Form 4.
- [052] FIG. 18 depicts the ^1H -NMR spectrum for Form 6.
- [053] FIG. 19 depicts the DSC thermogram for Form 6.
- [054] FIG. 20 depicts the XRPD overlay for Form 6, after 7 days at 40 °C/75% RH.
- [055] FIG. 21 depicts the ^1H -NMR spectrum for Form 7.
- [056] FIG. 22 depicts the DSC thermogram for Form 7.
- [057] FIG. 23 depicts the ^1H -NMR spectrum for Form 8.
- [058] FIG. 24 depicts the DSC thermogram for Form 8.
- [059] FIG. 25 depicts the XRPD diffractogram for anhydrous Form 9.
- [060] FIG. 26 depicts the heat-cool-heat DSC thermogram showing second heat ramp following dehydration of Form 3 during heat ramp one into Form 9.
- [061] FIG. 27 depicts the XRPD diffractogram for anhydrous Form 10.
- [062] FIG. 28 depicts the DSC thermogram of anhydrous Form 10.
- [063] FIG. 29 depicts the flow diagram for treatment of solubility assessment of Compound A at 50 °C.
- [064] FIG. 30 depicts the flow diagram for treatment of solubility assessment of Compound A at 5 °C.
- [065] FIG. 31 depicts overlayed XRPD diffractograms of Forms 4, 5 and 6 obtained from solubility assessment.
- [066] FIG. 32 depicts a simulated XRPD pattern of Compound A monohydrate, Form 3 (100(2) K).
- [067] FIG. 33 depicts an overlay of simulated diffractogram with experimental Compound A monohydrate, Form 3.
- [068] FIG. 34A depicts the XRPD diffractogram for anhydrous Form 12.
- [069] FIG. 34B depicts the XRPD diffractogram for anhydrous Form 12 (upper trace) compared to XRPD diffractogram for Form 3 monohydrate (lower trace).
- [070] FIG. 35 depicts the TGA and DSC overlay for anhydrous Form 12.
- [071] FIG. 36 depicts the DVS plot for anhydrous Form 12 at 25 °C.
- [072] FIG. 37 depicts the DVS plot for anhydrous Form 12 at varying humidity (sorption isotherm).

[073] FIGs. 38A and 38B depict the optical microscopy images of anhydrous Form 12.

[074] FIG. 39 depicts an overlay of XRPD diffractograms of Form 3 monohydrate and anhydrous Form 12 obtained at 25 °C during competitive slurry study.

[075] FIG. 40 depicts an overlay of XRPD diffractograms of Form 3 monohydrate and anhydrous Form 12 obtained at 50 °C during competitive slurry study.

DETAILED DESCRIPTION

[076] Autoimmune diseases are associated with the overproduction of pro-inflammatory factors. One of them is interleukin-1 (IL-1), produced by activated macrophages, monocytes, fibroblasts, and other components of the innate immune system like dendritic cells, involved in a variety of cellular activities, including cell proliferation, differentiation, and apoptosis (Masters, S. L., et al. *Annu. Rev. Immunol.* 2009. 27:621–68).

[077] Cytokines from the IL-1 family are highly active and, as important mediators of inflammation, primarily associated with acute and chronic inflammation (Sims, J. et al., *Nature Reviews Immunology* 10, 89-102 (February 2010)). The overproduction of IL-1 is considered to be a mediator of some autoimmune and autoinflammatory diseases. Autoinflammatory diseases are characterised by recurrent and unprovoked inflammation in the absence of autoantibodies, infection, or antigen-specific T lymphocytes.

[078] Pro-inflammatory cytokines of the IL-1 superfamily include IL-1 α , IL-1 β , IL-18, and IL-36 α , β , λ and are produced in response to pathogens and other cellular stressors as part of a host innate immune response. Unlike many other secreted cytokines, which are processed and released via the standard cellular secretory apparatus consisting of the endoplasmic reticulum and Golgi apparatus, IL-1 family members lack leader sequences required for endoplasmic reticulum entry and thus are retained intracellularly following translation. In addition, IL-1 β , IL-18, and IL-36 α , β , λ are synthesised as procytokines that require proteolytic activation to become optimal ligands for binding to their cognate receptors on target cells.

[079] In the case of IL-1 α , IL-1 β and IL-18, it is now appreciated that a multimeric protein complex known as an inflammasome is responsible for activating the proforms of IL-1 β and IL-18 and for release of these cytokines extracellularly. An inflammasome complex typically consists of a sensor molecule, such as an NLR (Nucleotide-Oligomerisation Domain (NOD)-like receptor), an adaptor molecule ASC (Apoptosis-associated speck-like protein containing a CARD (Caspase Recruitment Domain)) and procaspase-1. In response to a variety of “danger signals”, including pathogen-associated molecule patterns (PAMPs) and danger

associated molecular patterns (DAMPs), subunits of an inflammasome oligomerise to form a supramolecular structure within the cell. PAMPs include molecules such as peptidoglycan, viral DNA or RNA and bacterial DNA or RNA. DAMPs, on the other hand, consist of a wide range of endogenous or exogenous sterile triggers including monosodium urate crystals, silica, alum, asbestos, fatty acids, ceramides, cholesterol crystals and aggregates of beta-amyloid peptide. Assembly of an inflammasome platform facilitates autocatalysis of procaspase-1 yielding a highly active cysteine protease responsible for activation and release of pro-IL-1 β and pro-IL-18. Thus, release of these highly inflammatory cytokines is achieved only in response to inflammasome sensors detecting and responding to specific molecular danger signals.

[080] In humans, 22 NLR proteins are divided into four NLR subfamilies according to their N-terminal domains. NLRA contains a CARD-AT domain, NLRB (NAIP) contains a BIR domain, NLRC (including NOD1 and NOD2) contains a CARD domain, and NLRP contains a pyrin domain. Multiple NLR family members are associated with inflammasome formation including NLRP1, NLRP3, NLRP6, NLRP7, NLRP12 and NLRC4 (IPAF).

[081] Two other structurally distinct inflammasome structures containing a PYHIN domain (pyrin and HIN domain containing protein) namely Absent in Melanoma 2 (AIM2) and IFN λ -inducible protein 16 (IFI16) (Latz et al., Nat Rev Immunol 2013 13(6) 397-311) serve as intracellular DNA sensors. Pyrin (encoded by the MEFV gene) represents another type of inflammasome platform associated with proIL-1 β activation (Chae et al., Immunity 34, 755-768, 2011).

[082] Requiring assembly of an inflammasome platform to achieve activation and release of IL-1 β and IL-18 from monocytes and macrophages ensures their production is carefully orchestrated via a 2-step process. First, the cell must encounter a priming ligand (such as the TLR4 receptor ligand LPS, or an inflammatory cytokine such as TNF α) which leads to NF κ B dependent transcription of NLRP3, pro-IL-1 β and pro-IL-18. The newly translated procytokines remain intracellular and inactive unless producing cells encounter a second signal leading to activation of an inflammasome scaffold and maturation of procaspase-1.

[083] In addition to proteolytic activation of pro-IL-1 β and pro-IL-18, active caspase-1 also triggers a form of inflammatory cell death known as pyroptosis through cleavage of gasdermin-D. Pyroptosis allows the mature forms of IL-1 β and IL-18 to be externalised along with release of alarmin molecules (compounds that promote inflammation and activate innate and adaptive immunity) such as high mobility group box 1 protein (HMGB1), IL-33, and IL-1 α .

[084] Although inflammasome activation appears to have evolved as an important component of host immunity to pathogens, the NLRP3 inflammasome is unique in its ability activate in response to endogenous and exogenous sterile danger signals. Many such sterile signals have been elucidated, and their formation is associated with specific disease states. For example, uric acid crystals found in gout patients are effective triggers of NLRP3 activation. Similarly, cholesterol crystals found in atherosclerotic patients can also promote NLRP3 activation. Recognition of the role of sterile danger signals as NLRP3 activators led to IL-1 β and IL-18 being implicated in a diverse range of pathophysiological indications including metabolic, physiologic, inflammatory, hematologic and immunologic disorders.

[085] A link to human disease is best exemplified by discovery that mutations in the NLRP3 gene which lead to gain-of-function confer a range of autoinflammatory conditions collectively known as cryopyrin-associated periodic syndromes (CAPS) including familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS) and Neonatal onset multisystem inflammatory disease (NOMID) (Hoffman et al., Nat. Genet. 29(3) (2001) 301-305). Likewise, sterile mediator-induced activation of NLRP3 has been implicated in a wide range of disorders including joint degeneration (gout, rheumatoid arthritis, osteoarthritis), cardiometabolic (type 2 diabetes, atherosclerosis, hypertension), Central Nervous System (Alzheimer's Disease, Parkinson's disease, multiple sclerosis), gastrointestinal (Crohn's disease, ulcerative colitis), lung (chronic obstructive pulmonary disease (COPD), asthma, idiopathic pulmonary fibrosis) and liver (fibrosis, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis (NASH)). It is further believed that NLRP3 activation promotes kidney inflammation and thus contributes to chronic kidney disease (CKD).

[086] Current treatment options for diseases where IL-1 is implicated as a contributor to pathogenesis include the IL-1 receptor antagonist anakinra, an Fc-containing fusion construct of the extracellular domains of the IL-1 receptor and IL-1 receptor accessory protein (riloncept) and the anti-IL-1 β monoclonal antibody canakinumab. For example, canakinumab is licensed for CAPS, Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), Familial Mediterranean Fever (FMF) and gout.

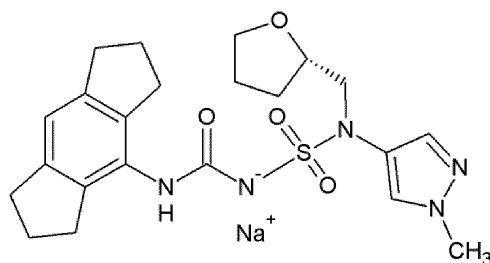
[087] Some small molecules have been reported to inhibit function of the NLRP3 inflammasome. Glyburide, for example, is a specific inhibitor of NLRP3 activation, albeit at micromolar concentrations which are unlikely attainable *in vivo*. Non-specific agents such as parthenolide, Bay 11-7082, and 3,4-methylenedioxy- β -nitrostyrene are reported to impair

NLRP3 activation but are expected to possess limited therapeutic utility due to their sharing of a common structural feature consisting of an olefin activated by substitution with an electron withdrawing group; this can lead to undesirable formation of covalent adducts with protein-bearing thiol groups. A number of natural products, for example β -hydroxybutyrate, sulforaphane, quercetin, and salvianolic acid, also are reported to suppress NLRP3 activation. Likewise, numerous effectors/modulators of other molecular targets have been reported to impair NLRP3 activation including agonists of the G-protein coupled receptor TGR5, an inhibitor of sodium-glucose co-transport epigliflozin, the dopamine receptor antagonist A-68930, the serotonin reuptake inhibitor fluoxetine, fenamate non-steroidal anti-inflammatory drugs, and the β -adrenergic receptor blocker nebivolol. Utility of these molecules as therapeutics for the chronic treatment of NLRP3-dependent inflammatory disorders remains to be established.

[088] The disclosure relates to compounds useful for the specific modulation of NLRP3-dependent cellular processes. In particular, compounds with improved physicochemical, pharmacological and pharmaceutical properties to existing NLRP3-modulating compounds are desired.

Morphic Forms of the Present Disclosure

[089] It is understood that “Compound A” as used herein, refers to a compound with the structure shown below:



Molecular Formula: $C_{22}H_{28}N_5NaO_4S$

Formula Weight: 481.543589

(Compound A).

[090] It is understood that the chemical name of Compound A is Sodium [(1,2,3,5,6,7-hexahydro-s-indacen-4-yl)carbamoyl][(1-methyl-1H-pyrazol-4-yl)((2S)-oxolan-2-yl)methyl)sulfamoyl]azanide; 1-(1,2,3,5,6,7-hexahydro-s-indacen-4-yl)-3-[(1-methyl-1H-pyrazol-4-yl)((2S)-oxolan-2-yl)methyl)sulfamoyl]urea, Sodium salt; or sodium (S)-((1,2,3,5,6,7-hexahydro-s-indacen-4-yl)carbamoyl)(N-(1-methyl-1H-pyrazol-4-yl)-N-((tetrahydrofuran-2-yl)methyl)sulfamoyl)amide. It is understood that Compound A

may be prepared as described in Example 2 in WO2022/051582 (incorporated herein by reference).

[091] In some aspects, the present disclosure provides a morphic form of Compound A.

[092] In some embodiments, the morphic form is a crystalline form of Compound A.

[093] In some aspects, the morphic form of Compound A is amorphous.

[094] In some aspects, the morphic form of Compound A is a crystalline form.

[095] In some aspects, the morphic form of Compound A is an anhydrous form.

[096] In some aspects, the morphic form of Compound A is a dihydrate.

[097] In some aspects, the morphic form of Compound A is a monohydrate.

[098] In some aspects, the morphic form of Compound A is solvated.

[099] In some aspects, the morphic form of Compound A is non-solvated.

[0100] In some aspects, the morphic form of Compound A is an anhydrous Form 1.

[0101] In some aspects, the morphic form of Compound A is a dihydrate Form 2.

[0102] In some aspects, the morphic form of Compound A is a monohydrate Form 3.

[0103] In some aspects, the morphic form of Compound A is crystalline having Form 4.

[0104] In some aspects, the morphic form of Compound A is crystalline having Form 5.

[0105] In some aspects, the morphic form of Compound A is crystalline having Form 6.

[0106] In some aspects, the morphic form of Compound A is crystalline having Form 7.

[0107] In some aspects, the morphic form of Compound A is crystalline having Form 8.

[0108] In some aspects, the morphic form of Compound A is an anhydrous Form 9.

[0109] In some aspects, the morphic form of Compound A is an anhydrous Form 10.

[0110] In some aspects, the morphic form of Compound A is an anhydrous Form 12.

[0111] In some embodiments, the morphic form is Form 1 of Compound A.

[0112] In some embodiments, the morphic form is Form 2 of Compound A.

[0113] In some embodiments, the morphic form is Form 3 of Compound A.

[0114] In some embodiments, the morphic form is Form 4 of Compound A.

[0115] In some embodiments, the morphic form is Form 5 of Compound A.

[0116] In some embodiments, the morphic form is Form 6 of Compound A.

[0117] In some embodiments, the morphic form is Form 7 of Compound A.

[0118] In some embodiments, the morphic form is Form 8 of Compound A.

[0119] In some embodiments, the morphic form is Form 9 of Compound A.

[0120] In some embodiments, the morphic form is Form 10 of Compound A.

[0121] In some embodiments, the morphic form is Form 12 of Compound A.

Form 1

[0122] In some embodiments, the morphic form of Compound A is anhydrous Form 1.

X-Ray Powder Diffraction (XRPD) Characterizations

[0123] In some embodiments, Form 1 of Compound A is characterized by an XRPD pattern comprising signals at 4.5 ± 0.5 , 18.1 ± 0.5 , and 18.3 ± 0.5 °2 θ (e.g., 4.5 ± 0.2 , 18.1 ± 0.2 , and 18.3 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.5 ± 0.1 , 18.1 ± 0.1 , and 18.3 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.5, 18.1, and 18.3 °2 θ using Cu K α radiation))).

[0124] In some embodiments, Form 1 of Compound A is characterized by an XRPD pattern comprising signals at 4.5 ± 0.5 , 18.1 ± 0.5 , 18.3 ± 0.5 , and 22.7 ± 0.5 °2 θ (e.g., 4.5 ± 0.2 , 18.1 ± 0.2 , 18.3 ± 0.2 , and 22.7 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.5 ± 0.1 , 18.1 ± 0.1 , 18.3 ± 0.1 , and 22.7 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.5, 18.1, 18.3, and 22.7 °2 θ using Cu K α radiation))).

[0125] In some embodiments, Form 1 of Compound A is characterized by an XRPD pattern comprising signals at 4.5 ± 0.5 , 18.1 ± 0.5 , 18.3 ± 0.5 , 19.0 ± 0.5 , and 22.7 ± 0.5 °2 θ (e.g., 4.5 ± 0.2 , 18.1 ± 0.2 , 18.3 ± 0.2 , 19.0 ± 0.2 , and 22.7 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.5 ± 0.1 , 18.1 ± 0.1 , 18.3 ± 0.1 , 19.0 ± 0.1 , and 22.7 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.5, 18.1, 18.3, 19.0, and 22.7 °2 θ using Cu K α radiation))).

[0126] In some embodiments, Form 1 of Compound A is characterized by an XRPD pattern comprising signals at 4.5 ± 0.5 , 18.1 ± 0.5 , 18.3 ± 0.5 , 19.0 ± 0.5 , 22.7 ± 0.5 , and 23.4 ± 0.5 °2 θ (e.g., 4.5 ± 0.2 , 18.1 ± 0.2 , 18.3 ± 0.2 , 19.0 ± 0.2 , 22.7 ± 0.2 , and 23.4 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.5 ± 0.1 , 18.1 ± 0.1 , 18.3 ± 0.1 , 19.0 ± 0.1 , 22.7 ± 0.1 , and 23.4 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.5, 18.1, 18.3, 19.0, 22.7, and 23.4 °2 θ using Cu K α radiation))).

[0127] In some embodiments, Form 1 of Compound A is characterized by an XRPD pattern comprising signals at 4.5 ± 0.5 , 13.3 ± 0.5 , 18.1 ± 0.5 , 18.3 ± 0.5 , 19.0 ± 0.5 , 22.7 ± 0.5 , and 23.4 ± 0.5 °2 θ (e.g., 4.5 ± 0.2 , 13.3 ± 0.2 , 18.1 ± 0.2 , 18.3 ± 0.2 , 19.0 ± 0.2 , 22.7 ± 0.2 , and 23.4 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.5 ± 0.1 , 13.3 ± 0.1 , 18.1 ± 0.1 , 18.3 ± 0.1 , 19.0 ± 0.1 , 22.7 ± 0.1 , and 23.4 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.5, 13.3, 18.1, 18.3, 19.0, 22.7, and 23.4 °2 θ using Cu K α radiation))).

[0128] In some embodiments, Form 1 of Compound A is characterized by an XRPD pattern comprising signals at 4.5 ± 0.5 , 13.3 ± 0.5 , 16.2 ± 0.5 , 18.1 ± 0.5 , 18.3 ± 0.5 , 19.0 ± 0.5 , 22.7 ± 0.5 , and 23.4 ± 0.5 °2 θ (e.g., 4.5 ± 0.2 , 13.3 ± 0.2 , 16.2 ± 0.2 , 18.1 ± 0.2 , 18.3 ± 0.2 , 19.0 ± 0.2 , 22.7 ± 0.2 , and 23.4 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.5 ± 0.1 , 13.3 ± 0.1 , 16.2 ± 0.1 , 18.1 ± 0.1 ,

18.3±0.1, 19.0±0.1, 22.7±0.1, and 23.4±0.1°2θ using Cu Kα radiation (e.g., 4.5, 13.3, 16.2, 18.1, 18.3, 19.0, 22.7, and 23.4 °2θ using Cu Kα radiation))).

[0129] In some embodiments, Form 1 of Compound A is characterized by an XRPD pattern having at least one signal selected from 4.5±0.5, 18.1±0.5, and 18.3±0.5 °2θ (e.g., 4.5±0.2, 18.1±0.2, and 18.3±0.2 °2θ using Cu Kα radiation (e.g., 4.5±0.1, 18.1±0.1, and 18.3±0.1 °2θ using Cu Kα radiation (e.g., 4.5, 18.1, and 18.3 °2θ using Cu Kα radiation))).

[0130] In some embodiments, Form 1 of Compound A is characterized by an XRPD pattern having at least two signals selected from 4.5±0.5, 18.1±0.5, and 18.3±0.5 °2θ (e.g., 4.5±0.2, 18.1±0.2, and 18.3±0.2 °2θ using Cu Kα radiation (e.g., 4.5±0.1, 18.1±0.1, and 18.3±0.1 °2θ using Cu Kα radiation (e.g., 4.5, 18.1, and 18.3 °2θ using Cu Kα radiation))).

[0131] In some embodiments, Form 1 of Compound A is characterized by an XRPD pattern having at least three signals selected from 4.5±0.5, 18.1±0.5, 18.3±0.5, and 22.7±0.5 °2θ (e.g., 4.5±0.2, 18.1±0.2, 18.3±0.2, and 22.7±0.2 °2θ using Cu Kα radiation (e.g., 4.5±0.1, 18.1±0.1, 18.3±0.1, and 22.7±0.1 °2θ using Cu Kα radiation (e.g., 4.5, 18.1, 18.3, and 22.7°2θ using Cu Kα radiation))).

[0132] In some embodiments, e.g., Form 1 of Compound A is characterized by an XRPD pattern having at least four signals selected from 4.5±0.5, 18.1±0.5, 18.3±0.5, 19.0±0.5, and 22.7±0.5 °2θ (e.g., 4.5±0.2, 18.1±0.2, 18.3±0.2, 19.0±0.2, and 22.7±0.2 °2θ using Cu Kα radiation (e.g., 4.5±0.1, 18.1±0.1, 18.3±0.1, 19.0±0.1, and 22.7±0.1 °2θ using Cu Kα radiation (e.g., 4.5, 18.1, 18.3, 19.0, and 22.7 °2θ using Cu Kα radiation))).

[0133] In some embodiments, Form 1 of Compound A is characterized by an XRPD pattern having at least five signals selected from 4.5±0.5, 18.1±0.5, 18.3±0.5, 19.0±0.5, 22.7±0.5, and 23.4±0.5 °2θ (e.g., 4.5±0.2, 18.1±0.2, 18.3±0.2, 19.0±0.2, 22.7±0.2, and 23.4±0.2 °2θ using Cu Kα radiation (e.g., 4.5±0.1, 18.1±0.1, 18.3±0.1, 19.0±0.1, 22.7±0.1, and 23.4±0.1 °2θ using Cu Kα radiation (e.g., 4.5, 18.1, 18.3, 19.0, 22.7, and 23.4 °2θ using Cu Kα radiation))).

[0134] In some embodiments, Form 1 of Compound A is characterized by an XRPD pattern having at least five signals selected from 4.5±0.5, 13.3±0.5, 18.1±0.5, 18.3±0.5, 19.0±0.5, 22.7±0.5, and 23.4±0.5 °2θ (e.g., 4.5±0.2, 13.3±0.2, 18.1±0.2, 18.3±0.2, 19.0±0.2, 22.7±0.2, and 23.4±0.2 °2θ using Cu Kα radiation (e.g., 4.5±0.1, 13.3±0.1, 18.1±0.1, 18.3±0.1, 19.0±0.1, 22.7±0.1, and 23.4±0.1 °2θ using Cu Kα radiation (e.g., 4.5, 13.3, 18.1, 18.3, 19.0, 22.7, and 23.4 °2θ using Cu Kα radiation))).

[0135] In some embodiments, Form 1 of Compound A is characterized by an XRPD pattern comprising one or more signals as described in Table 1 below.

[0136] In some embodiments, Form 1 of Compound A is characterized by an XRPD pattern comprising two or more signals as described in Table 1 below.

[0137] In some embodiments, Form 1 of Compound A is characterized by an XRPD pattern comprising three or more signals as described in Table 1 below.

[0138] In some embodiments, Form 1 of Compound A is characterized by an XRPD pattern comprising four or more signals as described in Table 1 below.

Table 1 XRPD Signals for anhydrous Form 1

Angle (2 θ °)	Intensity (%)	Angle (2 θ °)	Intensity (%)
4.5	100.0	23.2	6.8
8.6	8.9	23.4	9.8
9.2	9.2	24.0	4.6
10.2	5.0	24.2	7.8
11.7	5.3	24.4	5.6
13.3	9.7	25.9	5.3
13.6	5.4	26.3	1.7
15.1	4.5	26.8	5.6
15.6	1.5	27.3	8.1
16.2	9.7	27.6	2.5
16.3	6.6	28.1	1.6
17.2	2.6	28.5	2.5
18.1	33.3	29.7	2.0
18.3	24.1	30.5	3.8
19.0	10.2	32.0	5.3
21.0	2.9	32.4	2.8
22.7	10.8		

*The values shown in the above table are approximate value and subject to instrument differentiation and standard error.

[0139] In some embodiments, Form 1 of Compound A is characterized by an XRPD pattern substantially similar to that set forth in FIG. 2.

Thermal Gravimetric Analysis (TGA) Characterization

[0140] In some embodiments, Form 1 of Compound A is characterized by a degradation event up to 190 $\pm$ 40 °C, 190 $\pm$ 30 °C, 190 $\pm$ 20 °C, 190 $\pm$ 15 °C, 190 $\pm$ 10 °C, or 190 $\pm$ 5 °C (e.g., up to about 190 °C), as measured by TGA.

Differential Scanning Calorimetry (DSC) Characterizations

[0141] In some embodiments, Form 1 of Compound A is characterized by an endothermic event up to 75 ± 20 °C, 75 ± 15 °C, 75 ± 10 °C, or 75 ± 5 °C (e.g., about 75°C), as measured by DSC.

[0142] In some embodiments, Form 1 of Compound A is characterized by an endothermic event with an onset at 146 ± 20 °C, 146 ± 15 °C, 146 ± 10 °C, or 146 ± 5 °C (e.g., about 146°C), as measured by DSC.

Other Characterizations

[0143] In some embodiments, Form 1 of Compound A is characterized by a water uptake (e.g., from 0 % to 40 % RH) of about 1 %, about 0.9 %, about 0.8 %, about 0.7 %, about 0.6 %, about 0.5 %, about 0.4 %, about 0.3 %, about 0.2 %, or less than about 0.1 %, as measured by gravimetric vapor sorption (GVS).

[0144] In some embodiments, Form 1 of Compound A is a crystalline solid.

[0145] In some embodiments, Form 1 hydrates under ambient conditions.

[0146] In some embodiments, Form 1 is obtained from heating Form 2 above 100 °C.

[0147] In some embodiments, Form 1 is obtained from dehydrating Form 2 at 0% RH.

[0148] In some embodiments, Form 1 hydrates to Form 2 under ambient conditions.

[0149] In some embodiments, Form 1 is formed when Form 2 is heated at 100 °C at 0% RH.

Form 2

[0150] In some embodiments, the morphic form of Compound A is dihydrate Form 2.

X-Ray Powder Diffraction (XRPD) Characterizations

[0151] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern comprising signals at 4.2 ± 0.5 , 16.7 ± 0.5 , and 16.8 ± 0.5 °2 θ (e.g., 4.2 ± 0.2 , 16.7 ± 0.2 , and 16.8 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.2 ± 0.1 , 16.7 ± 0.1 , and 16.8 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.2, 16.7, and 16.8 °2 θ using Cu K α radiation))).

[0152] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern comprising signals at 4.2 ± 0.5 , 16.7 ± 0.5 , 16.8 ± 0.5 , and 18.2 ± 0.5 °2 θ (e.g., 4.2 ± 0.2 , 16.7 ± 0.2 , 16.8 ± 0.2 , and 18.2 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.2 ± 0.1 , 16.7 ± 0.1 , 16.8 ± 0.1 , and 18.2 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.2, 16.7, 16.8, and 18.2 °2 θ using Cu K α radiation))).

[0153] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern comprising signals at 4.2 ± 0.5 , 10.4 ± 0.5 , 16.7 ± 0.5 , 16.8 ± 0.5 , and 18.2 ± 0.5 °2 θ (e.g., 4.2 ± 0.2 , 10.4 ± 0.2 , 16.7 ± 0.2 , 16.8 ± 0.2 , and 18.2 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.2 ± 0.1 , 10.4 ± 0.1 , 16.7 ± 0.1 , 16.8 ± 0.1 , and 18.2 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.2, 10.4, 16.7, 16.8, and 18.2 °2 θ using Cu K α radiation))).

[0154] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern comprising signals at 4.2 ± 0.5 , 8.4 ± 0.5 , 10.4 ± 0.5 , 16.7 ± 0.5 , 16.8 ± 0.5 , and 18.2 ± 0.5 °2 θ (e.g., 4.2 ± 0.2 , 8.4 ± 0.2 , 10.4 ± 0.2 , 16.7 ± 0.2 , 16.8 ± 0.2 , and 18.2 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.2 ± 0.1 , 8.4 ± 0.1 , 10.4 ± 0.1 , 16.7 ± 0.1 , 16.8 ± 0.1 , and 18.2 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.2, 8.4, 10.4, 16.7, 16.8, and 18.2 °2 θ using Cu K α radiation))).

[0155] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern comprising signals at 4.2 ± 0.5 , 8.4 ± 0.5 , 10.4 ± 0.5 , 16.7 ± 0.5 , 16.8 ± 0.5 , 18.2 ± 0.5 , and 20.8 ± 0.5 °2 θ (e.g., 4.2 ± 0.2 , 8.4 ± 0.2 , 10.4 ± 0.2 , 16.7 ± 0.2 , 16.8 ± 0.2 , 18.2 ± 0.2 , and 20.8 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.2 ± 0.1 , 8.4 ± 0.1 , 10.4 ± 0.1 , 16.7 ± 0.1 , 16.8 ± 0.1 , 18.2 ± 0.1 , and 20.8 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.2, 8.4, 10.4, 16.7, 16.8, 18.2, and 20.8 °2 θ using Cu K α radiation))).

[0156] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern comprising signals at 4.2 ± 0.5 , 8.4 ± 0.5 , 10.4 ± 0.5 , 16.7 ± 0.5 , 16.8 ± 0.5 , 18.2 ± 0.5 , 20.8 ± 0.5 , and 21.1 ± 0.5 °2 θ (e.g., 4.2 ± 0.2 , 8.4 ± 0.2 , 10.4 ± 0.2 , 16.7 ± 0.2 , 16.8 ± 0.2 , 18.2 ± 0.2 , 20.8 ± 0.2 , and 21.1 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.2 ± 0.1 , 8.4 ± 0.1 , 10.4 ± 0.1 , 16.7 ± 0.1 , 16.8 ± 0.1 , 18.2 ± 0.1 , 20.8 ± 0.1 , and 21.1 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.2, 8.4, 10.4, 16.7, 16.8, 18.2, 20.8, and 21.1 °2 θ using Cu K α radiation))).

[0157] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern having at least one signal selected from 4.2 ± 0.5 , 16.7 ± 0.5 , and 16.8 ± 0.5 °2 θ (e.g., 4.2 ± 0.2 , 16.7 ± 0.2 , and 16.8 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.2 ± 0.1 , 16.7 ± 0.1 , and 16.8 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.2, 16.7, and 16.8 °2 θ using Cu K α radiation))).

[0158] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern having at least two signals selected from 4.2 ± 0.5 , 16.7 ± 0.5 , and 16.8 ± 0.5 °2 θ (e.g., 4.2 ± 0.2 , 16.7 ± 0.2 , and 16.8 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.2 ± 0.1 , 16.7 ± 0.1 , and 16.8 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.2, 16.7, and 16.8 °2 θ using Cu K α radiation))).

[0159] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern having at least three signals selected from 4.2 ± 0.5 , 16.7 ± 0.5 , 16.8 ± 0.5 , and 18.2 ± 0.5 °2 θ

(e.g., 4.2 ± 0.2 , 16.7 ± 0.2 , 16.8 ± 0.2 , and 18.2 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.2 ± 0.1 , 16.7 ± 0.1 , 16.8 ± 0.1 , and 18.2 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.2, 16.7, 16.8, and 18.2 °2 θ using Cu K α radiation))).

[0160] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern having at least four signals selected from 4.2 ± 0.5 , 10.4 ± 0.5 , 16.7 ± 0.5 , 16.8 ± 0.5 , and 18.2 ± 0.5 °2 θ (e.g., 4.2 ± 0.2 , 10.4 ± 0.2 , 16.7 ± 0.2 , 16.8 ± 0.2 , and 18.2 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.2 ± 0.1 , 10.4 ± 0.1 , 16.7 ± 0.1 , 16.8 ± 0.1 , and 18.2 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.2, 10.4, 16.7, 16.8, and 18.2 °2 θ using Cu K α radiation))).

[0161] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern having at least five signals selected from 4.2 ± 0.5 , 8.4 ± 0.5 , 10.4 ± 0.5 , 16.7 ± 0.5 , 16.8 ± 0.5 , and 18.2 ± 0.5 °2 θ (e.g., 4.2 ± 0.2 , 8.4 ± 0.2 , 10.4 ± 0.2 , 16.7 ± 0.2 , 16.8 ± 0.2 , and 18.2 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.2 ± 0.1 , 8.4 ± 0.1 , 10.4 ± 0.1 , 16.7 ± 0.1 , 16.8 ± 0.1 , and 18.2 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.2, 8.4, 10.4, 16.7, 16.8, and 18.2 °2 θ using Cu K α radiation))).

[0162] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern having at least five signals selected from 4.2 ± 0.5 , 8.4 ± 0.5 , 10.4 ± 0.5 , 16.7 ± 0.5 , 16.8 ± 0.5 , 18.2 ± 0.5 , and 20.8 ± 0.5 °2 θ (e.g., 4.2 ± 0.2 , 8.4 ± 0.2 , 10.4 ± 0.2 , 16.7 ± 0.2 , 16.8 ± 0.2 , 18.2 ± 0.2 , and 20.8 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.2 ± 0.1 , 8.4 ± 0.1 , 10.4 ± 0.1 , 16.7 ± 0.1 , 16.8 ± 0.1 , 18.2 ± 0.1 , and 20.8 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.2, 8.4, 10.4, 16.7, 16.8, 18.2, and 20.8 °2 θ using Cu K α radiation))).

[0163] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern comprising one or more signals as described in Table 2 below.

[0164] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern comprising two or more signals as described in Table 2 below.

[0165] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern comprising three or more signals as described in Table 2 below.

[0166] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern comprising four or more signals as described in Table 2 below.

Table 2 XRPD Signals for Form 2 dihydrate

Angle (2 θ °)	Intensity (%)	Angle (2 θ °)	Intensity (%)
4.2	100.0	24.7	18.1
8.4	35.0	25.2	10.3
10.2	16.6	25.3	10.5
10.4	44.8	25.6	7.0

Angle (2 θ °)	Intensity (%)	Angle (2 θ °)	Intensity (%)
13.1	19.9	26.1	8.1
13.5	11.1	26.6	25.7
16.3	9.3	27.1	3.9
16.7	50.3	28.3	4.4
16.8	55.3	28.9	4.6
18.2	47.8	29.1	7.2
18.6	17.0	29.5	5.8
19.3	5.8	29.8	6.9
20.8	32.5	30.0	4.3
21.1	32.1	30.3	3.4
23.0	14.9	30.7	3.6
23.3	13.6	31.1	3.2
23.5	14.2	31.7	15.2
24.3	31.7		

*The values shown in the above table are approximate value and subject to instrument differentiation and standard error.

[0167] In some embodiments, Form 2 of Compound A is characterized by an XRPD pattern substantially similar to that set forth in FIG. 4.

TGA Characterization

[0168] In some embodiments, Form 2 of Compound A is characterized by a degradation event up to 105 $\pm$ 40 °C, 105 $\pm$ 30 °C, 105 $\pm$ 20 °C, 105 $\pm$ 15 °C, 105 $\pm$ 10 °C, or 105 $\pm$ 5 °C (e.g., up to about 105 °C), as measured by TGA.

DSC Characterizations

[0169] In some embodiments, Form 2 of Compound A is characterized by an endothermic event with an onset at 50 $\pm$ 20 °C, 50 $\pm$ 15 °C, 50 $\pm$ 10 °C, or 50 $\pm$ 5 °C (e.g., about 50 °C), as measured by DSC.

[0170] In some embodiments, Form 2 of Compound A is characterized by an endothermic event with an onset at 144 $\pm$ 20 °C, 144 $\pm$ 15 °C, 144 $\pm$ 10 °C, or 144 $\pm$ 5 °C (e.g., about 144 °C), as measured by DSC.

Other Characterizations

[0171] In some embodiments, Form 2 of Compound A is characterized by a water uptake (e.g., from 0 % to 90 % RH) of 9.1 ± 0.5 %, 9.1 ± 0.4 %, 9.1 ± 0.3 %, 9.1 ± 0.2 %, 9.1 ± 0.1 %, or 9.1 ± 0.05 % (e.g., about 9.1 %), as measured by GVS.

[0172] In some embodiments, Form 2 of Compound A is characterized by an uptake (e.g., from 40 % to 70 % RH) of 2.2 ± 0.05 %, 2.2 ± 0.04 %, 2.2 ± 0.03 %, 2.2 ± 0.02 %, or 2.2 ± 0.01 % (e.g., about 2.2 %), as measured by GVS.

[0173] In some embodiments, Form 2 of Compound A is characterized by an uptake (e.g., from 40 % to 70 % RH) of 6.1 ± 0.05 %, 6.1 ± 0.04 %, 6.1 ± 0.03 %, 6.1 ± 0.02 %, or 6.1 ± 0.01 % (e.g., about 6.1 %), as measured by GVS.

[0174] In some embodiments, Form 2 of Compound A is characterized by a reversible hysteresis (e.g., from 70 % to 10 % RH), as measured by GVS.

[0175] In some embodiments, Form 2 of Compound A is a crystalline solid,

[0176] In some embodiments, the crystalline solid Form 2 is an agglomerated block crystalline form.

[0177] In some embodiments, Form 2 is obtained from storing amorphous Compound A at 25 °C/97% RH

[0178] In some embodiments, Form 2 is obtained from storing amorphous Compound A at 40 °C/75% RH.

[0179] In some embodiments, Form 2 is formed when the amorphous Compound A is stored at 60 °C/75% RH.

[0180] In some embodiments, Form 2 is obtained by crystallizing amorphous Compound A from EtOAc/water.

[0181] In some embodiments, Form 2 is formed when the amorphous Compound A is stored at 60 °C/75% RH and further crystallized from EtOAc/water.

[0182] In some embodiments, Form 2 is formed when the amorphous Compound A is stored at 60 °C/75% RH and further crystallized from EtOAc/water followed by liquid-assisted grinding.

[0183] In some embodiments, the liquid-assisted grinding is with water.

[0184] In some embodiments, Form 2 converts to a monohydrate when stored at 60 °C/75% RH.

[0185] In some embodiments, Form 2 converts to Form 3 when stored at 60 °C/75% RH.

[0186] In some embodiments, Form 2 is formed when Form 3 is stored at 25 °C/97% RH.

Form 3

[0187] In some embodiments, the morphic form of Compound A is monohydrate Form 3.

X-Ray Powder Diffraction (XRPD) Characterizations

[0188] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.4 ± 0.5 , and 17.8 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 8.4 ± 0.2 , and 17.8 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 8.4 ± 0.1 , and 17.8 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 8.4, and 17.8 °2 θ using Cu K α radiation))).

[0189] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.4 ± 0.5 , 17.8 ± 0.5 , and 19.0 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 8.4 ± 0.2 , 17.8 ± 0.2 , and 19.0 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 8.4 ± 0.1 , 17.8 ± 0.1 , and 19.0 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 8.4, 17.8, and 19.0 °2 θ using Cu K α radiation))).

[0190] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.4 ± 0.5 , 17.8 ± 0.5 , 19.0 ± 0.5 , and 22.3 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 8.4 ± 0.2 , 17.8 ± 0.2 , 19.0 ± 0.2 , and 22.3 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 8.4 ± 0.1 , 17.8 ± 0.1 , 19.0 ± 0.1 , and 22.3 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 8.4, 17.8, 19.0, and 22.3 °2 θ using Cu K α radiation))).

[0191] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.4 ± 0.5 , 17.8 ± 0.5 , 19.0 ± 0.5 , 19.6 ± 0.5 , and 22.3 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 8.4 ± 0.2 , 17.8 ± 0.2 , 19.0 ± 0.2 , 19.6 ± 0.2 , and 22.3 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 8.4 ± 0.1 , 17.8 ± 0.1 , 19.0 ± 0.1 , 19.6 ± 0.1 , and 22.3 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 8.4, 17.8, 19.0, 19.6, and 22.3 °2 θ using Cu K α radiation))).

[0192] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.4 ± 0.5 , 17.8 ± 0.5 , 19.0 ± 0.5 , 19.6 ± 0.5 , 20.9 ± 0.5 , and 22.3 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 8.4 ± 0.2 , 17.8 ± 0.2 , 19.0 ± 0.2 , 19.6 ± 0.2 , 20.9 ± 0.2 , and 22.3 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 8.4 ± 0.1 , 17.8 ± 0.1 , 19.0 ± 0.1 , 19.6 ± 0.1 , 20.9 ± 0.1 , and 22.3 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 8.4, 17.8, 19.0, 19.6, 20.9, and 22.3 °2 θ using Cu K α radiation))).

[0193] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.4 ± 0.5 , 14.3 ± 0.5 , 17.8 ± 0.5 , 19.0 ± 0.5 , 19.6 ± 0.5 , 20.9 ± 0.5 , and 22.3 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 8.4 ± 0.2 , 14.3 ± 0.2 , 17.8 ± 0.2 , 19.0 ± 0.2 , 19.6 ± 0.2 , 20.9 ± 0.2 , and 22.3 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 8.4 ± 0.1 , 14.3 ± 0.1 , 17.8 ± 0.1 , 19.0 ± 0.1 ,

19.6±0.1, 20.9±0.1, and 22.3±0.1 °2θ using Cu Kα radiation (e.g., 4.4, 8.4, 14.3, 17.8, 19.0, 19.6, 20.9, and 22.3 °2θ using Cu Kα radiation))).

[0194] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern having at least one signal selected from 4.4±0.5, 8.4±0.5, and 17.8±0.5 °2θ (e.g., 4.4±0.2, 8.4±0.2, and 17.8±0.2 °2θ using Cu Kα radiation (e.g., 4.4±0.1, 8.4±0.1, and 17.8±0.1 °2θ using Cu Kα radiation (e.g., 4.4, 8.4, and 17.8 °2θ using Cu Kα radiation))).

[0195] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern having at least two signals selected from 4.4±0.5, 8.4±0.5, and 17.8±0.5 °2θ (e.g., 4.4±0.2, 8.4±0.2, and 17.8±0.2 °2θ using Cu Kα radiation (e.g., 4.4±0.1, 8.4±0.1, and 17.8±0.1 °2θ using Cu Kα radiation (e.g., 4.4, 8.4, and 17.8 °2θ using Cu Kα radiation))).

[0196] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern having at least three signals selected from 4.4±0.5, 8.4±0.5, 17.8±0.5, and 19.0±0.5 °2θ (e.g., 4.4±0.2, 8.4±0.2, 17.8±0.2, and 19.0±0.2 °2θ using Cu Kα radiation (e.g., 4.4±0.1, 8.4±0.1, 17.8±0.1, and 19.0±0.1 °2θ using Cu Kα radiation (e.g., 4.4, 8.4, 17.8, and 19.0 °2θ using Cu Kα radiation))).

[0197] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern having at least four signals selected from 4.4±0.5, 8.4±0.5, 17.8±0.5, 19.0±0.5, and 22.3±0.5 °2θ (e.g., 4.4±0.2, 8.4±0.2, 17.8±0.2, 19.0±0.2, and 22.3±0.2 °2θ using Cu Kα radiation (e.g., 4.4±0.1, 8.4±0.1, 17.8±0.1, 19.0±0.1, and 22.3±0.1 °2θ using Cu Kα radiation (e.g., 4.4, 8.4, 17.8, 19.0, and 22.3 °2θ using Cu Kα radiation))).

[0198] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern having at least five signals selected from 4.4±0.5, 8.4±0.5, 17.8±0.5, 19.0±0.5, 19.6±0.5, and 22.3±0.5 °2θ (e.g., 4.4±0.2, 8.4±0.2, 17.8±0.2, 19.0±0.2, 19.6±0.2, and 22.3±0.2 °2θ using Cu Kα radiation (e.g., 4.4±0.1, 8.4±0.1, 17.8±0.1, 19.0±0.1, 19.6±0.1, and 22.3±0.1 °2θ using Cu Kα radiation (e.g., 4.4, 8.4, 17.8, 19.0, 19.6, and 22.3 °2θ using Cu Kα radiation))).

[0199] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern having at least five signals selected from 4.4±0.5, 8.4±0.5, 17.8±0.5, 19.0±0.5, 19.6±0.5, 20.9±0.5, and 22.3±0.5 °2θ (e.g., 4.4±0.2, 8.4±0.2, 17.8±0.2, 19.0±0.2, 19.6±0.2, 20.9±0.2, and 22.3±0.2 °2θ using Cu Kα radiation (e.g., 4.4±0.1, 8.4±0.1, 17.8±0.1, 19.0±0.1, 19.6±0.1, 20.9±0.1, and 22.3±0.1 °2θ using Cu Kα radiation (e.g., 4.4, 8.4, 17.8, 19.0, 19.6, 20.9, and 22.3 °2θ using Cu Kα radiation))).

[0200] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern comprising one or more signals as described in Table 3 below.

[0201] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern comprising two or more signals as described in Table 3 below.

[0202] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern comprising three or more signals as described in Table 3 below.

[0203] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern comprising four or more signals as described in Table 3 below.

Table 3 XRPD Signals for Form 3 Monohydrate

Angle (2θ °)	Intensity (%)	Angle (2θ °)	Intensity (%)
4.4	55.7	21.9	14.9
8.4	100.0	22.3	22.5
8.9	11.5	22.4	16.9
11.1	5.9	22.9	9.8
11.4	13.1	23.2	7.6
12.0	8.0	23.6	6.8
14.2	16.9	24.4	7.5
14.3	18.3	24.8	5.3
15.1	10.6	25.2	7.2
16.8	7.0	26.8	17.7
17.3	14.3	27.4	5.7
17.8	31.0	27.8	4.5
19.0	30.9	29.1	5.3
19.2	16.1	29.4	12.2
19.6	19.8	29.8	5.0
20.6	15.1	30.1	4.2
20.9	18.6	31.0	5.5
21.3	16.1	31.4	4.8
21.5	13.0		

*The values shown in the above table are approximate value and subject to instrument differentiation and standard error.

[0204] In some embodiments, Form 3 of Compound A is characterized by an XRPD pattern substantially similar to that set forth in FIG. 10.

TGA Characterizations

[0205] In some embodiments, Form 3 of Compound A is characterized by a degradation event up to 85 ± 40 °C, 85 ± 30 °C, 85 ± 20 °C, 85 ± 15 °C, 85 ± 10 °C, or 85 ± 5 °C (e.g., up to about 85 °C), as measured by TGA.

[0206] In some embodiments, Form 3 of Compound A is characterized by a degradation event onset at 85 ± 40 °C, 85 ± 30 °C, 85 ± 20 °C, 85 ± 15 °C, 85 ± 10 °C, or 85 ± 5 °C (e.g., about 85 °C), as measured by TGA.

DSC Characterizations

[0207] In some embodiments, Form 3 of Compound A is characterized by an endothermic event with an onset at 34 ± 20 °C, 34 ± 15 °C, 34 ± 10 °C, or 34 ± 5 °C (e.g., about 34 °C), as measured by DSC.

[0208] In some embodiments, Form 3 of Compound A is characterized by an endothermic event with an onset at 102 ± 20 °C, 102 ± 15 °C, 102 ± 10 °C, or 102 ± 5 °C (e.g., about 102 °C), as measured by DSC.

[0209] In some embodiments, Form 3 of Compound A is characterized by an endothermic event with an onset at 152 ± 20 °C, 152 ± 15 °C, 152 ± 10 °C, or 152 ± 5 °C (e.g., about 152 °C), as measured by DSC.

Other Characterizations

[0210] In some embodiments, Form 3 of Compound A is characterized by an uptake (e.g., from 40 % to 80 % RH) of 2.3 ± 0.5 %, 2.3 ± 0.4 %, 2.3 ± 0.3 %, 2.3 ± 0.2 %, 2.3 ± 0.1 %, or 2.3 ± 0.05 % (e.g., about 2.3 %), as measured by GVS.

[0211] In some embodiments, Form 3 of Compound A is characterized by an uptake (e.g., from 80 % to 90 % RH) of 8.9 ± 0.5 %, 8.9 ± 0.4 %, 8.9 ± 0.3 %, 8.9 ± 0.2 %, 8.9 ± 0.1 %, or 8.9 ± 0.05 % (e.g., about 8.9 %), as measured by GVS.

[0212] In some embodiments, Form 3 of Compound A is characterized by an uptake (e.g., from 40 % to 80 % RH) of 5.1 ± 0.5 %, 5.1 ± 0.4 %, 5.1 ± 0.3 %, 5.1 ± 0.2 %, 5.1 ± 0.1 %, or 5.1 ± 0.05 % (e.g., about 5.1 %), as measured by GVS.

[0213] In some embodiments, Form 3 of Compound A is characterized by a reversible hysteresis (e.g., from 70 % to 10 % RH), as measured by GVS.

[0214] In some embodiments, Form 3 of Compound A is a crystalline solid.

[0215] In some embodiments, the crystalline solid Form 3 is an agglomerated block crystalline form.

[0216] In some embodiments, Form 3 is formed when the amorphous Compound A is stored at 25 °C/97% RH.

[0217] In some embodiments, Form 3 is formed when the amorphous Compound A is stored at 25 °C/97% RH and further crystallized from EtOAc/water.

[0218] In some embodiments, Form 3 is formed when the amorphous Compound A is stored at 40 °C/75% RH.

[0219] In some embodiments, Form 3 is formed when the amorphous Compound A is stored at 40 °C/75% RH and further crystallized from EtOAc/water.

[0220] In some embodiments, Form 3 is obtained from storing Form 2 at 60 °C/75% RH.

[0221] In some embodiments, Form 3 is formed when the anhydrous Compound A is held under ambient conditions.

[0222] In some embodiments, Form 3 is obtained by crystallizing amorphous Compound A from EtOAc/water.

[0223] In some embodiments, Form 3 is obtained from liquid assistance grinding of amorphous Compound A with water.

[0224] In some embodiments, Form 3 is formed when the anhydrous Form 9 is held under ambient conditions.

[0225] In some embodiments, Form 3 converts to Form 9 when heated to 120 °C.

[0226] In some embodiments, Form 3 is formed when a solvate of Compound A is stored at 40 °C/75% RH.

[0227] In some embodiments, Form 3 is formed when Form 4 is stored at 40 °C/75% RH.

[0228] In some embodiments, Form 3 is formed when Form 6 is stored at 40 °C/75% RH.

[0229] In some embodiments, Form 3 is formed when Form 7 is stored at 40 °C/75% RH.

[0230] In some embodiments, Form 3 is formed when Form 8 is stored at 40 °C/75% RH.

[0231] In some embodiments, Form 3 of Compound A is a crystalline solid having crystal data as provided in Table AA.

[0232] In some embodiments, Form 3 of Compound A is a crystalline solid having one or more of the following characteristics:

a) a crystal size of 0.300 x 0.250 x 0.200 mm;

b) a crystal habit of colourless cut rod;

c) a crystal system of monoclinic;

d) a space group of $P2_1$;

e) unit cell dimensions of $a = 10.17100(10)$ Å, $a = 90^\circ$, $b = 12.04740(10)$ Å, $b = 89.8050(10)^\circ$, $c = 20.0561(2)$ Å, $g = 90^\circ$;

- f) a volume of 2457.54(4) Å³;
- g) a density (calculated) of 1.350 Mg/m³;
- h) an absorption coefficient or 1.708 mm⁻¹; and/or
- i) $F(000)$ of 1056.

[0233] In some embodiments, Form 3 of Compound A is a crystalline solid having a crystal size of 0.300 x 0.250 x 0.200 mm.

[0234] In some embodiments, Form 3 of Compound A is a crystalline solid having a crystal habit of colourless cut rod.

[0235] In some embodiments, Form 3 of Compound A is a crystalline solid having a crystal system of monoclinic.

[0236] In some embodiments, Form 3 of Compound A is a crystalline solid having a space group of $P2_1$.

[0237] In some embodiments, Form 3 of Compound A is a crystalline solid having unit cell dimensions of $a = 10.17100(10)$ Å, $a = 90^\circ$, $b = 12.04740(10)$ Å, $b = 89.8050(10)^\circ$, $c = 20.0561(2)$ Å, $\gamma = 90^\circ$.

[0238] In some embodiments, Form 3 of Compound A is a crystalline solid having a volume of 2457.54(4) Å³.

[0239] In some embodiments, Form 3 of Compound A is a crystalline solid having a density (calculated) of 1.350 Mg/m³.

[0240] In some embodiments, Form 3 of Compound A is a crystalline solid having an absorption coefficient or 1.708 mm⁻¹.

[0241] In some embodiments, Form 3 of Compound A is a crystalline solid having an $F(000)$ of 1056.

Form 4

[0242] In some embodiments, the morphic form of Compound A is Form 4.

DSC Characterizations

[0243] In some embodiments, Form 4 of Compound A is characterized by an endothermic event with an onset at 25 ± 20 °C, 25 ± 15 °C, 25 ± 10 °C, or 25 ± 5 °C (e.g., about 25 °C), as measured by DSC.

[0244] In some embodiments, Form 4 of Compound A is characterized by an endothermic event with an onset at 122 ± 20 °C, 122 ± 15 °C, 122 ± 10 °C, or 122 ± 5 °C (e.g., about 122 °C), as measured by DSC.

Other Characterizations

[0245] In some embodiments, Form 4 of Compound A is characterized by a ¹H-NMR spectrum substantially similar to that set forth in FIG. 16.

[0246] In some embodiments, Form 4 is formed when the amorphous Compound A undergoes solvent addition, isothermal maturation, an additional maturation step, and liquid assisted grinding.

[0247] In some embodiments, Form 4 is obtained from addition of heptane to amorphous Compound A and IPA solution.

[0248] In some embodiments, Form 4 is obtained from 24-hour isothermal (5 °C) maturation of amorphous Compound A in IPA slurry.

[0249] In some embodiments, Form 4 is obtained from RT/50 °C maturation of amorphous Compound A in IPA/heptane.

[0250] In some embodiments, Form 4 is obtained from liquid assisted grinding of amorphous Compound A with IPA.

Form 5

[0251] In some embodiments, the morphic form of Compound A is Form 5.

Other Characterizations

[0252] In some embodiments, Form 5 is obtained from heptane addition of amorphous Compound A and acetone solution followed by three-day slurry.

Form 6

[0253] In some embodiments, the morphic form of Compound A is Form 6.

X-Ray Powder Diffraction (XRPD) Characterizations

[0254] In some embodiments, Form 6 of Compound A is characterized by an XRPD pattern substantially similar to that set forth in FIG. 20.

DSC Characterizations

[0255] In some embodiments, Form 6 of Compound A is characterized by an endothermic event up to 80 ± 20 °C, 80 ± 15 °C, 80 ± 10 °C, or 80 ± 5 °C (e.g., about 80 °C), as measured by DSC.

[0256] In some embodiments, Form 6 of Compound A is characterized by an endothermic event with an onset at 109 ± 20 °C, 109 ± 15 °C, 109 ± 10 °C, or 109 ± 5 °C (e.g., about 109 °C), as measured by DSC.

Other Characterizations

[0257] In some embodiments, Form 6 is formed when the amorphous Compound A undergoes cooling crystallization and liquid-assisted grinding.

[0258] In some embodiments, Form 6 is obtained from cooling crystallization of a solution of amorphous Compound A and 2-methyl-1-propanol.

[0259] In some embodiments, Form 6 is obtained from a 5 °C isothermal slurry of a solution of amorphous Compound A and 2-methyl-1-propanol.

[0260] In some embodiments, Form 6 is obtained from liquid-assisted grinding of amorphous Compound A with 2-methyl-1-propanol.

Form 7

[0261] In some embodiments, the morphic form of Compound A is Form 7.

DSC Characterizations

[0262] In some embodiments, Form 7 of Compound A is characterized by an endothermic event with an onset at 86 ± 20 °C, 86 ± 15 °C, 86 ± 10 °C, or 86 ± 5 °C (e.g., about 86 °C), as measured by DSC.

[0263] In some embodiments, Form 7 of Compound A is characterized by an endothermic event with an onset at 103 ± 20 °C, 103 ± 15 °C, 103 ± 10 °C, or 103 ± 5 °C (e.g., about 103 °C), as measured by DSC.

[0264] In some embodiments, Form 7 of Compound A is characterized by an endothermic event with an onset at 144 ± 20 °C, 144 ± 15 °C, 144 ± 10 °C, or 144 ± 5 °C (e.g., about 144 °C), as measured by DSC.

[0265] In some embodiments, Form 7 of Compound A is characterized by two overlapping endotherms between 140 ± 20 °C and 170 ± 20 °C, 140 ± 15 °C and 170 ± 15 °C, 140 ± 10 °C and 170 ± 10 °C, or 140 ± 5 °C and 170 ± 5 °C (e.g., between about 140 °C and 170 °C), as measured by DSC.

[0266] In some embodiments, Form 7 of Compound A is characterized by an endothermic event with a shoulder observed up to 130 ± 20 °C, 130 ± 15 °C, 130 ± 10 °C, or 130 ± 5 °C (e.g., up to about 130 °C), as measured by DSC.

Other Characterizations

[0267] In some embodiments, Form 7 is formed when the amorphous Compound A undergoes solvent at least one maturation cycle and liquid assisted grinding.

[0268] In some embodiments, Form 7 is obtained from amorphous Compound A maturation at 50-25 °C in Heptane/EtOH (9:1 v/v).

[0269] In some embodiments, Form 7 is obtained from amorphous Compound A liquid-assisted grinding with water/MeOH.

Form 8

[0270] In some embodiments, the morphic form of Compound A is Form 8.

DSC Characterizations

[0271] In some embodiments, Form 8 of Compound A is characterized by an endothermic event with an onset at 88 ± 20 °C, 88 ± 15 °C, 88 ± 10 °C, or 88 ± 5 °C (e.g., about 88 °C), as measured by DSC.

[0272] In some embodiments, Form 8 of Compound A is characterized by an endothermic event with an onset at 101 ± 20 °C, 101 ± 15 °C, 101 ± 10 °C, or 101 ± 5 °C (e.g., about 101 °C), as measured by DSC.

Other Characterizations

[0273] In some embodiments, Form 8 is formed when the amorphous Compound A undergoes at least one maturation cycle.

[0274] In some embodiments, Form 8 is obtained from maturation amorphous Compound A at 50-25 °C in Heptane/2-Methyl-1-propanol (9:1 v/v)

Form 9

[0275] In some embodiments, the morphic form of Compound A is anhydrous Form 9.

X-Ray Powder Diffraction (XRPD) Characterizations

[0276] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern comprising signals at 8.0 ± 0.5 , 21.3 ± 0.5 , and 22.1 ± 0.5 °2 θ (e.g., 8.0 ± 0.2 , 21.3 ± 0.2 , and 22.1 ± 0.2 °2 θ using Cu K α radiation (e.g., 8.0 ± 0.1 , 21.3 ± 0.1 , and 22.1 ± 0.1 °2 θ using Cu K α radiation (e.g., 8.0, 21.3, and 22.1 °2 θ using Cu K α radiation))).

[0277] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern comprising signals at 8.0 ± 0.5 , 21.3 ± 0.5 , 22.1 ± 0.5 , and 22.9 ± 0.5 °2 θ (e.g., 8.0 ± 0.2 , 21.3 ± 0.2 , 22.1 ± 0.2 , and 22.9 ± 0.2 °2 θ using Cu K α radiation (e.g., 8.0 ± 0.1 , 21.3 ± 0.1 , 22.1 ± 0.1 , and 22.9 ± 0.1 °2 θ using Cu K α radiation (e.g., 8.0, 21.3, 22.1, and 22.9 °2 θ using Cu K α radiation))).

[0278] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern comprising signals at 8.0 ± 0.5 , 18.2 ± 0.5 , 21.3 ± 0.5 , 22.1 ± 0.5 , and 22.9 ± 0.5 °2 θ (e.g., 8.0 ± 0.2 , 18.2 ± 0.2 , 21.3 ± 0.2 , 22.1 ± 0.2 , and 22.9 ± 0.2 °2 θ using Cu K α radiation (e.g., 8.0 ± 0.1 , 18.2 ± 0.1 , 21.3 ± 0.1 , 22.1 ± 0.1 , and 22.9 ± 0.1 °2 θ using Cu K α radiation (e.g., 8.0, 18.2, 21.3, 22.1, and 22.9 °2 θ using Cu K α radiation))).

[0279] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern comprising signals at 8.0 ± 0.5 , 18.2 ± 0.5 , 19.7 ± 0.5 , 21.3 ± 0.5 , 22.1 ± 0.5 , and 22.9 ± 0.5 °2 θ (e.g., 8.0 ± 0.2 , 18.2 ± 0.2 , 19.7 ± 0.2 , 21.3 ± 0.2 , 22.1 ± 0.2 , and 22.9 ± 0.2 °2 θ using Cu K α radiation (e.g., 8.0 ± 0.1 , 18.2 ± 0.1 , 19.7 ± 0.1 , 21.3 ± 0.1 , 22.1 ± 0.1 , and 22.9 ± 0.1 °2 θ using Cu K α radiation (e.g., 8.0, 18.2, 19.7, 21.3, 22.1, and 22.9 °2 θ using Cu K α radiation))).

[0280] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern comprising signals at 8.0 ± 0.5 , 18.2 ± 0.5 , 19.7 ± 0.5 , 21.3 ± 0.5 , 22.1 ± 0.5 , 22.9 ± 0.5 , and 25.3 ± 0.5 °2 θ (e.g., 8.0 ± 0.2 , 18.2 ± 0.2 , 19.7 ± 0.2 , 21.3 ± 0.2 , 22.1 ± 0.2 , 22.9 ± 0.2 , and 25.3 ± 0.2 °2 θ using Cu K α radiation (e.g., 8.0 ± 0.1 , 18.2 ± 0.1 , 19.7 ± 0.1 , 21.3 ± 0.1 , 22.1 ± 0.1 , 22.9 ± 0.1 , and 25.3 ± 0.1 °2 θ using Cu K α radiation (e.g., 8.0, 18.2, 19.7, 21.3, 22.1, 22.9, and 25.3 °2 θ using Cu K α radiation))).

[0281] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern comprising signals at 8.0 ± 0.5 , 18.2 ± 0.5 , 19.7 ± 0.5 , 21.3 ± 0.5 , 22.1 ± 0.5 , 22.9 ± 0.5 , 24.6 ± 0.5 , and 25.3 ± 0.5 $^{\circ}2\theta$ (e.g., 8.0 ± 0.2 , 18.2 ± 0.2 , 19.7 ± 0.2 , 21.3 ± 0.2 , 22.1 ± 0.2 , 22.9 ± 0.2 , 24.6 ± 0.2 , and 25.3 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 8.0 ± 0.1 , 18.2 ± 0.1 , 19.7 ± 0.1 , 21.3 ± 0.1 , 22.1 ± 0.1 , 22.9 ± 0.1 , 24.6 ± 0.1 , and 25.3 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 8.0, 18.2, 19.7, 21.3, 22.1, 22.9, 24.6, and 25.3 $^{\circ}2\theta$ using Cu K α radiation))).

[0282] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern having at least one signal selected from 8.0 ± 0.5 , 21.3 ± 0.5 , and 22.1 ± 0.5 $^{\circ}2\theta$ (e.g., 8.0 ± 0.2 , 21.3 ± 0.2 , and 22.1 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 8.0 ± 0.1 , 21.3 ± 0.1 , and 22.1 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 8.0, 21.3, and 22.1 $^{\circ}2\theta$ using Cu K α radiation))).

[0283] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern having at least two signals selected from 8.0 ± 0.5 , 21.3 ± 0.5 , and 22.1 ± 0.5 $^{\circ}2\theta$ (e.g., 8.0 ± 0.2 , 21.3 ± 0.2 , and 22.1 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 8.0 ± 0.1 , 21.3 ± 0.1 , and 22.1 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 8.0, 21.3, and 22.1 $^{\circ}2\theta$ using Cu K α radiation))).

[0284] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern having at least three signals selected from 8.0 ± 0.5 , 21.3 ± 0.5 , 22.1 ± 0.5 , and 22.9 ± 0.5 $^{\circ}2\theta$ (e.g., 8.0 ± 0.2 , 21.3 ± 0.2 , 22.1 ± 0.2 , and 22.9 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 8.0 ± 0.1 , 21.3 ± 0.1 , 22.1 ± 0.1 , and 22.9 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 8.0, 21.3, 22.1, and 22.9 $^{\circ}2\theta$ using Cu K α radiation))).

[0285] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern having at least four signals selected from 8.0 ± 0.5 , 18.2 ± 0.5 , 21.3 ± 0.5 , 22.1 ± 0.5 , and 22.9 ± 0.5 $^{\circ}2\theta$ (e.g., 8.0 ± 0.2 , 18.2 ± 0.2 , 21.3 ± 0.2 , 22.1 ± 0.2 , and 22.9 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 8.0 ± 0.1 , 18.2 ± 0.1 , 21.3 ± 0.1 , 22.1 ± 0.1 , and 22.9 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 8.0, 18.2, 21.3, 22.1, and 22.9 $^{\circ}2\theta$ using Cu K α radiation))).

[0286] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern having at least five signals selected from 8.0 ± 0.5 , 18.2 ± 0.5 , 19.7 ± 0.5 , 21.3 ± 0.5 , 22.1 ± 0.5 , and 22.9 ± 0.5 $^{\circ}2\theta$ (e.g., 8.0 ± 0.2 , 18.2 ± 0.2 , 19.7 ± 0.2 , 21.3 ± 0.2 , 22.1 ± 0.2 , and 22.9 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 8.0 ± 0.1 , 18.2 ± 0.1 , 19.7 ± 0.1 , 21.3 ± 0.1 , 22.1 ± 0.1 , and 22.9 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 8.0, 18.2, 19.7, 21.3, 22.1, and 22.9 $^{\circ}2\theta$ using Cu K α radiation))).

[0287] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern having at least five signals selected from 8.0 ± 0.5 , 18.2 ± 0.5 , 19.7 ± 0.5 , 21.3 ± 0.5 , 22.1 ± 0.5 , 22.9 ± 0.5 , and 25.3 ± 0.5 $^{\circ}2\theta$ (e.g., 8.0 ± 0.2 , 18.2 ± 0.2 , 19.7 ± 0.2 , 21.3 ± 0.2 , 22.1 ± 0.2 , 22.9 ± 0.2 ,

and 25.3 ± 0.2 °2 θ using Cu K α radiation (e.g., 8.0 ± 0.1 , 18.2 ± 0.1 , 19.7 ± 0.1 , 21.3 ± 0.1 , 22.1 ± 0.1 , 22.9 ± 0.1 , and 25.3 ± 0.1 °2 θ using Cu K α radiation (e.g., 8.0, 18.2, 19.7, 21.3, 22.1, 22.9, and 25.3 °2 θ using Cu K α radiation))).

[0288] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern comprising one or more signals as described in Table 4 below.

[0289] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern comprising two or more signals as described in Table 4 below.

[0290] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern comprising three or more signals as described in Table 4 below.

[0291] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern comprising four or more signals as described in Table 4 below.

Table 4 XRPD Signals for Anhydrous Form 9

Angle (° 2 θ)	Intensity (%)	Angle (° 2 θ)	Intensity (%)
4.6	46.4	19.3	59.3
7.2	43.3	19.7	66.0
8.0	100.0	20.7	50.3
9.1	30.4	21.3	98.9
10.8	24.7	22.1	90.5
11.1	27.6	22.9	79.3
12.9	24.6	23.9	49.3
14.6	47.3	24.6	61.3
15.7	42.7	25.3	61.5
16.4	55.7	26.0	41.3
17.1	55.4	26.5	42.3
18.2	72.4	27.5	52.1
18.7	48.7	29.0	43.5
19.0	56.8	29.8	43.1

*The values shown in the above table are approximate value and subject to instrument differentiation and standard error.

[0292] In some embodiments, Form 9 of Compound A is characterized by an XRPD pattern substantially similar to that set forth in FIG. 25.

DSC Characterization

[0293] In some embodiments, Form 9 of Compound A is characterized by an endothermic event with an onset at 149 ± 20 °C, 149 ± 15 °C, 149 ± 10 °C, or 149 ± 5 °C (e.g., about 149 °C), as measured by DSC.

[0294] *Other Characterizations* In some embodiments, Form 9 is obtained from heating Form 3 at 120 °C.

Form 10

[0295] In some embodiments, the morphic form of Compound A is anhydrous Form 10.

X-Ray Powder Diffraction (XRPD) Characterizations

[0296] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.3 ± 0.5 , and 17.5 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 8.3 ± 0.2 , and 17.5 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 8.3 ± 0.1 , and 17.5 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 8.3, and 17.5 °2 θ using Cu K α radiation))).

[0297] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.3 ± 0.5 , 17.5 ± 0.5 , and 19.2 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 8.3 ± 0.2 , 17.5 ± 0.2 , and 19.2 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 8.3 ± 0.1 , 17.5 ± 0.1 , and 19.2 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 8.3, 17.5, and 19.2 °2 θ using Cu K α radiation))).

[0298] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.3 ± 0.5 , 14.9 ± 0.5 , 17.5 ± 0.5 , and 19.2 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 8.3 ± 0.2 , 14.9 ± 0.2 , 17.5 ± 0.2 , and 19.2 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 8.3 ± 0.1 , 14.9 ± 0.1 , 17.5 ± 0.1 , and 19.2 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 8.3, 14.9, 17.5, and 19.2 °2 θ using Cu K α radiation))).

[0299] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 4.7 ± 0.5 , 8.3 ± 0.5 , 14.9 ± 0.5 , 17.5 ± 0.5 , and 19.2 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 4.7 ± 0.2 , 8.3 ± 0.2 , 14.9 ± 0.2 , 17.5 ± 0.2 , and 19.2 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 4.7 ± 0.1 , 8.3 ± 0.1 , 14.9 ± 0.1 , 17.5 ± 0.1 , and 19.2 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 4.7, 8.3, 14.9, 17.5, and 19.2 °2 θ using Cu K α radiation))).

[0300] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 4.7 ± 0.5 , 7.4 ± 0.5 , 8.3 ± 0.5 , 14.9 ± 0.5 , 17.5 ± 0.5 , and 19.2 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 4.7 ± 0.2 , 7.4 ± 0.2 , 8.3 ± 0.2 , 14.9 ± 0.2 , 17.5 ± 0.2 , and 19.2 ± 0.2 °2 θ using Cu

K α radiation (e.g., 4.4 ± 0.1 , 4.7 ± 0.1 , 7.4 ± 0.1 , 8.3 ± 0.1 , 14.9 ± 0.1 , 17.5 ± 0.1 , and 19.2 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 4.7, 7.4, 8.3, 14.9, 17.5, and 19.2 °2 θ using Cu K α radiation))).

[0301] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 4.7 ± 0.5 , 7.4 ± 0.5 , 8.3 ± 0.5 , 14.9 ± 0.5 , 17.5 ± 0.5 , 19.2 ± 0.5 , and 23.3 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 4.7 ± 0.2 , 7.4 ± 0.2 , 8.3 ± 0.2 , 14.9 ± 0.2 , 17.5 ± 0.2 , 19.2 ± 0.2 , and 23.3 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 4.7 ± 0.1 , 7.4 ± 0.1 , 8.3 ± 0.1 , 14.9 ± 0.1 , 17.5 ± 0.1 , 19.2 ± 0.1 , and 23.3 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 4.7, 7.4, 8.3, 14.9, 17.5, 19.2, and 23.3 °2 θ using Cu K α radiation))).

[0302] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern having at least one signal selected from 4.4 ± 0.5 , 8.3 ± 0.5 , and 17.5 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 8.3 ± 0.2 , and 17.5 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 8.3 ± 0.1 , and 17.5 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 8.3, and 17.5 °2 θ using Cu K α radiation))).

[0303] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern having at least two signals selected from 4.4 ± 0.5 , 8.3 ± 0.5 , and 17.5 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 8.3 ± 0.2 , and 17.5 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 8.3 ± 0.1 , and 17.5 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 8.3, and 17.5 °2 θ using Cu K α radiation))).

[0304] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern having at least three signals selected from 4.4 ± 0.5 , 8.3 ± 0.5 , 17.5 ± 0.5 , and 19.2 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 8.3 ± 0.2 , 17.5 ± 0.2 , and 19.2 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 8.3 ± 0.1 , 17.5 ± 0.1 , and 19.2 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 8.3, 17.5, and 19.2 °2 θ using Cu K α radiation))).

[0305] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern having at least four signals selected from 4.4 ± 0.5 , 8.3 ± 0.5 , 14.9 ± 0.5 , 17.5 ± 0.5 , and 19.2 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 8.3 ± 0.2 , 14.9 ± 0.2 , 17.5 ± 0.2 , and 19.2 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 8.3 ± 0.1 , 14.9 ± 0.1 , 17.5 ± 0.1 , and 19.2 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 8.3, 14.9, 17.5, and 19.2 °2 θ using Cu K α radiation))).

[0306] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern having at least five signals selected from 4.4 ± 0.5 , 4.7 ± 0.5 , 8.3 ± 0.5 , 14.9 ± 0.5 , 17.5 ± 0.5 , and 19.2 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 4.7 ± 0.2 , 8.3 ± 0.2 , 14.9 ± 0.2 , 17.5 ± 0.2 , and 19.2 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 4.7 ± 0.1 , 8.3 ± 0.1 , 14.9 ± 0.1 , 17.5 ± 0.1 , and 19.2 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 4.7, 8.3, 14.9, 17.5, and 19.2 °2 θ using Cu K α radiation))).

[0307] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern having at least five signals selected from 4.4 ± 0.5 , 4.7 ± 0.5 , 7.4 ± 0.5 , 8.3 ± 0.5 , 14.9 ± 0.5 , 17.5 ± 0.5 , and 19.2 ± 0.5 °2 θ (e.g., 4.4 ± 0.2 , 4.7 ± 0.2 , 7.4 ± 0.2 , 8.3 ± 0.2 , 14.9 ± 0.2 , 17.5 ± 0.2 , and 19.2 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.4 ± 0.1 , 4.7 ± 0.1 , 7.4 ± 0.1 , 8.3 ± 0.1 , 14.9 ± 0.1 , 17.5 ± 0.1 , and 19.2 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.4, 4.7, 7.4, 8.3, 14.9, 17.5, and 19.2 °2 θ using Cu K α radiation))).

[0308] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern comprising one or more signals as described in Table 5 below.

[0309] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern comprising two or more signals as described in Table 5 below.

[0310] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern comprising three or more signals as described in Table 5 below.

[0311] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern comprising four or more signals as described in Table 5 below.

Table 5 XRPD Signals for Anhydrous Form 10

Angle (° 2 θ)	Intensity (%)	Angle (° 2 θ)	Intensity (%)
4.4	100.0	16.5	7.6
4.7	15.2	17.5	23.8
7.4	13.7	17.8	8.9
8.3	36.4	19.2	22.5
11.2	4.7	19.6	10.0
11.8	7.0	20.4	9.6
12.0	8.9	20.9	9.3
12.6	5.4	21.4	10.6
13.1	9.3	22.1	10.6
14.9	17.4	23.3	13.4
15.6	9.4	26.3	8.8
16.1	6.5		

*The values shown in the above table are approximate value and subject to instrument differentiation and standard error.

[0312] In some embodiments, Form 10 of Compound A is characterized by an XRPD pattern substantially similar to that set forth in FIG. 27.

DSC Characterizations

[0313] In some embodiments, Form 10 of Compound A is characterized by an endothermic event with an onset at 149 ± 20 °C, 149 ± 15 °C, 149 ± 10 °C, or 149 ± 5 °C (e.g., about 149 °C), as measured by DSC.

[0314] In some embodiments, Form 10 of Compound A is characterized by an endothermic event with an onset at 165 ± 20 °C, 165 ± 15 °C, 165 ± 10 °C, or 165 ± 5 °C (e.g., about 165 °C), as measured by DSC.

Other Characterizations

[0315] In some embodiments, Form 10 is formed when a solvate of Compound A is heated between about 70 °C to about 100 °C.

[0316] In some embodiments, Form 10 is formed when Form 7 is heated between about 70 °C to about 100 °C.

[0317] In some embodiments, Form 10 is obtained from heating Form 7 between 70 and 100 °C.

Form 12

[0318] In some embodiments, the morphic form of Compound A is anhydrous Form 12.

X-Ray Powder Diffraction (XRPD) Characterizations

[0319] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising signals at 4.1 ± 0.5 , 4.7 ± 0.5 , and 8.2 ± 0.5 °2 θ (e.g., 4.1 ± 0.2 , 4.7 ± 0.2 , and 8.2 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.1 ± 0.1 , 4.7 ± 0.1 , and 8.2 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.1, 4.7, and 8.2 °2 θ using Cu K α radiation))).

[0320] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising signals at 4.1 ± 0.5 , 4.7 ± 0.5 , 8.2 ± 0.5 , and 8.7 ± 0.5 °2 θ (e.g., 4.1 ± 0.2 , 4.7 ± 0.2 , 8.2 ± 0.2 , and 8.7 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.1 ± 0.1 , 4.7 ± 0.1 , 8.2 ± 0.1 , and 8.7 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.1, 4.7, 8.2, and 8.7 °2 θ using Cu K α radiation))).

[0321] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising signals at 4.1 ± 0.5 , 4.7 ± 0.5 , 8.2 ± 0.5 , 8.7 ± 0.5 , and 12.4 ± 0.5 °2 θ (e.g., 4.1 ± 0.2 , 4.7 ± 0.2 , 8.2 ± 0.2 , 8.7 ± 0.2 , and 12.4 ± 0.2 °2 θ using Cu K α radiation (e.g., 4.1 ± 0.1 , 4.7 ± 0.1 , 8.2 ± 0.1 , 8.7 ± 0.1 , and 12.4 ± 0.1 °2 θ using Cu K α radiation (e.g., 4.1, 4.7, 8.2, 8.7, and 12.4 °2 θ using Cu K α radiation))).

[0322] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising signals at 4.1 ± 0.5 , 4.7 ± 0.5 , 8.2 ± 0.5 , 8.7 ± 0.5 , 10.2 ± 0.5 , and 12.4 ± 0.5 $^{\circ}2\theta$ (e.g., 4.1 ± 0.2 , 4.7 ± 0.2 , 8.2 ± 0.2 , 8.7 ± 0.2 , 10.2 ± 0.2 , and 12.4 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1 ± 0.1 , 4.7 ± 0.1 , 8.2 ± 0.1 , 8.7 ± 0.1 , 10.2 ± 0.1 , and 12.4 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1, 4.7, 8.2, 8.7, 10.2, and 12.4 $^{\circ}2\theta$ using Cu K α radiation))).

[0323] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising signals at 4.1 ± 0.5 , 4.7 ± 0.5 , 8.2 ± 0.5 , 8.7 ± 0.5 , 10.2 ± 0.5 , 11.3 ± 0.5 , and 12.4 ± 0.5 $^{\circ}2\theta$ (e.g., 4.1 ± 0.2 , 4.7 ± 0.2 , 8.2 ± 0.2 , 8.7 ± 0.2 , 10.2 ± 0.2 , 11.3 ± 0.2 , and 12.4 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1 ± 0.1 , 4.7 ± 0.1 , 8.2 ± 0.1 , 8.7 ± 0.1 , 10.2 ± 0.1 , 11.3 ± 0.1 , and 12.4 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1, 4.7, 8.2, 8.7, 10.2, 11.3, and 12.4 $^{\circ}2\theta$ using Cu K α radiation))).

[0324] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising signals at 4.1 ± 0.5 , 4.7 ± 0.5 , 8.2 ± 0.5 , 8.7 ± 0.5 , 10.2 ± 0.5 , 11.3 ± 0.5 , 12.4 ± 0.5 , and 18.8 ± 0.5 $^{\circ}2\theta$ (e.g., 4.1 ± 0.2 , 4.7 ± 0.2 , 8.2 ± 0.2 , 8.7 ± 0.2 , 10.2 ± 0.2 , 11.3 ± 0.2 , 12.4 ± 0.2 , and 18.8 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1 ± 0.1 , 4.7 ± 0.1 , 8.2 ± 0.1 , 8.7 ± 0.1 , 10.2 ± 0.1 , 11.3 ± 0.1 , 12.4 ± 0.1 , and 18.8 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1, 4.7, 8.2, 8.7, 10.2, 11.3, 12.4, and 18.8 $^{\circ}2\theta$ using Cu K α radiation))).

[0325] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least one signal selected from 4.1 ± 0.5 , 4.7 ± 0.5 , and 8.2 ± 0.5 $^{\circ}2\theta$ (e.g., 4.1 ± 0.2 , 4.7 ± 0.2 , and 8.2 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1 ± 0.1 , 4.7 ± 0.1 , and 8.2 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1, 4.7, and 8.2 $^{\circ}2\theta$ using Cu K α radiation))).

[0326] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least two signals selected from 4.1 ± 0.5 , 4.7 ± 0.5 , and 8.2 ± 0.5 $^{\circ}2\theta$ (e.g., 4.1 ± 0.2 , 4.7 ± 0.2 , and 8.2 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1 ± 0.1 , 4.7 ± 0.1 , and 8.2 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1, 4.7, and 8.2 $^{\circ}2\theta$ using Cu K α radiation))).

[0327] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least three signals selected from 4.1 ± 0.5 , 4.7 ± 0.5 , 8.2 ± 0.5 , and 8.7 ± 0.5 $^{\circ}2\theta$ (e.g., 4.1 ± 0.2 , 4.7 ± 0.2 , 8.2 ± 0.2 , and 8.7 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1 ± 0.1 , 4.7 ± 0.1 , 8.2 ± 0.1 , and 8.7 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1, 4.7, 8.2, and 8.7 $^{\circ}2\theta$ using Cu K α radiation))).

[0328] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least four signals selected from 4.1 ± 0.5 , 4.7 ± 0.5 , 8.2 ± 0.5 , 8.7 ± 0.5 , and 12.4 ± 0.5 $^{\circ}2\theta$ (e.g., 4.1 ± 0.2 , 4.7 ± 0.2 , 8.2 ± 0.2 , 8.7 ± 0.2 , and 12.4 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g.,

4.1±0.1, 4.7±0.1, 8.2±0.1, 8.7±0.1, and 12.4±0.1 °2θ using Cu Kα radiation (e.g., 4.1, 4.7, 8.2, 8.7, and 12.4 °2θ using Cu Kα radiation))).

[0329] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least five signals selected from 4.1±0.5, 4.7±0.5, 8.2±0.5, 8.7±0.5, 10.2±0.5, and 12.4±0.5 °2θ (e.g., 4.1±0.2, 4.7±0.2, 8.2±0.2, 8.7±0.2, 10.2±0.2, and 12.4±0.2 °2θ using Cu Kα radiation (e.g., 4.1±0.1, 4.7±0.1, 8.2±0.1, 8.7±0.1, 10.2±0.1, and 12.4±0.1 °2θ using Cu Kα radiation (e.g., 4.1, 4.7, 8.2, 8.7, 10.2, and 12.4 °2θ using Cu Kα radiation))).

[0330] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least six signals selected from 4.1±0.5, 4.7±0.5, 8.2±0.5, 8.7±0.5, 10.2±0.5, 11.3±0.5, and 12.4±0.5 °2θ (e.g., 4.1±0.2, 4.7±0.2, 8.2±0.2, 8.7±0.2, 10.2±0.2, 11.3±0.2, and 12.4±0.2 °2θ using Cu Kα radiation (e.g., 4.1±0.1, 4.7±0.1, 8.2±0.1, 8.7±0.1, 10.2±0.1, 11.3±0.1, and 12.4±0.1 °2θ using Cu Kα radiation (e.g., 4.1, 4.7, 8.2, 8.7, 10.2, 11.3, and 12.4 °2θ using Cu Kα radiation))).

[0331] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising signals at 4.1±0.5, 8.2±0.5, and 8.7±0.5 °2θ (e.g., 4.1±0.2, 8.2±0.2, and 8.7±0.2 °2θ using Cu Kα radiation (e.g., 4.1±0.1, 8.2±0.1, and 8.7±0.1 °2θ using Cu Kα radiation (e.g., 4.1, 8.2, and 8.7 °2θ using Cu Kα radiation))).

[0332] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising signals at 4.1±0.5, 8.2±0.5, 8.7±0.5, and 12.4±0.5 °2θ (e.g., 4.1±0.2, 8.2±0.2, 8.7±0.2, and 12.4±0.2 °2θ using Cu Kα radiation (e.g., 4.1±0.1, 8.2±0.1, 8.7±0.1, and 12.4±0.1 °2θ using Cu Kα radiation (e.g., 4.1, 8.2, 8.7, and 12.4 °2θ using Cu Kα radiation))).

[0333] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising signals at 4.1±0.5, 8.2±0.5, 8.7±0.5, 10.2±0.5, and 12.4±0.5 °2θ (e.g., 4.1±0.2, 8.2±0.2, 8.7±0.2, 10.2±0.2, and 12.4±0.2 °2θ using Cu Kα radiation (e.g., 4.1±0.1, 8.2±0.1, 8.7±0.1, 10.2±0.1, and 12.4±0.1 °2θ using Cu Kα radiation (e.g., 4.1, 8.2, 8.7, 10.2, and 12.4 °2θ using Cu Kα radiation))).

[0334] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising signals at 4.1±0.5, 8.2±0.5, 8.7±0.5, 10.2±0.5, 11.3±0.5, and 12.4±0.5 °2θ (e.g., 4.1±0.2, 8.2±0.2, 8.7±0.2, 10.2±0.2, 11.3±0.2, and 12.4±0.2 °2θ using Cu Kα radiation (e.g., 4.1±0.1, 8.2±0.1, 8.7±0.1, 10.2±0.1, 11.3±0.1, and 12.4±0.1 °2θ using Cu Kα radiation (e.g., 4.1, 8.2, 8.7, 10.2, 11.3, and 12.4 °2θ using Cu Kα radiation))).

[0335] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising signals at 4.1 ± 0.5 , 8.2 ± 0.5 , 8.7 ± 0.5 , 10.2 ± 0.5 , 11.3 ± 0.5 , 12.4 ± 0.5 , and 18.8 ± 0.5 $^{\circ}2\theta$ (e.g., 4.1 ± 0.2 , 8.2 ± 0.2 , 8.7 ± 0.2 , 10.2 ± 0.2 , 11.3 ± 0.2 , 12.4 ± 0.2 , and 18.8 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1 ± 0.1 , 8.2 ± 0.1 , 8.7 ± 0.1 , 10.2 ± 0.1 , 11.3 ± 0.1 , 12.4 ± 0.1 , and 18.8 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1, 8.2, 8.7, 10.2, 11.3, 12.4, and 18.8 $^{\circ}2\theta$ using Cu K α radiation))).

[0336] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least one signal selected from 4.1 ± 0.5 , 8.2 ± 0.5 , and 8.7 ± 0.5 $^{\circ}2\theta$ (e.g., 4.1 ± 0.2 , 8.2 ± 0.2 , and 8.7 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1 ± 0.1 , 8.2 ± 0.1 , and 8.7 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1, 8.2, and 8.7 $^{\circ}2\theta$ using Cu K α radiation))).

[0337] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least two signals selected from 4.1 ± 0.5 , 8.2 ± 0.5 , and 8.7 ± 0.5 $^{\circ}2\theta$ (e.g., 4.1 ± 0.2 , 8.2 ± 0.2 , and 8.7 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1 ± 0.1 , 8.2 ± 0.1 , and 8.7 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1, 8.2, and 8.7 $^{\circ}2\theta$ using Cu K α radiation))).

[0338] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least three signals selected from 4.1 ± 0.5 , 8.2 ± 0.5 , 8.7 ± 0.5 , and 12.4 ± 0.5 $^{\circ}2\theta$ (e.g., 4.1 ± 0.2 , 8.2 ± 0.2 , 8.7 ± 0.2 , and 12.4 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1 ± 0.1 , 8.2 ± 0.1 , 8.7 ± 0.1 , and 12.4 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1, 8.2, 8.7, and 12.4 $^{\circ}2\theta$ using Cu K α radiation))).

[0339] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least four signals selected from 4.1 ± 0.5 , 8.2 ± 0.5 , 8.7 ± 0.5 , 10.2 ± 0.5 , and 12.4 ± 0.5 $^{\circ}2\theta$ (e.g., 4.1 ± 0.2 , 8.2 ± 0.2 , 8.7 ± 0.2 , 10.2 ± 0.2 , and 12.4 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1 ± 0.1 , 8.2 ± 0.1 , 8.7 ± 0.1 , 10.2 ± 0.1 , and 12.4 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1, 8.2, 8.7, 10.2, and 12.4 $^{\circ}2\theta$ using Cu K α radiation))).

[0340] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least five signals selected from 4.1 ± 0.5 , 8.2 ± 0.5 , 8.7 ± 0.5 , 10.2 ± 0.5 , 11.3 ± 0.5 , and 12.4 ± 0.5 $^{\circ}2\theta$ (e.g., 4.1 ± 0.2 , 8.2 ± 0.2 , 8.7 ± 0.2 , 10.2 ± 0.2 , 11.3 ± 0.2 , and 12.4 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1 ± 0.1 , 8.2 ± 0.1 , 8.7 ± 0.1 , 10.2 ± 0.1 , 11.3 ± 0.1 , and 12.4 ± 0.1 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1, 8.2, 8.7, 10.2, 11.3, and 12.4 $^{\circ}2\theta$ using Cu K α radiation))).

[0341] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least six signals selected from 4.1 ± 0.5 , 8.2 ± 0.5 , 8.7 ± 0.5 , 10.2 ± 0.5 , 11.3 ± 0.5 , 12.4 ± 0.5 , and 18.8 ± 0.5 $^{\circ}2\theta$ (e.g., 4.1 ± 0.2 , 8.2 ± 0.2 , 8.7 ± 0.2 , 10.2 ± 0.2 , 11.3 ± 0.2 , 12.4 ± 0.2 , and 18.8 ± 0.2 $^{\circ}2\theta$ using Cu K α radiation (e.g., 4.1 ± 0.1 , 8.2 ± 0.1 , 8.7 ± 0.1 , 10.2 ± 0.1 , 11.3 ± 0.1 ,

12.4±0.1, and 18.8±0.1 °2θ using Cu Kα radiation (e.g., 4.1, 8.2, 8.7, 10.2, 11.3, 12.4, and 18.8 °2θ using Cu Kα radiation))).

[0342] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising signals at 8.2±0.5 and 8.7±0.5 °2θ (e.g., 8.2±0.2 and 8.7±0.2 °2θ using Cu Kα radiation (e.g., 8.2±0.1 and 8.7±0.1 °2θ using Cu Kα radiation (e.g., 8.2 and 8.7 °2θ using Cu Kα radiation))).

[0343] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising signals at 8.2±0.5, 8.7±0.5, and 12.4±0.5 °2θ (e.g., 8.2±0.2, 8.7±0.2, and 12.4±0.2 °2θ using Cu Kα radiation (e.g., 8.2±0.1, 8.7±0.1, and 12.4±0.1 °2θ using Cu Kα radiation (e.g., 8.2, 8.7, and 12.4 °2θ using Cu Kα radiation))).

[0344] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising signals at 8.2±0.5, 8.7±0.5, 10.2±0.5, and 12.4±0.5 °2θ (e.g., 8.2±0.2, 8.7±0.2, 10.2±0.2, and 12.4±0.2 °2θ using Cu Kα radiation (e.g., 8.2±0.1, 8.7±0.1, 10.2±0.1, and 12.4±0.1 °2θ using Cu Kα radiation (e.g., 8.2, 8.7, 10.2, and 12.4 °2θ using Cu Kα radiation))).

[0345] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising signals at 8.2±0.5, 8.7±0.5, 10.2±0.5, 11.3±0.5, and 12.4±0.5 °2θ (e.g., 8.2±0.2, 8.7±0.2, 10.2±0.2, 11.3±0.2, and 12.4±0.2 °2θ using Cu Kα radiation (e.g., 8.2±0.1, 8.7±0.1, 10.2±0.1, 11.3±0.1, and 12.4±0.1 °2θ using Cu Kα radiation (e.g., 8.2, 8.7, 10.2, 11.3, and 12.4 °2θ using Cu Kα radiation))).

[0346] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising signals at 8.2±0.5, 8.7±0.5, 10.2±0.5, 11.3±0.5, 12.4±0.5, and 18.8±0.5 °2θ (e.g., 8.2±0.2, 8.7±0.2, 10.2±0.2, 11.3±0.2, 12.4±0.2, and 18.8±0.2 °2θ using Cu Kα radiation (e.g., 8.2±0.1, 8.7±0.1, 10.2±0.1, 11.3±0.1, 12.4±0.1, and 18.8±0.1 °2θ using Cu Kα radiation (e.g., 8.2, 8.7, 10.2, 11.3, 12.4, and 18.8 °2θ using Cu Kα radiation))).

[0347] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least one signal selected from 8.2±0.5 and 8.7±0.5 °2θ (e.g., 8.2±0.2 and 8.7±0.2 °2θ using Cu Kα radiation (e.g., 8.2±0.1 and 8.7±0.1 °2θ using Cu Kα radiation (e.g., 8.2 and 8.7 °2θ using Cu Kα radiation))).

[0348] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least two signals selected from 8.2±0.5, 8.7±0.5, and 12.4±0.5 °2θ (e.g., 8.2±0.2,

8.7±0.2, and 12.4±0.2 °2θ using Cu Kα radiation (e.g., 8.2±0.1, 8.7±0.1, and 12.4±0.1 °2θ using Cu Kα radiation (e.g., 8.2, 8.7, and 12.4 °2θ using Cu Kα radiation))).

[0349] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least three signals selected from 8.2±0.5, 8.7±0.5, 10.2±0.5, and 12.4±0.5 °2θ (e.g., 8.2±0.2, 8.7±0.2, 10.2±0.2, and 12.4±0.2 °2θ using Cu Kα radiation (e.g., 8.2±0.1, 8.7±0.1, 10.2±0.1, and 12.4±0.1 °2θ using Cu Kα radiation (e.g., 8.2, 8.7, 10.2, and 12.4 °2θ using Cu Kα radiation))).

[0350] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least four signals selected from 8.2±0.5, 8.7±0.5, 10.2±0.5, 11.3±0.5, and 12.4±0.5 °2θ (e.g., 8.2±0.2, 8.7±0.2, 10.2±0.2, 11.3±0.2, and 12.4±0.2 °2θ using Cu Kα radiation (e.g., 8.2±0.1, 8.7±0.1, 10.2±0.1, 11.3±0.1, and 12.4±0.1 °2θ using Cu Kα radiation (e.g., 8.2, 8.7, 10.2, 11.3, and 12.4 °2θ using Cu Kα radiation))).

[0351] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern having at least five signals selected from 8.2±0.5, 8.7±0.5, 10.2±0.5, 11.3±0.5, 12.4±0.5, and 18.8±0.5 °2θ (e.g., 8.2±0.2, 8.7±0.2, 10.2±0.2, 11.3±0.2, 12.4±0.2, and 18.8±0.2 °2θ using Cu Kα radiation (e.g., 8.2±0.1, 8.7±0.1, 10.2±0.1, 11.3±0.1, 12.4±0.1, and 18.8±0.1 °2θ using Cu Kα radiation (e.g., 8.2, 8.7, 10.2, 11.3, 12.4, and 18.8 °2θ using Cu Kα radiation))).

[0352] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern comprising one or more signals as described in Table 5-1 below.

Table 5-1 XRPD Signals for Form 12

Angle (2θ °)	Intensity (%)
4.1	16.9
4.7	100.0
6.7	3.1
8.2	51.3
8.7	15.2
10.2	8.2
10.9	3.2
11.3	6.8
12.4	10.2
14.0	3.4
15.0	4.9
16.9	2.4
18.8	6.6
20.6	3.0
22.0	6.2

Angle (2 θ °)	Intensity (%)
22.8	2.4
24.2	4.0

[0353] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern substantially similar to that set forth in FIG. 34A.

[0354] In some embodiments, Form 12 of Compound A is characterized by an XRPD pattern substantially similar to that set forth in FIG. 34B (upper trace).

TGA Characterizations

[0355] In some embodiments, Form 12 of Compound A is characterized by negligible weight loss up to 150 $\pm$ 40 °C, 150 $\pm$ 30 °C, 150 $\pm$ 20 °C, 150 $\pm$ 15 °C, 150 $\pm$ 10 °C, or 150 $\pm$ 5 °C (e.g., up to about 150 °C) followed by thermal degradation, as measured by TGA.

[0356] In some embodiments, Form 12 of Compound A is characterized by thermal degradation starting at 150 $\pm$ 40 °C, 150 $\pm$ 30 °C, 150 $\pm$ 20 °C, 150 $\pm$ 15 °C, 150 $\pm$ 10 °C, or 150 $\pm$ 5 °C (e.g., at about 150 °C), as measured by TGA.

DSC Characterizations

[0357] In some embodiments, Form 12 of Compound A is characterized by an endothermic event with an onset at 178 $\pm$ 20 °C, 178 $\pm$ 15 °C, 178 $\pm$ 10 °C, or 178 $\pm$ 5 °C (e.g., about 178 °C), as measured by DSC.

[0358] In some embodiments, Form 12 of Compound A is characterized by a melt endotherm of 185 $\pm$ 20 °C, 185 $\pm$ 15 °C, 185 $\pm$ 10 °C, or 185 $\pm$ 5 °C (e.g., about 185 °C), as measured by DSC.

Other Characterizations

[0359] In some embodiments, Form 12 of Compound A is characterized by an uptake (e.g., from 0 % to 80 % RH) of 1.0 $\pm$ 0.5 %, 1.0 $\pm$ 0.4 %, 1.0 $\pm$ 0.3 %, 1.0 $\pm$ 0.2 %, 1.0 $\pm$ 0.1 %, or 1.0 $\pm$ 0.05 % (e.g., about 1.0%), as measured by DVS.

[0360] In some embodiments, Form 12 of Compound A is characterized by an uptake (e.g., after 80 % RH) of 33 $\pm$ 5 %, 33 $\pm$ 4 %, 33 $\pm$ 3 %, 33 $\pm$ 2 %, 33 $\pm$ 1 %, or 33 $\pm$ 0.5 % (e.g., about 33 %), as measured by DVS.

[0361] In some embodiments, Form 12 of Compound A is stable up to 80% RH at 25 °C.

[0362] In some embodiments, Form 12 of Compound A is a crystalline solid.

[0363] In some embodiments, the crystalline solid Form 12 of Compound A has a needle shaped crystal morphology.

Solid Forms

[0364] In some embodiments, the morphic form of Compound A is one of the forms provided in Table 6.

[0365] In some embodiments, the morphic form of Compound A is Form 1 as prepared by the Method in Table 6.

[0366] In some embodiments, the morphic form of Compound A is Form 2 as prepared by the Method in Table 6.

[0367] In some embodiments, the morphic form of Compound A is Form 3 as prepared by the Method in Table 6.

[0368] In some embodiments, the morphic form of Compound A is Form 4 as prepared by the Method in Table 6.

[0369] In some embodiments, the morphic form of Compound A is Form 5 as prepared by the Method in Table 6.

[0370] In some embodiments, the morphic form of Compound A is Form 6 as prepared by the Method in Table 6.

[0371] In some embodiments, the morphic form of Compound A is Form 7 as prepared by the Method in Table 6.

[0372] In some embodiments, the morphic form of Compound A is Form 8 as prepared by the Method in Table 6.

[0373] In some embodiments, the morphic form of Compound A is Form 9 as prepared by the Method in Table 6.

[0374] In some embodiments, the morphic form of Compound A is Form 10 as prepared by the Method in Table 6.

[0375] In some embodiments, the morphic form of Compound A is Form 12 as prepared by the Method in Table 6.

Table 6 Solid Form Assignment for Forms Identified from Polymorph and Hydrate Screening of Compound A

Form/Pattern	Method	Assignments
Form 1	post-GVS of amorphous material, Heat Form 2 above 100 °C	Non-solvated

Form/Pattern	Method	Assignments
Form 2	25 °C/97% RH and 40 °C/75% RH, crystallization from EtOAc/water	Dihydrate
Form 3	60 °C/75% RH, LAG with water, crystallization from EtOAc/water	Monohydrate
Form 4	Various from IPA	IPA solvate
Form 5	Cool from acetone	Unknown – deliquesced after XRPD analysis
Form 6	Various from 2-Methyl-1-propanol	2-Methyl-1-propanol solvate
Form 7	Maturation 50-25 °C in Heptane/EtOH (9:1 v/v), ball milling water/MeOH	Possible solvate or mixed solvate/hydrate
Form 8	Maturation 50-25 °C in Heptane/2-Methyl-1-propanol (9:1 v/v)	2-Methyl-1-propanol solvate
Form 9	Heat Form 3 to 120 °C	Non-solvated
Form 10	Heat Form 7 Observed at 70 and 100 °C (from different samples)	Non-solvated
Form 12	Dissolving Form 4 in EtOAc and water, heating to 45 °C, cooling to 30 °C after 30 min, and aging at 30 °C for 65 h, followed by magnetic stirring of the solution	Anhydrous

Key: LAG – liquid-assisted grinding

[0376] In some embodiments, the morphic form of Compound A is prepared using one of the methods provided in FIG. 1 or the Examples.

Other Properties of the Crystalline Forms

[0377] In some embodiments, the morphic form of Compound A has a purity of about 80% or greater, about 85% or greater, about 90% or greater, about 91% or greater, about 92% or greater, about 93% or greater, about 94% or greater, about 95% or greater, about 96% or greater, about 97% or greater, about 98% or greater, about 99% or greater, about 99.1% or greater, about 99.2% or greater, about 99.3% or greater, about 99.4% or greater, about 99.5% or greater, about 99.6% or greater, about 99.7% or greater, about 99.8% or greater, or about 99.9% or greater.

[0378] In some embodiments, the morphic form of Compound A has a morphic purity of about 80% or greater, about 85% or greater, about 90% or greater, about 91% or greater, about 92% or greater, about 93% or greater, about 94% or greater, about 95% or greater, about 96% or greater, about 97% or greater, about 98% or greater, about 99% or greater, about 99.1% or greater, about 99.2% or greater, about 99.3% or greater, about 99.4% or

greater, about 99.5% or greater, about 99.6% or greater, about 99.7% or greater, about 99.8% or greater, or about 99.9% or greater.

[0379] In some embodiments, the morphic form of Compound A exhibits less than about 20%, about 15%, about 10%, about 9%, about 8%, about 7%, about 6%, about 5%, about 4%, about 3%, about 2%, about 1%, about 0.9%, about 0.8%, about 0.7%, about 0.6%, about 0.5%, about 0.4%, about 0.3%, about 0.2%, or about 0.1% impurities over 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, one week, two weeks, three weeks, one month, two months, three months, or four months.

[0380] In some embodiments, the morphic form of Compound A exhibits less than about 20%, about 15%, about 10%, about 9%, about 8%, about 7%, about 6%, about 5%, about 4%, about 3%, about 2%, about 1%, about 0.9%, about 0.8%, about 0.7%, about 0.6%, about 0.5%, about 0.4%, about 0.3%, about 0.2%, or about 0.1% of a different morphic form of Compound A over 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, one week, two weeks, three weeks, one month, two months, three months, or four months.

[0381] In some embodiments, the morphic form of Compound A exhibits less than about 20%, about 15%, about 10%, about 9%, about 8%, about 7%, about 6%, about 5%, about 4%, about 3%, about 2%, about 1%, about 0.9%, about 0.8%, about 0.7%, about 0.6%, about 0.5%, about 0.4%, about 0.3%, about 0.2%, or about 0.1% impurity, under 25 °C and 97% relative humidity (RH), over 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, one week, two weeks, three weeks, one month, two months, three months, or four months.

[0382] In some embodiments, the morphic form of Compound A exhibits less than about 20%, about 15%, about 10%, about 9%, about 8%, about 7%, about 6%, about 5%, about 4%, about 3%, about 2%, about 1%, about 0.9%, about 0.8%, about 0.7%, about 0.6%, about 0.5%, about 0.4%, about 0.3%, about 0.2%, or about 0.1% impurity, under 40 °C and 75% relative humidity (RH), over 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, one week, two weeks, three weeks, one month, two months, three months, or four months.

Methods of Preparing the Crystalline Forms

[0383] In some aspects, the present disclosure provides a method of preparing a crystalline form of Compound A described herein.

[0384] In some aspects, the present disclosure provides a method of preparing a crystalline form of Compound A, comprising one or more steps as described herein.

[0385] In some aspects, the present disclosure provides a compound obtainable by, or obtained by, or directly obtained by a method for preparing a crystalline form of Compound A as described herein (See, e.g., FIG. 1).

[0386] In some embodiments, the prepared crystalline form of Compound A has a higher purity as compared to Compound A being prepared by a comparable method (e.g., by 1% or greater, 2% or greater, 3% or greater, 4% or greater, 5% or greater, 10% or greater, 15% or greater, 20% or greater, 25% or greater, 30% or greater, 35% or greater, 40% or greater, 45% or greater, or 50% or greater).

[0387] In some embodiments, the prepared crystalline form of Compound A has a higher morphic purity as compared to Compound A being prepared by a comparable method (e.g., by 1% or greater, 2% or greater, 3% or greater, 4% or greater, 5% or greater, 10% or greater, 15% or greater, 20% or greater, 25% or greater, 30% or greater, 35% or greater, 40% or greater, 45% or greater, or 50% or greater).

[0388] In some embodiments, the morphic form of Compound A exhibits fewer impurities as compared to Compound A being prepared by a comparable method (e.g., by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, or about 50%), under 25 °C and 97% relative humidity (RH), over 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, one week, two weeks, three weeks, one month, two months, three months, or four months.

[0389] In some embodiments, the morphic form of Compound A exhibits less impurity as compared to Compound A being prepared by a comparable method (e.g., by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, or about 50%), under 40 °C and 75% relative humidity (RH), over 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, one week, two weeks, three weeks, one month, two months, three months, or four months.

[0390] The crystalline form of Compound A can be prepared by any suitable technique known in the art. Particular processes for the preparation of these compounds are described further in the accompanying examples.

[0391] Conveniently, the reaction of the compounds is carried out in the presence of a suitable solvent, which is preferably inert under the respective reaction conditions. Examples of suitable solvents comprise but are not limited to hydrocarbons, such as hexane, petroleum ether, benzene, toluene or xylene; chlorinated hydrocarbons, such as trichloroethylene, 1,2-dichloroethane, tetrachloromethane, chloroform or dichloromethane; alcohols, such as methanol, ethanol, isopropanol, n-propanol, n-butanol or tert-butanol; ethers, such as diethyl

ether, diisopropyl ether, tetrahydrofuran (THF), 2-methyltetrahydrofuran, cyclopentylmethyl ether (CPME), methyl tert-butyl ether (MTBE) or dioxane; glycol ethers, such as ethylene glycol monomethyl or monoethyl ether or ethylene glycol dimethyl ether (diglyme); ketones, such as acetone, methylisobutylketone (MIBK) or butanone; amides, such as acetamide, dimethylacetamide, dimethylformamide (DMF) or N-methylpyrrolidinone (NMP); nitriles, such as acetonitrile; sulphoxides, such as dimethyl sulphoxide (DMSO); nitro compounds, such as nitromethane or nitrobenzene; esters, such as ethyl acetate or methyl acetate, or mixtures of the said solvents or mixtures with water.

[0392] Reaction times are generally in the range between a fraction of a minute and several days, depending on the reactivity of the respective compounds and the respective reaction conditions. Suitable reaction times are readily determinable by methods known in the art, for example reaction monitoring. Based on the reaction temperatures given above, suitable reaction times generally lie in the range between about 5 minutes and about 48 hours.

Biological Assays

[0393] Compounds described herein can be characterised using a variety of assays known to those skilled in the art to determine whether the compounds have biological activity. For example, the molecules can be characterised by conventional assays, including but not limited to those assays described below, to determine whether they have a predicted activity, binding activity and/or binding specificity.

[0394] Furthermore, high-throughput screening can be used to speed up analysis using such assays. As a result, it can be possible to rapidly screen the molecules described herein for activity, using techniques known in the art. General methodologies for performing high-throughput screening are described, for example, in Devlin (1998) High Throughput Screening, Marcel Dekker; and U.S. Patent No. 5,763,263. High-throughput assays can use one or more different assay techniques including, but not limited to, those described below.

[0395] Various *in vitro* or *in vivo* biological assays may be suitable for detecting the effect of the compounds of the present disclosure. These *in vitro* or *in vivo* biological assays can include, but are not limited to, enzymatic activity assays, electrophoretic mobility shift assays, reporter gene assays, *in vitro* cell viability assays, and the assays described herein.

[0396] In some embodiments, the biological assay is a biological assay testing inhibitory activity against IL-1 β release upon NLRP3 activation in peripheral blood mononuclear cells (PBMC).

[0397] In some embodiments, the biological assay is a PBMC IC₅₀ Determination Assay.

[0398] In some embodiments, the compound is tested for their inhibitory activity against IL-1 β release upon NLRP3 activation in blood cells (e.g., peripheral blood mononuclear cells (PBMC)).

[0399] In some embodiments, PBMC are isolated and seeded into the wells of a plate and incubated for a period of time (e.g., for 3 hours with a lipopolysaccharide). Following incubation, the medium is exchanged and the compound added to the well (e.g., a compound of the present disclosure) and the cells may be incubated. Next, the cells are stimulated (e.g., with ATP or nigericin) and the cell culture media are collected for analysis.

[0400] In some embodiments, the release of IL-1 β into the media is determined by a quantitative detection of IL-1 β in the media (e.g., using ELISA).

[0401] In some embodiments, PBMC are isolated (e.g., from buffy coats). Isolated cells are seeded into wells and incubated (e.g., for 3 hours with lipopolysaccharide). The compound is then be added and the cells incubated. Next, the cells are stimulated and the media from the wells are collected for analysis.

[0402] In some embodiments, the release of IL-1 β into the media is determined by quantitative detection (e.g., of IL-1 β in media using HTRF®).

Compositions

[0403] In some embodiments, the composition comprises a mixture of Forms of Compound A.

[0404] In some embodiments, the composition comprises a mixture of morphic forms of Compound A provided in Table 6.

[0405] In some embodiments, the composition comprises a mixture of Form 1 and one more additional form of Compound A provided in Table 6.

[0406] In some embodiments, the composition comprises a mixture of Form 2 and one more additional form of Compound A provided in Table 6.

[0407] In some embodiments, the composition comprises a mixture of Form 3 and one more additional form of Compound A provided in Table 6.

[0408] In some embodiments, the composition comprises a mixture of Form 4 and one more additional form of Compound A provided in Table 6.

[0409] In some embodiments, the composition comprises a mixture of Form 5 and one more additional form of Compound A provided in Table 6.

[0410] In some embodiments, the composition comprises a mixture of Form 6 and one more additional form of Compound A provided in Table 6.

[0411] In some embodiments, the composition comprises a mixture of Form 7 and one more additional form of Compound A provided in Table 6.

[0412] In some embodiments, the composition comprises a mixture of Form 8 and one more additional form of Compound A provided in Table 6.

[0413] In some embodiments, the composition comprises a mixture of Form 9 and one more additional form of Compound A provided in Table 6.

[0414] In some embodiments, the composition comprises a mixture of Form 10 and one more additional form of Compound A provided in Table 6.

[0415] In some embodiments, the composition comprises a mixture of Form 12 and one more additional form of Compound A provided in Table 6.

[0416] In some embodiments, the composition is a pharmaceutical composition.

[0417] In some aspects, the present disclosure provides pharmaceutical compositions comprising a crystalline form of Compound A described herein, and one or more pharmaceutically acceptable carrier, diluent, or excipient.

[0418] The pharmaceutical compositions containing active compounds of the present disclosure may be manufactured in a manner that is generally known, *e.g.*, by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping, or lyophilizing processes. Pharmaceutical compositions may be formulated in a conventional manner using one or more pharmaceutically acceptable carrier comprising one or more excipient and/or auxiliary that facilitates processing of the active compound into preparations that can be used pharmaceutically. A person with skill in the art would understand that the appropriate formulation may be dependent upon the route of administration chosen.

[0419] Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers may include physiological saline, bacteriostatic water, Cremophor EL (BASF, Parsippany, N.J.) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringeability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating

such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol and sorbitol, and sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

[0420] Sterile injectable solutions can be prepared by incorporating the active compound in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle that contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, methods of preparation are vacuum drying and freeze-drying that yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

[0421] Oral compositions may include one or more inert diluent or one or more edible pharmaceutically acceptable carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

[0422] For administration by inhalation, the compounds are delivered in the form of an aerosol spray from a pressurized container or dispenser, which contains a suitable propellant, *e.g.*, a gas such as carbon dioxide, or a nebulizer.

[0423] Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be

permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

[0424] The active compounds can be prepared with one or more pharmaceutically acceptable carrier that may protect the compound against rapid elimination from the body, such as a controlled release formulation, including an implant and microencapsulated delivery system. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art.

[0425] It may be especially advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the disclosure is dictated by and directly dependent on the unique characteristics of the active compound and the particular therapeutic effect to be achieved.

[0426] In therapeutic applications, the dosages of the pharmaceutical compositions used in accordance with the disclosure vary depending on the agent, the age, weight, and clinical condition of the recipient patient, and the experience and judgment of the clinician or practitioner administering the therapy, among other factors affecting the selected dosage. Generally, the dose should be sufficient to result in slowing, and preferably regressing, the symptoms of the disease and also preferably causing complete regression of the disease.

[0427] It is understood that the pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

Methods of Use

[0428] In some aspects, the present disclosure provides a method of preventing or treating a disease or disorder in a subject, comprising administering to the subject a pharmaceutically effective amount of a morphic form of Compound A described herein.

[0429] In some aspects, the present disclosure provides a method of treating a disease or disorder in a subject, comprising administering to the subject a pharmaceutically effective amount of a morphic form of Compound A described herein.

[0430] In some aspects, the present disclosure provides a method of preventing or treating a disease or disorder in a subject, comprising administering to the subject a morphic form of Compound A described herein.

[0431] In some aspects, the present disclosure provides a method of treating a disease or disorder in a subject, comprising administering to the subject a morphic form of Compound A described herein.

[0432] In some aspects, the present disclosure provides a morphic form of Compound A described herein for use in preventing or treating a disease or disorder in a subject.

[0433] In some aspects, the present disclosure provides a morphic form of Compound A described herein for use in treating a disease or disorder in a subject.

[0434] In some aspects, the present disclosure provides use of a morphic form of Compound A described herein in the manufacture of a medicament for preventing or treating a disease or disorder in a subject.

[0435] In some aspects, the present disclosure provides use of a morphic form of Compound A described herein in the manufacture of a medicament for treating a disease or disorder in a subject.

[0436] In some aspects, the present disclosure provides use of a morphic form of Compound A described herein for preventing or treating a disease or disorder in a subject.

[0437] In some aspects, the present disclosure provides use of a morphic form of Compound A described herein for treating a disease or disorder in a subject.

[0438] In some embodiments, the disease or disorder is associated with an implicated inflammasome activity. In some embodiments, the disease or disorder is a disease or disorder in which inflammasome activity is implicated.

[0439] In some embodiments, the disease or disorder is an inflammatory disorder, autoinflammatory disorder, an autoimmune disorder, a neurodegenerative disease, or cancer.

[0440] In some embodiments, the disease or disorder is an inflammatory disorder, autoinflammatory disorder and/or an autoimmune disorder.

[0441] In some embodiments, the disease or disorder is selected from cryopyrin-associated autoinflammatory syndrome (CAPS; e.g., familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), chronic infantile neurological cutaneous and articular (CINCA) syndrome/ neonatal-onset multisystem inflammatory disease (NOMID)), familial

Mediterranean fever (FMF), nonalcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), gout, rheumatoid arthritis, osteoarthritis, Crohn's disease, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), fibrosis, obesity, type 2 diabetes, multiple sclerosis, dermatological disease (e.g., acne), neuroinflammation occurring in protein misfolding diseases (e.g., Prion diseases and ocular (eye) disease(s)).

[0442] In some embodiments, the disease or disorder is a neurodegenerative disease.

[0443] In some embodiments, the disease or disorder is Parkinson's disease or Alzheimer's disease.

[0444] In some embodiments, the disease or disorder is a dermatological disease.

[0445] In some embodiments, the dermatological disease is acne.

[0446] In some embodiments, the disease or disorder is cancer.

[0447] In some embodiments, the disease or disorder is an ocular (eye) disease.

[0448] In some embodiments, the ocular (eye) disease is macular degeneration, diabetic retinopathy, Behçet's disease, uveitis, xerophthalmia, glaucoma, or ocular hypertension.

[0449] In some embodiments, the cancer is metastasising cancer, gastrointestinal cancer, skin cancer, non-small-cell lung carcinoma, brain cancer (e.g. glioblastoma) or colorectal adenocarcinoma.

[0450] In some aspects, the present disclosure provides a method of inhibiting inflammasome (e.g., the NLRP3 inflammasome) activity in a subject (e.g., in vitro or in vivo), comprising contacting a cell with an effective amount of a crystalline form of Compound A.

[0451] In some aspects, the present disclosure provides a crystalline form of Compound A described herein for use in inhibiting inflammasome (e.g., the NLRP3 inflammasome) activity in a subject (e.g., in vitro or in vivo).

[0452] In some aspects, the present disclosure provides use of a crystalline form of Compound A described herein in the manufacture of a medicament for inhibiting inflammasome (e.g., the NLRP3 inflammasome) activity (e.g., in vitro or in vivo).

[0453] In some embodiments, the inflammasome is NLRP3 inflammasome.

[0454] In some embodiments, the subject is an animal.

[0455] In some embodiments, the subject is a mammal.

[0456] In some embodiments, the subject is a human.

[0457] In some embodiments, the subject is a cell.

[0458] In some embodiments, the subject is a cell population.

Definitions

[0459] Unless otherwise stated, the following terms used in the specification and claims have the following meanings set out below.

[0460] It is understood that the compounds of the present disclosure can exist in either hydrated or unhydrated (the anhydrous) form or as solvates with other solvent molecules. Nonlimiting examples of hydrates may include monohydrates and dihydrates. Nonlimiting examples of solvates may include ethanol solvates and acetone solvates.

[0461] As used herein, the expressions “one or more of A, B, or C,” “one or more A, B, or C,” “one or more of A, B, and C,” “one or more A, B, and C,” “selected from the group consisting of A, B, and C”, “selected from A, B, and C”, and the like are used interchangeably and all refer to a selection from a group consisting of A, B, and/or C, i.e., one or more As, one or more Bs, one or more Cs, or any combination thereof, unless indicated otherwise.

[0462] Terms of degree such as "about," "substantially" (e.g., “substantially similar”), and "approximately" as used herein mean a reasonable amount of deviation of the modified term such that the end result is not significantly changed. These terms of degree should be construed as including a deviation of at least $\pm 5\%$ of the modified term if this deviation would not negate the meaning of the word it modifies.

[0463] It is to be understood that the present disclosure provides methods for the synthesis of a crystalline form of Compound A.

[0464] It is to be understood that, throughout the description, where compositions are described as having, including, or comprising specific components, it is contemplated that compositions also consist essentially of, or consist of, the recited components. Similarly, where methods or processes are described as having, including, or comprising specific process steps, the processes also consist essentially of, or consist of, the recited processing steps. Further, it should be understood that the order of steps or order for performing certain actions is immaterial so long as the invention remains operable. Moreover, two or more steps or actions can be conducted simultaneously.

[0465] It is to be understood that the synthetic processes of the disclosure can tolerate a wide variety of functional groups, therefore, various substituted starting materials can be used.

[0466] It is to be understood that a crystalline form of Compound A can be prepared in a variety of ways using commercially available starting materials, compounds known in the literature, or from readily prepared intermediates, by employing standard synthetic methods and procedures either known to those skilled in the art, or which will be apparent to the

skilled artisan in light of the teachings herein. Standard synthetic methods and procedures for the preparation of organic molecules and functional group transformations and manipulations can be obtained from the relevant scientific literature or from standard textbooks in the field. Although not limited to any one or several sources, classic texts such as Smith, M. B., March, J., *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 5th edition, John Wiley & Sons: New York, 2001; Greene, T.W., Wuts, P.G. M., *Protective Groups in Organic Synthesis*, 3rd edition, John Wiley & Sons: New York, 1999; R. Larock, *Comprehensive Organic Transformations*, VCH Publishers (1989); L. Fieser and M. Fieser, *Fieser and Fieser's Reagents for Organic Synthesis*, John Wiley and Sons (1994); and L. Paquette, ed., *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons (1995), incorporated by reference herein, are useful and recognised reference textbooks of organic synthesis known to those in the art

[0467] One of ordinary skill in the art will note that, during the reaction sequences and synthetic scheme described herein, the order of certain steps may be changed, such as the introduction and removal of protecting groups. One of ordinary skill in the art will recognise that certain groups may require protection from the reaction conditions via the use of protecting groups. Protecting groups may also be used to differentiate similar functional groups in molecules. A list of protecting groups and how to introduce and remove these groups can be found in Greene, T.W., Wuts, P.G. M., *Protective Groups in Organic Synthesis*, 3rd edition, John Wiley & Sons: New York, 1999.

[0468] It is to be understood that, unless otherwise stated, any description of a method of treatment or prevention includes use of a crystalline form of Compound A to provide such treatment or prevention as is described herein. It is to be further understood, unless otherwise stated, any description of a method of treatment or prevention includes use of a crystalline form of Compound A to prepare a medicament to treat or prevent such condition. The treatment or prevention includes treatment or prevention of human or non-human animals including rodents and other disease models.

[0469] It is to be understood that, unless otherwise stated, any description of a method of treatment includes use of a crystalline form of Compound A to provide such treatment as is described herein. It is to be further understood, unless otherwise stated, any description of a method of treatment includes use of a crystalline form of Compound A to prepare a medicament to treat such condition. The treatment includes treatment of human or non-human animals including rodents and other disease models.

[0470] In some embodiments, a signal is a peak.

[0471] As used herein, the term “subject” includes human and non-human animals, as well as cell lines, cell cultures, tissues, and organs. In some embodiments, the subject is a mammal. The mammal can be *e.g.*, a human or appropriate non-human mammal, such as primate, mouse, rat, dog, cat, cow, horse, goat, camel, sheep or a pig. The subject can also be a bird or fowl. In some embodiments, the subject is a human.

[0472] As used herein, the term “subject in need thereof” refers to a subject having a disease or having an increased risk of developing the disease. A subject in need thereof can be one who has been previously diagnosed or identified as having a disease or disorder disclosed herein. A subject in need thereof can also be one who is suffering from a disease or disorder disclosed herein. Alternatively, a subject in need thereof can be one who has an increased risk of developing such disease or disorder relative to the population at large (*i.e.*, a subject who is predisposed to developing such disorder relative to the population at large). A subject in need thereof can be refractory or resistant to a disease or disorder disclosed herein (*i.e.*, a disease or disorder disclosed herein that does not respond or has not yet responded to treatment). The subject may be resistant at start of treatment or may become resistant during treatment. In some embodiments, the subject in need thereof received and failed all known effective therapies for a disease or disorder disclosed herein. In some embodiments, the subject in need thereof received at least one prior therapy.

[0473] As used herein, the term “treating” or “treat” describes the management and care of a patient for the purpose of combating a disease, condition, or disorder and includes the administration of a compound of the present disclosure, polymorph or solvate thereof, to alleviate the symptoms or complications of a disease, condition or disorder, or to eliminate the disease, condition or disorder. The term “treat” can also include treatment of a cell *in vitro* or an animal model.

[0474] It is to be understood that a morphic form of Compound A, can or may also be used to prevent a relevant disease, condition or disorder, or used to identify suitable candidates for such purposes.

[0475] As used herein, the term “preventing,” “prevent,” or “protecting against” describes reducing or eliminating the onset of the symptoms or complications of such disease, condition or disorder.

[0476] It is to be understood that “solubility” or “solubility rating” refers to the property of a polymorph disclosed herein to dissolve in a liquid solvent and form a homogeneous solution. In some embodiments, solubility is expressed as a concentration, either by mass of solute per unit volume of solvent (*e.g.*, g of solute per kg of solvent, g per dL (100 mL), mg/ml, etc.),

molarity, molality, mole fraction, or other similar descriptions of concentration. A person of skill in the art may understand that the maximum equilibrium amount of solute that can dissolve per amount of solvent is the solubility of that solute in that solvent under the specified conditions, including temperature, pressure, pH, and the nature of the solvent. In some embodiments, solubility is measured at physiological pH, or non-physiological pH, for example, at about pH 5.0, about pH 6.0, about pH 7.0, about pH 7.4, about pH 7.6, about pH 7.8, or about pH 8.0 (e.g., about pH 5-8). In some embodiments, solubility is measured in water or a physiological buffer, for example PBS, NaCl (with or without NaPO₄), or FaSSIF. In some embodiments, solubility is measured in a biological fluid (solvent) (e.g., blood or serum). In some embodiments, the temperature is be about room temperature (e.g., about 20, about 21, about 22, about 23, about 24, or about 25°C) or about body temperature (about 37°C). In some embodiments, an agent has a solubility rating of at least about 0.1, about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, about 19, about 20, about 25, about 30, about 40, about 50, about 60, about 70, about 80, about 90 or about 100 mg/ml at room temperature or at 37 °C.

[0477] As used herein, “stable” refers to a polymorph that maintains purity, appearance, and/or analytical parameters over a defined time and temperature as compared to the polymorph as isolated. In some embodiments, the “stable” polymorph exhibits less than about 10%, about 9%, about 8%, about 7%, about 6%, about 5%, about 4%, about 3%, about 2%, about 1%, about 0.9%, about 0.8%, about 0.7%, about 0.6%, about 0.5%, about 0.4%, about 0.3%, about 0.2%, or about 0.1% impurity over a set period of time (e.g., 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, one week, two weeks, three weeks, one month, two months, three months, or four months). For example, a polymorph is stable if after two weeks at room temperature the DSC and TGA profiles are consistent with the originally isolated polymorph.

[0478] It is to be understood that one skilled in the art may refer to general reference texts for detailed descriptions of known techniques discussed herein or equivalent techniques. These texts include Ausubel *et al.*, *Current Protocols in Molecular Biology*, John Wiley and Sons, Inc. (2005); Sambrook *et al.*, *Molecular Cloning, A Laboratory Manual* (3rd edition), Cold Spring Harbor Press, Cold Spring Harbor, New York (2000); Coligan *et al.*, *Current Protocols in Immunology*, John Wiley & Sons, N.Y.; Enna *et al.*, *Current Protocols in Pharmacology*, John Wiley & Sons, N.Y.; Fingl *et al.*, *The Pharmacological Basis of Therapeutics* (1975), *Remington's Pharmaceutical Sciences*, Mack Publishing Co., Easton,

PA, 18th edition (1990). These texts can, of course, also be referred to in making or using an aspect of the disclosure.

[0479] It is to be understood that the present disclosure also provides pharmaceutical compositions comprising a crystalline form of Compound A in combination with at least one excipient, diluent, or carrier (e.g., a pharmaceutically acceptable excipient, diluent, or carrier).

[0480] As used herein, the term “pharmaceutical composition” is a formulation containing a crystalline form of Compound A in a form suitable for administration to a subject. In some embodiments, the pharmaceutical composition is in bulk or in unit dosage form. The unit dosage form is any of a variety of forms, including, for example, a capsule, an IV bag, a tablet, a single pump on an aerosol inhaler or a vial. The quantity of active ingredient (*e.g.*, a formulation of the disclosed compound or hydrate, solvate or isomer thereof) in a unit dose of composition is an effective amount and is varied according to the particular treatment involved. One skilled in the art will appreciate that it is sometimes necessary to make routine variations to the dosage depending on the age and condition of the patient. The dosage will also depend on the route of administration. A variety of routes are contemplated, including oral, pulmonary, rectal, parenteral, transdermal, subcutaneous, intravenous, intramuscular, intraperitoneal, inhalational, buccal, sublingual, intrapleural, intrathecal, intranasal, intravitreal, and the like. Dosage forms for the topical or transdermal administration of a compound of this disclosure include powders, sprays, ointments, pastes, creams, lotions, gels, solutions, patches and inhalants. In one embodiment, the active compound is mixed under sterile conditions with one or more pharmaceutically acceptable carrier, and with any preservatives, buffers, or propellants that are required.

[0481] As used herein, the term “pharmaceutically acceptable” refers to those compounds, anions, cations, materials, compositions, carriers, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

[0482] As used herein, the term “pharmaceutically acceptable excipient” means an excipient that is useful in preparing a pharmaceutical composition that is generally safe, non-toxic and neither biologically nor otherwise undesirable, and includes excipient that is acceptable for veterinary use as well as human pharmaceutical use. A “pharmaceutically acceptable excipient” as used in the specification and claims may include both one and more than one such excipient.

[0483] It is to be understood that a pharmaceutical composition of the disclosure is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, *e.g.*, intravenous, intradermal, subcutaneous, oral (*e.g.*, ingestion), inhalation, transdermal (topical), and transmucosal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulphite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates, and agents for the adjustment of tonicity such as sodium chloride or dextrose. The pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

[0484] It is to be understood that a compound or pharmaceutical composition of the disclosure can be administered to a subject in many of the well-known methods currently used for chemotherapeutic treatment. For example, a compound of the disclosure may be injected into the blood stream or body cavities or taken orally or applied through the skin with patches. The dose chosen should be sufficient to constitute effective treatment but not so high as to cause unacceptable side effects. The state of the disease condition (*e.g.*, a disease or disorder disclosed herein) and the health of the patient should preferably be closely monitored during and for a reasonable period after treatment.

[0485] As used herein, the term “therapeutically effective amount”, refers to an amount of a pharmaceutical agent to treat, ameliorate, or prevent an identified disease or condition, or to exhibit a detectable therapeutic or inhibitory effect. The effect can be detected by any assay method known in the art. The precise effective amount for a subject will depend upon the subject’s body weight, size, and health; the nature and extent of the condition; and the therapeutic or combination of therapeutics selected for administration. Therapeutically effective amounts for a given situation can be determined by routine experimentation that is within the skill and judgment of the clinician.

[0486] As used herein, the term “effective amount”, refers to an amount of a pharmaceutical agent to treat or ameliorate an identified disease or condition, or to exhibit a detectable therapeutic or inhibitory effect. The effect can be detected by any assay method known in the art. The precise effective amount for a subject will depend upon the subject’s body weight, size, and health; the nature and extent of the condition; and the therapeutic or combination of

therapeutics selected for administration. Therapeutically effective amounts for a given situation can be determined by routine experimentation that is within the skill and judgment of the clinician.

[0487] It is to be understood that, for any compound, the therapeutically effective amount or effective amount can be estimated initially either in cell culture assays, *e.g.*, of neoplastic cells, or in animal models, usually rats, mice, rabbits, dogs, or pigs. The animal model may also be used to determine the appropriate concentration range and route of administration. Such information can then be used to determine useful doses and routes for administration in humans. Therapeutic/prophylactic efficacy and toxicity may be determined by standard pharmaceutical procedures in cell cultures or experimental animals, *e.g.*, ED₅₀ (the dose therapeutically effective in 50% of the population) and LD₅₀ (the dose lethal to 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index, and it can be expressed as the ratio, LD₅₀/ED₅₀. Pharmaceutical compositions that exhibit large therapeutic indices are preferred. The dosage may vary within this range depending upon the dosage form employed, sensitivity of the patient, and the route of administration.

[0488] Dosage and administration are adjusted to provide sufficient levels of the active agent(s) or to maintain the desired effect. Factors which may be taken into account include the severity of the disease state, general health of the subject, age, weight, and gender of the subject, diet, time and frequency of administration, drug combination(s), reaction sensitivities, and tolerance/response to therapy.

[0489] The pharmaceutical compositions containing a crystalline form of Compound A may be manufactured in a manner that is generally known, *e.g.*, by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping, or lyophilising processes. Pharmaceutical compositions may be formulated in a conventional manner using one or more pharmaceutically acceptable carrier comprising excipients and/or auxiliaries that facilitate processing of a crystalline form of Compound A into preparations that can be used pharmaceutically. The appropriate formulation is dependent upon the route of administration chosen.

[0490] The crystalline form of Compound A can be prepared with one or more pharmaceutically acceptable carrier, diluent, or excipient that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including an implant and microencapsulated delivery system.

[0491] It is to be understood that the pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

[0492] Techniques for formulation and administration of the disclosed compounds of the disclosure can be found in *Remington: the Science and Practice of Pharmacy*, 19th edition, Mack Publishing Co., Easton, PA (1995). In some embodiments, a crystalline form of Compound A, is used in pharmaceutical preparations in combination with one or more pharmaceutically acceptable carrier or diluent. A suitable pharmaceutically acceptable carrier includes, but is not limited to, inert solid fillers or diluents and sterile aqueous or organic solutions. The compounds will be present in such pharmaceutical compositions in amounts sufficient to provide the desired dosage amount in the range described herein.

[0493] All percentages and ratios used herein, unless otherwise indicated, are by weight. Other features and advantages of the present disclosure are apparent from the different examples. The provided examples illustrate different components and methodology useful in practicing the present disclosure. The examples do not limit the claimed disclosure. Based on the present disclosure the skilled artisan can identify and employ other components and methodology useful for practicing the present disclosure.

[0494] In the synthetic scheme described herein, compounds may be drawn with one particular configuration for simplicity. Such particular configurations are not to be construed as limiting the disclosure to one or another isomer, tautomer, or stereoisomer, nor does it exclude mixtures of isomers, tautomers, or stereoisomers; however, it will be understood that a given isomer, tautomer, or stereoisomer may have a higher level of activity than another isomer, tautomer, or stereoisomer.

[0495] All publications and patent documents cited herein are incorporated herein by reference as if each such publication or document was specifically and individually indicated to be incorporated herein by reference. Citation of publications and patent documents is not intended as an admission that any is pertinent prior art, nor does it constitute any admission as to the contents or date of the same. The invention having now been described by way of written description, those of skill in the art will recognize that the invention can be practiced in a variety of embodiments and that the foregoing description and examples below are for purposes of illustration and not limitation of the claims that follow.

[0496] The disclosure having been described, the following examples are offered by way of illustration and not limitation.

EXAMPLES

Abbreviations:

Abbreviation	Definition
¹ H NMR	Proton Nuclear Magnetic Resonance
API	Active Pharmaceutical Ingredient
ASR	Analytical Service Report
BB	Broad Band
ca.	Approximately
DMSO	Dimethyl sulfoxide
DSC	Differential Scanning Calorimetry
DVS	Dynamic Vapour Sorption
eq	Equivalents
EtOAc	Ethyl acetate
EtOH	Ethanol
GVS	Gravimetric Vapour Sorption
H ₂ O	Water
HPLC	High Performance Liquid Chromatography
IC	Ion Chromatography
ID	Identification
IP	Intellectual Property
IPA	2-Propanol
i-PrOAc	Isopropyl acetate
KF	Karl Fischer
MAS	Magic Angle Spinning
MDSC	Modulated Differential Scanning Calorimetry
MeCN	Acetonitrile
MEK	Methyl ethyl ketone
MeOH	Methanol
MIBK	Methyl isobutyl ketone
N/A	Not Applicable
NMR	Nuclear Magnetic Resonance
No.	Number
n-PrOH	1-Propanol
PLM	Polarised Light Microscopy
RH	Relative Humidity
RT	Room Temperature
SEM	Scanning Electron Microscope
SSNMR	Solid State Nuclear Magnetic Resonance
TBME	<i>tert</i> -Butyl methyl ether
TGA	Thermal Gravimetric Analysis
THF	Tetrahydrofuran
vol	Volumes
VT-XRPD	Variable Temperature X-Ray Powder Diffraction
XRPD	X-Ray Powder Diffraction

Instrument and Methodology Details

[0497] The instrument and methodology details for the experiments carried out in the examples are described herein.

*X-Ray Powder Diffraction (XRPD)***[0498] Bruker AXS C2 GADDS:**

[0499] XRPD diffractograms were collected on a Bruker AXS C2 GADDS diffractometer using Cu K α radiation (40 kV, 40 mA), an automated XYZ stage, a laser video microscope for auto-sample positioning and a Vântec-500 2-dimensional area detector. X-ray optics consists of a single Göbel multilayer mirror coupled with a pinhole collimator of 0.3 mm. The beam divergence, i.e. the effective size of the X-ray beam on the sample, was approximately 4 mm. A θ - θ continuous scan mode was employed with a sample – detector distance of 20 cm which gives an effective 2θ range of $1.5^\circ - 32.5^\circ$. Typically, the sample was exposed to the X-ray beam for 120 seconds. The software used for data collection and analysis was GADDS for Win7/XP and Diffrac *Plus* EVA respectively.

[0500] **Ambient conditions:** Samples run under ambient conditions were prepared as flat plate specimens using powder as received without grinding. Samples were prepared and analysed on a glass slide, by lightly pressed the powder to obtain a flat surface for analysis.

[0501] **Non-ambient conditions:** For variable temperature (VT-XRPD) experiments samples were mounted on an Anton Paar DHS 900 hot stage at ambient conditions. The sample was then heated to the appropriate temperature at $20^\circ\text{C}/\text{min}$ and subsequently held isothermally for 1 minute before data collection. Samples were prepared and analysed on a silicon wafer mounted to the hot stage using a heat-conducting paste.

[0502] Bruker AXS D8 Advance:

[0503] XRPD diffractograms were collected on a Bruker D8 diffractometer using Cu K α radiation (40 kV, 40 mA) and a θ - 2θ goniometer fitted with a Ge monochromator. The incident beam passes through a 2.0 mm divergence slit followed by a 0.2 mm anti-scatter slit and knife edge. The diffracted beam passes through an 8.0 mm receiving slit with 2.5° Soller slits followed by the Lynxeye Detector. The software used for data collection and analysis was Diffrac *Plus* XRD Commander and Diffrac *Plus* EVA respectively.

[0504] Samples were run under ambient conditions as flat plate specimens using powder as received. The sample was prepared on a polished, zero-background (510) silicon wafer by gently pressing onto the flat surface or packed into a cut cavity. The sample was rotated in its own plane.

[0505] The details of the standard Pharmorphix data collection method are:

- Angular range: 2 to 42° 2 θ
- Step size: 0.05° 2 θ
- Collection time: 0.5 s/step (total collection time: 6.40 min)

[0506] **PANalytical Empyrean:**

[0507] XRPD diffractograms were collected on a PANalytical Empyrean diffractometer using Cu K α radiation (45 kV, 40 mA) in transmission geometry. A 0.5° slit, 4 mm mask and 0.04 rad Soller slits with a focusing mirror were used on the incident beam. A PIXcel^{3D} detector, placed on the diffracted beam, was fitted with a receiving slit and 0.04 rad Soller slits. The software used for data collection was X'Pert Data Collector using X'Pert Operator Interface. The data were analysed and presented using Diffraction *Plus* EVA or HighScore Plus.

[0508] Samples were prepared and analysed in either a metal or Millipore 96 well-plate in transmission mode. X-ray transparent film was used between the metal sheets on the metal well-plate and powders (approximately 1 – 2 mg) were used as received. The Millipore plate was used to isolate and analyse solids from suspensions by adding a small amount of suspension directly to the plate before filtration under a light vacuum.

[0509] The scan mode for the metal plate used the goni scan axis, whereas a 2 θ scan was utilised for the Millipore plate.

[0510] The details of the standard screening data collection method are:

- Angular range: 2.5 to 32.0° 2 θ
- Step size: 0.0130° 2 θ
- Collection time: 12.75 s/step (total collection time of 2.07 min)

[0511] **Non-ambient conditions:** XRPD diffractograms were collected on a PANalytical Empyrean diffractometer using Cu K α radiation (45 kV, 40 mA) in reflection geometry. The instrument is fitted with an Anton Paar CHC plus⁺ stage fitted with graphite/Kapton windows. A programmable divergence slit (in automatic mode), with a 10 mm fixed incident beam mask, Ni filter and 0.04 rad Soller slits were used on the incident beam. A PIXcel^{3D} detector, placed on the diffracted beam, was fitted with a programmable anti-scatter slit (in automatic mode) and 0.04 rad Soller slits.

[0512] The software used for data collection was X'Pert Data Collector and the data analysed and presented using Diffraction *Plus* EVA or Highscore Plus.

[0513] For variable temperature (VT-XRPD) experiments the samples were prepared and analysed in an Anton Paar chromed sample holder with silicon wafer insert. A

heating/cooling rate of 10 °C/min was used with a 2 min isothermal hold before the measurement started. The measurement parameters are as per the standard screening data collection method (detailed above). Measurements were taken at the following temperatures: 25, 30, 70, 125, 140, 160 and 25 °C.

[0514] **Bruker D2 Phaser Gen 2:**

[0515] X-Ray powder diffraction patterns of Form 12 were collected using a Bruker D2 Phaser Gen 2 using Cu K α radiation (30 kV, 10 mA), $\theta - \theta$ goniometer, divergence slit (0.2 mm) and an SSD160 (1D Mode) Detector with a 4.799° opening. The software used for data collection was Diffrac.Commander version 6.5.0.1. and the data were presented using Diffrac.Eva version 7.1.0.1. XRPD diffractograms were acquired under ambient conditions via reflection on a flat silica zero background plate with rotation at 15 revolutions per minute. The data collection range was 3.0-40.0 °2 θ with a step size of 0.02 2 θ and a collection time of 0.1 seconds per step.

Nuclear Magnetic Resonance (NMR)

[0516] **400 MHz Instrument, DRX400 Console:** ¹H NMR spectra were collected on a Bruker 400 MHz instrument equipped with an auto-sampler and controlled by a DRX400 console. Samples were prepared in DMSO-*d*₆ solvent, unless otherwise stated. Automated experiments were acquired using ICON-NMR configuration within Topspin software, using standard Bruker-loaded experiments (¹H). Off-line analysis was performed using ACD Spectrus Processor.

[0517] **400 MHz Instrument, AV3+ Console:** ¹H NMR spectra were collected on a Bruker 400 MHz instrument equipped with an auto-sampler and controlled by an AV3+ console with SMART probe. Samples were prepared in DMSO-*d*₆ solvent, unless otherwise stated. Automated experiments were acquired using ICON-NMR configuration within Topspin software, using standard Bruker-loaded experiments (¹H). Off-line analysis was performed using ACD Spectrus Processor.

Differential Scanning Calorimetry (DSC)

[0518] **TA Instruments Q2000:** DSC data were collected on a TA Instruments Q2000 equipped with a 50 position auto-sampler. Typically, 0.5 - 3 mg of each sample, in a pin-holed aluminium pan, was heated at 10 °C/min from 25 °C to 300 °C. A purge of dry nitrogen at 50 ml/min was maintained over the sample.

[0519] Modulated temperature DSC was carried out using an underlying heating rate of 2 °C/min and temperature modulation parameters of ± 0.636 °C (amplitude) every 60 seconds (period). The instrument control software was Advantage for Q Series and Thermal Advantage and the data were analysed using Universal Analysis or TRIOS.

[0520] DSC data of Form 12 was collected on a TA Instruments Q2000 DSC. A predefined amount of the sample, 2.0 to 10.0 mg, was placed in an aluminium pan and heated at 10 °C / minute from 40 °C to 300 °C, or varied as experimentation dictated. A purge of dry nitrogen at 100 mL / minute was maintained over the sample. The instrument control and data acquisition were acquired using Q Advantage software release version 5.5.23. The data was processed and presented using the TA Universal Analysis 2000 software version 4.5A build 4.5.0.5.

[0521] **TA Instruments Discovery DSC:** DSC data were collected on a TA Instruments Discovery DSC equipped with a 50 position auto-sampler. Typically, 0.5 - 3 mg of each sample, in a pin-holed aluminium pan, was heated at 10 °C/min from 25 °C to 300 °C. A purge of dry nitrogen at 50 ml/min was maintained over the sample.

[0522] The instrument control software was TRIOS and the data were analysed using TRIOS or Universal Analysis.

Thermo-Gravimetric Analysis (TGA)

[0523] **TA Instruments Q500:** TGA data were collected on a TA Instruments Q500 TGA, equipped with a 16 position auto-sampler. Typically, 5 - 10 mg of each sample was loaded onto a pre-tared aluminium DSC pan and heated at 10 °C/min from ambient temperature to 350 °C. A nitrogen purge at 60 ml/min was maintained over the sample. The instrument control software was Advantage for Q Series and Thermal Advantage and the data were analysed using Universal Analysis or TRIOS.

[0524] **TA Instruments Discovery TGA:** TGA data were collected on a TA Instruments Discovery TGA, equipped with a 25 position auto-sampler. Typically, 5 - 10 mg of each sample was loaded onto a pre-tared aluminium DSC pan and heated at 10 °C/min from ambient temperature to 350 °C. A nitrogen purge at 25 ml/min was maintained over the sample. The instrument control software was TRIOS and the data were analysed using TRIOS or Universal Analysis.

[0525] **TA Instruments Q5000 TGA:**

[0526] TGA data of Form 12 was collected on a TA Instruments Q5000 TGA. A predefined amount of the sample, 2.0 to 10.0 mg, was placed in an aluminium pan and heated at 10 °C /

minute from 40 °C to 300 °C, or varied as experimentation dictated. A purge of dry nitrogen at 25 mL / minute was maintained over the sample. The instrument control and data acquisition are acquired using Q Advantage software release version 5.5.23. The data was processed and presented using the TA Universal Analysis 2000 software version 4.5A build 4.5.0.5.

Polarised Light Microscopy (PLM)

[0527] **Leica LM/DM Polarised Light Microscope:** Samples were analysed on a Leica LM/DM polarised light microscope with a digital video camera for image capture. A small amount of each sample was placed on a glass slide, with or without immersion oil, and covered with a glass slip. The sample was viewed with appropriate magnification and partially polarised light, coupled to a λ false-colour filter. Images were captured using StudioCapture or Image ProPlus software.

[0528] **Nikon LM/DM Polarised Light Microscope:** Samples were studied on a Nikon SMZ1500 polarised light microscope with a digital video camera connected to a DS Camera control unit DS-L2 for image capture. The sample was viewed with appropriate magnification and partially polarised light, coupled to a λ false-colour filter.

Scanning Electron Microscopy (SEM)

[0529] Data were collected on a Phenom Pro Scanning Electron Microscope. A small quantity of sample was mounted onto an aluminium stub using conducting double-sided adhesive tape. A thin layer of gold was applied using a sputter coater (20 mA, 120 s).

Gravimetric Vapour Sorption (GVS)

[0530] Sorption isotherms were obtained using a SMS DVS Intrinsic moisture sorption analyser, controlled by DVS Intrinsic Control software. The sample temperature was maintained at 25 °C by the instrument controls. The humidity was controlled by mixing streams of dry and wet nitrogen, with a total flow rate of 200 ml/min. The relative humidity was measured by a calibrated Rotronic probe (dynamic range of 1.0 – 100 %RH), located near the sample. The weight change, (mass relaxation) of the sample as a function of %RH was constantly monitored by a microbalance (accuracy ± 0.005 mg).

[0531] Typically, 5 - 30 mg of sample was placed in a tared mesh stainless steel basket under ambient conditions. The sample was loaded and unloaded at 40 %RH and 25 °C (typical room conditions). A moisture sorption isotherm was performed as outlined below (2 scans

per complete cycle). The standard isotherm was performed at 25 °C at 10 %RH intervals over a 0 – 90 %RH range. Typically, a double cycle (4 scans) was carried out. Data analysis was carried out within Microsoft Excel using the DVS Analysis Suite.

Method for SMS DVS Intrinsic experiments

Parameter	Value
Adsorption – Scan 1	40 – 90
Desorption, Adsorption – Scan 2	90 – 0, 0 – 40
Intervals (%RH)	10
Number of Scans	4
Flow rate (ml/min)	200
Temperature (°C)	25
Stability (°C/min)	0.2
Sorption Time (hours)	6 hour time out
Number of cycles	2

[0532] The sample was recovered after completion of the isotherm and re-analysed by XRPD.

Chemical Purity Determination by HPLC

[0533] Purity analysis was performed on an Agilent HP1100/Infinity II 1260 series system equipped with a diode array detector and using OpenLAB software. The full method details are provided below:

HPLC method for chemical purity determinations

Parameter	Value		
Type of method	Reverse phase with gradient elution		
Sample Preparation	0.3 – 0.5 mg/ml in acetonitrile : water 1:1		
Column	Supelco Ascentis Express C18 2.7 µm 100 x 4.6 mm		
Column Temperature (°C)	25		
Injection (µl)	10		
Detection: Wavelength, Bandwidth (nm)	255, 90		
Flow Rate (ml/min)	2		
Phase A	0.1% TFA in water		
Phase B	0.085% TFA in acetonitrile		
Timetable	Time (min)	% Phase A	% Phase B
	0	95	5
	6	5	95
	6.2	95	5
	8	95	5

Water Determination by Karl Fischer Titration (KF)

[0534] The water content of each sample was measured on a Metrohm 874 Oven Sample Processor at 150 °C with 851 Titration Coulometer using Hydranal Coulomat AG oven reagent and nitrogen purge. Weighed solid samples were introduced into a sealed sample vial. Approximately 10 mg of sample was used per titration and duplicate determinations were made. An average of these results is presented unless otherwise stated. Data collection and analysis were performed using Tiamo software.

Thermodynamic Aqueous Solubility

[0535] Aqueous solubility was determined by suspending sufficient compound in relevant media to give a maximum final concentration of ≥ 10 mg/ml of the parent free-form of the compound. The suspension was equilibrated at 25 °C, on a Heidolph plate shaker set to 750 rpm for 24 hours. The pH of the saturated solution was then measured, and the suspension filtered through a glass fibre C filter (particle retention 1.2 μ m) and diluted appropriately. Quantitation was by HPLC with reference to a standard solution of approximately 0.15 mg/ml in DMSO. Different volumes of the standard, diluted and undiluted sample solutions were injected. The solubility was calculated using the peak areas determined by integration of the peak found at the same retention time as the principal peak in the standard injection.

HPLC method for solubility measurements

Parameter	Value		
Type of method	Reverse phase with gradient elution		
Column	Phenomenex Luna, C18 (2) 5 μ m 50 x 4.6 mm		
Column Temperature (°C)	25		
Standard Injections (μ l)	1, 2, 3, 4, 5, 7		
Test Injections (μ l)	1, 2, 3, 10, 15, 20		
Detection: Wavelength, Bandwidth (nm)	260,90		
Flow Rate (ml/min)	2		
Phase A	0.1% TFA in water		
Phase B	0.085% TFA in acetonitrile		
Timetable	Time (min)	% Phase A	% Phase B
	0.0	95	5
	1.0	80	20
	2.3	5	95
	3.3	5	95
	3.5	95	5
	4.4	95	5

[0536] Analysis was performed on an Agilent HP1100/ Infinity II 1260 series system equipped with a diode array detector and using OpenLAB software.

Ion Chromatography (IC)

[0537] Data were collected on a Metrohm 930 Compact IC Flex with 858 Professional autosampler and 800 Dosino dosage unit monitor, using IC MagicNet software. Accurately weighed samples were prepared as stock solutions in a suitable solvent. Quantification was achieved by comparison with standard solutions of known concentration of the ion being analysed. Analyses were performed in duplicate and an average of the values is given unless otherwise stated.

IC method for cation chromatography

Parameter	Value
Type of method	Cation exchange
Column	Metrosep C 4 – 250 (4.0 x 250 mm)
Column Temperature (°C)	Ambient
Injection (µl)	Various
Detection	Conductivity detector
Flow Rate (ml/min)	0.9
Eluent	1.7 mM nitric acid 0.7 mM dipicolinic acid in a 5% acetone aqueous solution.

IC method for anion chromatography

Parameter	Value
Type of method	Anion exchange
Column	Metrosep A Supp 5 – 150 (4.0 x 150 mm)
Column Temperature (°C)	Ambient
Injection (µl)	Various
Detection	Conductivity detector
Flow Rate (ml/min)	0.7
Eluent	3.2 mM sodium carbonate 1.0 mM sodium hydrogen carbonate in a 5% acetone aqueous solution.

[0538] *Dynamic Vapor Sorption (DVS)* Dynamic Vapour Sorption (DVS) of Form 12 was carried out using the TA Instruments Q5000 SA. A predefined amount of the sample, 2.0 to 10.0 mg, was placed in a platinum pan. The sample was allowed to equilibrate at 50 °C at 0% RH for a period of 60 minutes. The sample was then equilibrated at 25 °C before ramping the

humidity from 0 to 95% RH at 5% increments every hour. A similar ramp profile was used for desorption cycle. XRPD analysis was also performed on post DVS sample.

Optical Microscopy

[0539] Optical Microscopy of Form 12 was performed using the Nikon Eclipse E400 Optical Microscope equipped with 2, 4, 10, 25 and 40× objective lens. The microscope is coupled with a QImaging digital camera. The camera is controlled by the proprietary QCapture Pro 7 software. The camera software measurement tool is calibrated using a calibration slide (Pyser-SGI S8 Micrometer scale 1mm/0.01 mm).

Single Crystal X-Ray Diffraction (SCXRD)

[0540] Data were collected on a Rigaku Oxford Diffraction XtaLAB Synergy-S diffractometer equipped with a dualflex source (Cu at Zero), HyPix-6000HE detector and an Oxford Cryosystems Cobra cooling device. The data were collected using Cu K α radiation as stated in the experimental tables. Structures were solved and refined using the Shelx suite of programs and OLEX was used as an interface to view the structures with and produce figures. Unless otherwise stated, hydrogen atoms attached to carbon were placed geometrically and allowed to refine with a riding isotropic displacement parameter. A reference diffractogram for the crystal structure was generated using Mercury.

Example 1. Exemplary Preparation of Form 1.

[0541] Form 1 was first observed from recovering the GVS residue of amorphous Compound A. It was later shown that Form 1 can be prepared through heating Form 2 (dihydrate) above 100 °C. For the collection of a high resolution diffractogram and DSC thermogram Form 1 was recovered as a GVS residue of the dihydrate. The DSC was characterised by an endotherm with an onset ~143.9 °C.

[0542] Form 1 was characterized using a wide range of techniques to investigate the solid form and chemical properties. A summary of the results is shown below. Table A and Table B showed results of characterization of two batches of Form 1.

Table A Characterisation Data of Form 1

Form 1	
XRPD	Form 1
DSC	Endotherm onset 143.9 °C (26 J/g)

Table B Characterisation Data of Form 1

Form 1	
XRPD	Form 1
TGA	3 % weight loss, RT-190 °C
DSC	Broad endotherm RT-75 °C (21 J/g) Broad endotherm onset ~145.6 °C (28 J/g)
VT-XRPD	n/a
Tentative assignment	Anhydrous (readily rehydrates)

[0543] TGA thermogram of Form 1 showed a 3% w/w loss up to 190 °C. DSC thermogram of Form 1 showed a broad endotherm up to 75 °C occurred during this mass loss that suggested an uptake of water after which the sample was stored in a fridge at ambient (uncontrolled) humidity. When the sample was reanalysed by XRPD after 1 week, the sample had converted from Form 1 (anhydrous) to Form 2 (dihydrate). The XRPD indicated that in a humid environment at 5 °C the anhydrous Form 1 will readily uptake water from the atmosphere.

[0544] XRPD diffractogram and DSC thermogram of anhydrous Form 1 are provided in FIG. 2 and FIG. 3, respectively.

Example 2. Exemplary Preparation of Form 2 – Dihydrate.

[0545] Amorphous Compound A (500 mg) was placed in a crystallisation dish in a sealed container with saturated solution to give a 25 °C/75% RH environment for 4 days. The solid was amorphous and placed at 40 °C 75% RH for 4 days. An off-white glass was extracted and analysed initially by XRPD.

[0546] Alternatively, the dihydrate Form 2 was prepared from conversion of the amorphous Compound A at 25 °C/97 %RH or at 40 °C/30 %RH.

[0547] Specifically, the dihydrate Form 2 was prepared by solid-state conversion under static storage at 40 °C/75% RH and was recovered with comparative purity by HPLC to the input amorphous solid. The material appeared to convert to the crystalline hydrate via a glass showing the material may initially deliquesce prior to formation. The material was fully characterised. A summary of the results is shown below. Table C and Table D show results of characterization of two batches of Form 2.

Table Characterisation Summary for Dihydrate Form 2

	Form 2
Condition	40 °C/75% RH
Assignment	Dihydrate
XRPD	Form 2
HPLC	98.5 %
NMR	Matches expected structure, 29 protons No solvent present
TGA	6 % step loss weight loss 50-105 °C (1.7 eq. water)
DSC	Broad endotherm onset 49.8 °C (88 J/g), Endotherm onset 144.2 °C (27 J/g)
GVS	9.1% total water uptake between 0 – 90% RH 2.2 % uptake 40 – 70 % RH (1 st sorption cycle). 6.1 % uptake 40-70 % RH (2 nd sorption cycle) Reversible hysteresis 70% – 10 % RH (for later cycles)
XRPD – Post GVS	Converted to Form 1 (anhydrous)
SEM	Agglomerated blocks
KF	7.3% water content (2.1 mol. eq. H ₂ O)
IC	1 eq. Na
Solubility	pH 1.2: 0.07; residue Form 11 pH 6.0: 0.32; residue Form 11 pH 8.0: >10; residue Form 11

Table D Characterisation Data for Form 2

	Form 2
XRPD	Form 2
TGA	6 % weight loss from RT-90 °C (equates to 1.7 mol. eq. H ₂ O) [†]
DSC	Broad endotherm between 30 – 100 °C (140 J/g), Broad endotherm onset 143.4 (28 J/g) [‡]
VT-XRPD	30 °C – Form 2, Converts to Form 1 above 100 °C [‡]
Tentative Assignment	Hydrate

Key: [†] sample was from 40 °C/75% RH storage

[‡] sample was GVS sample that converted from Form 1 to Form 2

[0548] The structure of Form 2 was consistent by NMR with Compound A and no residual solvent was noted. The TGA thermogram had a 6% w/w loss up to 105 °C which overlapped with a broad endotherm with an onset at 49.8 °C (88 J/g) which is then followed by a second endotherm with onset at 144.2 °C (27 J/g). The KF analysis indicated 7.3% water content equating to 2.1 mol. eq. H₂O and between the thermal and KF analysis corroborated Form 2 being a dihydrate. The dihydrate has hygroscopic properties having a total 9.1 % water reuptake in the range 0 – 90% RH and a reversible hysteresis is observed between 10 – 70%

RH. This hysteresis is manifested in the recovered solid residue having converted to the anhydrous Form 1. The SEM was characterised by agglomerated block crystals which may originate from the conversion to the crystalline phase following deliquescing and passing through a glass-like phase. To understand the physical stability of Dihydrate Form 2, the material was held under nine different elevated temperature/humidity conditions as summarised in Table E.

Table E XRPD Analysis of Dihydrate Form 2 after Storage at Elevated Conditions.

RH	25 °C	40 °C	60 °C
30	Form 2	n/a	Form 2
50	Form 2	n/a	Form 2
75	Form 2	Form 2 (91.0%)	Form 3 (96.2%)
97	Form 2 (96.0%)	n/a	Brown Gum (81.7%)

HPLC purity where measured is provided in brackets

[0549] The dihydrate showed good physical stability at all humidity conditions investigated at 25 °C (30 – 97% RH) and 40 °C/75% RH. More nuanced behaviour was observed when held at 60 °C with the dihydrate persisting at 60 °C/50% RH and 60 °C/50% RH, however, it should be noted at high temperature and high humidity the physical stability drops. The material converted to monohydrate Form 3 at 60°C/75% RH only, where high temperature and water conditions appeared to facilitate an annealing type crystallisation to an alternative form. At 60 °C/97% RH, Form 2 converted to a brown gum which had 81.7% purity. Although the physical stability of Form 2 was good in many of the conditions, the HPLC purity suggest the chemical purity is less robust with drops noted after 7 days. It is recommended to store the final solid form in a controlled temperature and humidity environment to reduce chemical degradation over time.

[0550] Characterization data of Form 2 are provided in FIGS. 4-9.

[0551] In summary, Form 2 is a hygroscopic crystalline dihydrate of the sodium mono-salt of Compound A that displays good physical stability to elevated temperature and humidity (except at conditions above 60 °C/75% RH) and should be stored in controlled temperature and humidity environment to reduce chemical degradation over time.

Example 3. Exemplary Preparation of Form 3 - Monohydrate.

[0552] Amorphous Compound A (500 mg) was placed in a crystallisation dish in a sealed container with saturated solution to give a 60 °C/75% RH environment for 4 days. The

sample was very sticky and difficult to handle and was dried in a vacuum oven (RT, ~5 mbar) for 4 hrs.

[0553] As such, the monohydrate Form 3 was successfully generated from a solid-state conversion of amorphous Compound A at the elevated 60 °C/75% RH condition which appeared to potentially convert by passing through a glass-like phase first. Due to the high temperature and humidity condition for conversion, a small drop in chemical purity to 97.1% was determined by HPLC and IC analysis confirmed Form 3 to be a sodium mono-salt. The material was fully characterised. A summary of the results is shown below. Table F and Table G show results of characterization of two batches of Form 3.

[0554] The NMR matched the expected structure for Compound A and did not identify any residual solvent. The TGA thermogram was characterised by a 4% w/w total loss (two 2% weight loss events) up to 140 °C while the KF analysis showed there be to 3.7% water content (equivalent to 1 ml. eq. water). The DSC thermogram had two endotherms with an onset at 33.7 °C (15 J/g) and 101.8 °C (59 J/g) that overlap with the mass loss events of water loss. These are then followed by a final endotherm with an onset at 152.1 °C (13 J/g). Form 3 is hygroscopic with ~13% reversible water uptake between 0 – 90% RH and a hysteresis between 10 – 70% RH. The recovered GVS sample showed conversion to a mixture of anhydrous Form 1 and Form 3. The SEM was characterised by agglomerated blocks. As with the dihydrate, this block type morphology is likely a manifestation of crystallising through a glass-like phase in the solid-state.

Table F Characterisation Summary for Monohydrate Form 3

Form 3	
Condition	60 °C/75% RH
Assignment	Monohydrate
XRPD	Form 3
HPLC	97.1 %
NMR	Matches expected structure, 29 protons No solvent present
TGA	2 % weight loss RT – 85 °C (0.5 eq. water) 2% weight loss 85 – 140 °C (0.5 eq. water)
DSC	Broad endotherm onset 33.7 °C (15 J/g), endotherm onset 101.8 °C (59 J/g), endotherm onset 152.1 °C (13 J/g)
GVS	2.3 % uptake 40 – 80 % RH and 8.9 % uptake 80 – 90 %RH (1 st sorption cycle). 5.1 % uptake 40 – 80 % RH (2 nd sorption cycle) Reversible hysteresis 70% – 10 % RH (for later cycles)
XRPD – Post	Converted to a mixture of Form 1 and Form 3

Form 3	
GVS	
SEM	Agglomerated blocks
KF	3.7% water content (1 mol. eq. H ₂ O)
IC	1 eq. Na
Solubility (mg/ml)	pH 1.2: 0.06 pH 6.0: 0.33 pH 8.0: 10.2

Table G Characterisation Data of Form 3

Form 3	
XRPD	Form 3
TGA	3 % weight loss from RT-120 °C (equates to 0.83 mol. eq. H ₂ O)
DSC	Large broad endotherm, 50-120 °C (86 J/g), broad endotherm, onset 146.9 (34 J/g)
VT-XRPD	Crystalline Form 9 at 120 °C Converted back to Form 3 on cooling
Tentative assignment	Hydrate

[0555] The physical stability of monohydrate Form 3 was investigated under a range of elevated temperature and humidity conditions and summarised in Table H. Form 3 showed good physical stability remaining unchanged at all temperatures up to 75% RH. There was a form change to dihydrate Form 2 at 25 °C/97% RH and had a drop in purity to 92.5%. While at 60 °C/97% RH a brown gum with lowered purity to 81.7% was observed. As observed previously with Form 2 a drop in chemical purity where measured was noted.

Table H XRPD Analysis of Monohydrate Form 3 After Storage at Elevated Conditions.

RH	25 °C	40 °C	60 °C
30	Form 3	n/a	Form 3
50	Form 3	n/a	Form 3
75	Form 3	Form 3 (94.1%)	Form 3 (92.0%)
97	Form 2 (92.5)	n/a	Brown Gum (81.7%)

HPLC purity where measured is provided in parenthesis

[0556] Characterization data of Form 3 are provided in FIGS. 10-15.

[0557] To summarise, Form 3 is a hygroscopic crystalline monohydrate of the sodium mono-salt of Compound A. Form 3 shows good physical stability to elevated temperature and humidity conditions (except conversion to Form 2 at 25 °C/97% RH and becoming a brown gum at 60 °C/97% RH). It would be recommended to store Form 2 in a controlled temperature and humidity environment to avoid accelerate drops in chemical purity.

Example 4. Exemplary Preparation of Form 4.

[0558] Form 4 was obtained from IPA. Characterisation of this Form indicated that this was likely a solvate and was metastable when placed at 40 °C/75% RH. Characterization data of Form 4 are provided in FIGS. 16 and 17 and Table I.

Table I Characterisation data for Form 4

Solvent	Form	VT-XRPD	DSC	NMR	40 °C/75 %RH
IPA	4	N/A	Broad endotherm RT – 90 °C (32 J/g) Endotherm, onset: 122.2 °C (40 J/g)	0.64 mol. eq. IPA	Deliquesced Mixture Form 2 and Form 3

Key: N/A – not applicable

[0559] Form 4 was consistent with the structure by NMR and had ~0.6 mol. eq. IPA in the solid. The DSC thermogram had a broad endotherm up to 90 °C (32 J/g) which was likely associated with the MeOH loss and followed by a second endotherm with an onset at 122.2 °C (40 J/g). The solid showed limited physical stability deliquescing at 40 °C/75% RH which dried to a solid on removal which was a mixture of the hydrates, Form 2 and Form 3. Form 4 was tentatively assigned as a IPA solvate that showed limited physical stability.

Example 5. Exemplary Preparation of Form 5.

[0560] Form 5 was obtained from acetone. Characterisation of this Form indicated that this was likely a solvate and was metastable when placed at 40 °C/75% RH.

Example 6. Exemplary Preparation of Form 6.

[0561] Form 6 was obtained from 2-Methyl-1-propanol. Characterisation of Form 6 indicated that this was likely a solvate and was metastable when placed at 40 °C/75% RH. Characterization data of Form 6 are provided in FIGS. 18-20 and Table J.

Table J Characterisation data for Form 6

Solvent	Form	VT-XRPD	DSC	NMR	40 °C/75 %RH
2-Me-1-PrOH	6	N/A	Broad endotherm RT – 80 °C (25 J/g) Endotherm, onset: 109.0 °C (69 J/g)	0.91 mol. eq. 2-Me-1-PrOH	Deliquesced Mixture Form 2 and Form 3

Key: N/A – not applicable

[0562] Form 6 was shown to have ~0.9 mol. eq. 2-Me-1-PrOH by NMR. A broad endotherm up to 80 °C (25 J/g) was observed by DSC (likely associated with solvent vaporisation) which was then followed by a second endotherm with an onset at 109.0 °C (69 J/g). There was limited physical stability with the material deliquescing at 40 °C/75% RH and as this dried to a solid became a mixture of Form 2 and Form 3. Form 6 was tentatively assigned as a 2-Me-1-PrOH solvate with limited physical stability.

Example 7. Exemplary Preparation of Form 7.

[0563] Form 7 was isolated from heptane/EtOH and ~0.9 mol. eq. EtOH was identified by NMR. The DSC thermogram showed complicated behaviour where a broad endotherm with a shoulder was observed up to 130 °C (195 J/g) which was then followed by two overlapping endotherms between 140 – 170 °C (48 J/g).

[0564] Characterisation of this Form indicated that this was likely a solvate and was metastable when placed at 40 °C/75% RH.

[0565] Form 7 was also obtained from MeOH/water. Characterisation of Form 7 is summarized in Tables K and L and shown in in FIGs. 21 and 22.

Table K Characterisation data for Form 7

	Form 7
NMR	Consistent with structure, 0.5 eq. MeOH
DSC	Broad endotherm RT-70 °C (11 J/g), Large broad endotherm onset 71.1 °C (46 J/g), Endotherm onset 131.3 °C (2 J/g), Endotherm onset 148.8 °C (3 J/g) Large endotherm onset 160.5 °C (23 J/g)
HCH-DSC	Heat cycle 1 (up to 120 °C: Observe two broad endotherms Heat cycle 2 (up to 250 °C): no events until observe three endotherms at <i>ca.</i> 130, 150 and 160 °C
VT-XRPD	Form 7 observed at initial RT measurement Form 10 observed at 70 °C, 125 °C and 140 °C Amorphous diffractogram at 160 °C which persisted on cooling

Table L Characterisation data for Form 7

Solvent	Form	VT-XRPD	DSC	NMR	40 °C/75 %RH
EtOH	7	Form 10 at 100 °C	Broad endotherm with shoulder 50-130 °C (195 J/g), Broad overlapping endotherm 140-170 °C (48 J/g)	0.89 mol. eq. EtOH	Form 3 (monohydrate)

[0566] The NMR of the material identified 0.5 mol. eq. MeOH and the DSC showed complicated behaviour. There were two broad endotherms up to ~120 °C. These are then followed by two smaller endotherms with onsets at 131.3 °C (2 J/g) and 148.8 °C (3 J/g) followed by a larger endotherm with onset at 160.5 °C (23 J/g). The three endotherms above 130 °C were suspected to be due to anhydrous forms and a Heat-Cool-Heat DSC was run to see if these may be reduced by initially driving off the solvent. The second heat cycle was shown to still display the three endotherms. These three endotherms could be related to the three anhydrous forms identified and by all being endothermic transitions could imply an enantiotropic relationship between the anhydrous forms. To investigate this further a VT-XRPD was undertaken where Form 7 solvate is observe at the initial room temperature measurement. On heating the material converted to anhydrous Form 10 at 70 °C which persisted at 125 °C and 140 °C. At 160 °C the sample started to melt which persisted on cooling.

[0567] Despite measuring the XRPD in between the first two higher temperature endotherms only Form 10 was observed. As these two endotherms had a small enthalpy (2 – 3 J/g) it may be that only a small portion of the material converted to anhydrous Form 1 or Form 9 which was below the limit of detection for the instrument.

Example 8. Exemplary Preparation of Form 8.

[0568] Form 8 was isolated using a heptane/2-Me-1-PrOH mixture (9:1 v/v) and the NMR showed there to be 1 mol. eq. of 2-Me-1-PrOH and 0.4 mol. eq. heptane. The DSC was characterised by an overlapping endotherm with the first endotherm having an onset at 88.0 °C (4 J/g) and the second larger endotherm with onset at 100.6 °C (95 J/g). Form 8 converted

to Form 3 (monohydrate) after storage at 40 °C/75% RH. A tentative assignment as a potential 2-Me-1-PrOH or mixed solvate with limited physical stability.

[0569] Characterization data of Form 8 are provided in Table M and FIGs. 23 and 24.

Table M Characterisation Data for Form 8

Solvent	Form	VT-XRPD	DSC	NMR	40 °C/75 %RH
2-Me-1-PrOH	8	N/A	Overlapping endotherms, Endo 1, onset 88.0°C (4 J/g) Endo 2, onset: 100.6 °C (95 J/g)	1 mol. eq. 2-Me-1-Propanol, 0.4 mol. eq. heptane	Form 3 (monohydrate)

Key: N/A – not applicable

[0570] Characterisation of Form 8 indicated that this was likely a solvate and was metastable when placed at 40 °C/75% RH.

Example 9. Exemplary Preparation of Form 9 – Anhydrous.

[0571] To collect a phase pure diffractogram of Form 9, the monohydrate Form 3 had to be heated to 120 °C (and measured by VT-XRPD) and measured *in-situ* as Form 9 then converted back to Form 3 on cooling. The DSC had an endotherm with an onset temperature at 148.9 °C and was measured *in-situ* using a heat-cool-heat DSC experiment.

[0572] Characterization data of Form 9 are provided in Table N and FIGs. 25 and 26.

Table N Characterisation of Form 9

Form 9	
XRPD	Obtained at 125 °C Converted back to Form 3 on cooling back to RT
DSC	Endotherm onset 148.9 °C (30 J/g)

Example 10. Exemplary Preparation of Form 10 – Anhydrous.

[0573] To generate Form 10, the solvate(/mixed hydrate/solvate) Form 7 was heated to 70 °C whereby conversion to Form 10 was achieved. The DSC had a small endotherm with an onset at of 148.8 °C followed by a second endotherm 164.5 °C. Characterization data of Form 10 are provided in Table O and FIGs. 27 and 28.

Table O Characterisation of Form 10

Form 10	
XRPD	Obtained from heating Form 7 to 70 °C
DSC	Shallow endotherm onset 148.8 °C (2 J/g), endotherm onset 164.5 C (12 J/g)

Example 11. Solubility Study of Morphic Forms

[0574] The objective of this study was to understand the solubility in a range of solvents for future studies, as well as conduct polymorphism screens using solution-based methods.

[0575] **Procedure at 50 °C:** To amorphous Compound A (20 mg) sequential aliquots of solvent were added and the samples stirred at 50 °C with an observation was made after 10 minutes. This process was repeated until either a clear solution was obtained, or 70 total volumes of solvent were added.

[0576] Any suspensions at 50 °C were slurried at 50 °C for 24 hrs. Clear solutions at 50 °C were cooled to 5 °C at 0.1 °C/minute. If samples remained clear at 5 °C, antisolvent (heptane) was added in 1 relative volume aliquots at RT until 1:3 v/v ratio was achieved. If solvents were immiscible with the antisolvent, the samples were evaporated to dryness with a pierced lid. Any gums were subjected to ultrasound for 30 minutes. In all cases where a suspension was obtained, they were isolated by filtration under positive pressure through a frit and analysed by XRPD. The process flow for the samples are summarised in FIG. 29.

[0577] **Procedure at 5 °C:** To amorphous Compound A (20 mg) sequential aliquots of solvent were added and the samples stirred at 5 °C with an observation made after 10 minutes. This process was repeated until either a clear solution was obtained or 70 total volumes of solvent were added.

[0578] Any suspensions at 5 °C were slurried at 5 °C for 24hrs days. Clear samples were heated to 25 °C where antisolvent (cyclohexane or TBME depending on miscibility) was added 1 relative volume aliquots until 1:3 v/v ratio was achieved. If samples were still solutions after antisolvent addition, samples were evaporated to dryness by removing the vial cap. Any gums were subjected to ultrasound for 30 minutes. Any suspensions were isolated by filtration under positive pressure through a frit. All solids were analysed by XRPD. The process flow for the samples is summarised in FIG. 30.

[0579] The results of the solubility assessment at 50 °C and 5 °C are summarised in Table P and Table Q, respectively.

Table P Solubility Assessment at 50 °C, Observations and XRPD Analysis for Recovered Solids

ID	Solvent	10 vol	20 vol	30 vol	50 vol	70 vol	Observation	Treatment	Observation after treatment	XRPD
1	n-Heptane	X	X	X	X	X	Suspension	Slurry 50 °C	Solid	Amorphous
2	Ethyl acetate	X	X	X	X	X	Suspension	Slurry 50 °C	Gummed on filter	/
3	Isopropyl acetate	X	X	X	X	X	Suspension	Slurry 50 °C	Solid	Amorphous
4	MIBK	X	X	X	X	X	Suspension	Slurry 50 °C	Gummed on filter	/
5	2-Propanol	X	X	X	X	✓	Clear	Cool to 5 °C/heptane	Suspension	Form 4
6	MEK	✓	/	/	/	/	Clear	Cool to 5 °C/heptane	Gum	/
7	Acetone	✓	/	/	/	/	Clear	Cool to 5 °C/heptane	Solid*	Form 5
8	Ethanol	✓	/	/	/	/	Clear	Cool to 5 °C/heptane	Gum	/
9	Tetrahydrofuran	✓	/	/	/	/	Clear	Cool to 5 °C/heptane	Gum	/
10	Water	✓	/	/	/	/	Clear	Cool to 5 °C/evaporation	Clear/Gum	/
11	2-Methyl-1-propanol	X	✓	/	/	/	Clear	Cool to 5 °C	Suspension	Form 6
12	1,4-Dioxane	✓	/	/	/	/	Clear	Cool to 5 °C/heptane	Gum	/
13	IPA: Water (10%)	✓	/	/	/	/	Clear	Cool to 5 °C/ Evaporation	Gum	/
14	Acetone: Water (10%)	✓	/	/	/	/	Clear	Cool to 5 °C/ Evaporation	Gum	/

Key: X = suspension, ✓ = Clear, / = Not Conducted, *gum then became solid after 3 days slurry

Table Q Solubility Assessment at 5 °C, Observations and XRPD Analysis for Recovered Solids

ID	Solvent	10 vol	20 vol	30 vol	50 vol	70 vol	Observation	Treatment	Observation after treatment	XRPD
1	n-Heptane	X	X	X	X	X	Suspension	Maturation 24 hrs	Suspension	Amorphous
2	Ethyl acetate	X	X	X	X	X	Suspension	Maturation 24 hrs	Suspension	Gummed on filter
3	Isopropyl acetate	X	X	X	X	X	Suspension	Maturation 24 hrs	Suspension	Gummed on filter
4	MIBK	X	X	X	X	X	Suspension	Maturation 24 hrs	Suspension	Gummed on filter
5	2-Propanol	X	X	X	X	X	Suspension	Maturation 24 hrs	Suspension	Form 4
6	MEK	√	/	/	/	/	Clear	Cyclohexane addition/ultrasound	Gum	/
7	Acetone	√	/	/	/	/	Clear	Cyclohexane addition/ultrasound	Gum	/
8	Ethanol	√	/	/	/	/	Clear	Cyclohexane addition/ultrasound	Gum	/
9	Tetrahydrofuran	√	/	/	/	/	Clear	Cyclohexane addition/ultrasound	Gum	/
10	Water	√	/	/	/	/	Clear	TBME addition	Solution	/
11	2-Methyl-1-propanol	X	X	X	X	X	Suspension	Maturation 24 hrs	Suspension	Gummed on filter
12	1,4-Dioxane*	√	/	/	/	/	Clear	Cyclohexane addition/ultrasound	Gum	/
13	IPA: Water (10%)	√	/	/	/	/	Clear	TBME addition	Solution	/
14	Acetone: Water (10%)	√	/	/	/	/	Clear	TBME addition	Solution	/

X = suspension, √ = Clear, / = Not Conducted

[0580] At 50 °C amorphous Compound A was highly soluble in the majority of solvents tested (solutions in 8/14 solvent at 10 volumes) with good solubility in 2-Me-1-PrOH (20 volumes), poor solubility in IPA (70 volumes) and some undissolved material persisting in heptane, EtOAc, IPAc and MIBK up to 100 volumes. By contrast, at 5 °C there were 7 solvents where solubility was achieved in 10 volumes. In the remaining 6 solvents; heptane, EtOAc, IPAc, MIBK, IPA and 2-Me-1-PrOH; some material persisted up to 70 vol.

[0581] Following the solubility assessments a combination of cooling, anti-solvent addition, slurry maturation, evaporation and sonication were used as outlined in FIGs. 29 and 30 to generate solids to assess an initial propensity for polymorphism. To assess potential antisolvents for crystallisation approaches; heptane (50 °C samples), and cyclohexane or TBME (5°C samples raised to RT) were added to clear solutions. Only the addition of heptane to an acetone solution was successful in generating solids. In overview, where used, the three typical antisolvents heptane, cyclohexane and TBME were not successful for inducing crystallisation and resulted in samples gumming on addition to the solutions. Samples that were clear solutions after cooling from 50 °C and/or antisolvent addition were evaporated, however, these also resulted in gums forming. Samples from the 5 °C solubility assessment after antisolvent addition were treated to ultrasound for 1 hour to induce form change, however, this was unsuccessful and all remained gums.

[0582] Suspensions at 50 °C and 5 °C were slurried for 24 hours at their respective temperatures before isolation. It was found that samples from EtOAc and MIBK gummed on the filter during isolation, samples from IPAc either gummed on filter or gave an amorphous material and heptane yielded an amorphous solid.

[0583] Forms 4, 5 and 6 were obtained from IPA, acetone and 2-Me-1-PrOH, respectively (FIG. 31). Further characterisation was not possible as these solids deliquesced before this could be conducted.

Example 12. Polymorphism Screen.

[0584] The objective of the polymorph study was to identify any different forms of Compound A using maturation and solvent drop grinding techniques on the amorphous material.

[0585] **5 °C Isothermal Maturation Slurry:** Amorphous Compound A (40 mg) was placed in HPLC vials with a magnetic stir bar and the stated solvent volume was added at 5 °C and stirred

for 30 minutes after which an observation was made. If a suspension was obtained the sample was further slurried at 5 °C for 7 days. All suspensions were isolated by filtration under vacuum, and the solids analysed by XRPD. The observations and results are summarised in Table R.

[0586] **RT/50 °C Maturation Cycling:** Amorphous Compound A (40 mg) was placed in HPLC vials with a magnetic stir bar and the stated solvent volume was added at 50 °C and stirred for 30 minutes after which an observation was made. If a suspension was obtained then the sample was placed in a Heidolph shaker incubator with temperature cycling between 50 °C and RT 4 hours at each temperature) for 7 days. Suspensions were isolated by filtration under vacuum and analysed by XRPD. Gums on the wall of the vials were extracted to give a powder. The observations and results are summarised in Table S.

[0587] **Liquid-assisted Grinding:** Amorphous Compound A (40 mg) was placed in HPLC vials with a 2 stainless steel grinding beads, wetted with 10 µl of the stated solvent and was milled using a Fritsch planetary mill at 500 rpm for 2 hours. After milling, vial caps were removed to allow the solvent to evaporate. Any gums were treated to ultrasound for 4 hours and then placed in a vacuum oven at RT overnight (~5 mbar). All solids were analysed by XRPD. The observations and results are summarised in Table T.

[0588] Based on the 5 °C solubility assessment data, the compound was matured in neat heptane, EtOAc, IPAc, MIBK, IPA and 2-Me-1-PrOH in 10 volumes. Due to the high solubility observed in the other selected solvents, mixtures with heptane in 1:1 v/v ratio were used. The XRPD analysis of recovered solids saw Form 4 from IPA and Form 6 from 2-Me-1-PrOH being observed again. These were observed previously from solids generation after the solubility assessment.

[0589] The observations show that many of the solvent/heptane mixtures yielded gums which did not convert to solids over the 7 days. In addition there were three suspensions observed from EtOAc, IPAc and MIBK that formed gums on isolation. The suspensions in heptane could be successfully isolated and was amorphous by XRPD and the suspension 10% water/IPA) / heptane (1:1 v/v) dissolved during isolation on the filter block.

Table R Observations and XRPD Analysis for 5 °C Isothermal Maturation

ID	Solvent	Vol.	Observation after 24 hrs	Observation after 3 days	Observation after 7 days	XRPD
1	Heptane	10	Suspension	Suspension	Suspension	Amorphous
2	EtOAc	10	Suspension	Suspension	Suspension	Gum
3	IPAc	10	Suspension	Suspension	Suspension	Gum
4	MIBK	10	Suspension	Suspension	Suspension	Gum
5	IPA	10	Suspension	Suspension	Suspension	Form 4
6	MEK/heptane (1:1)	5	Gum	Gum	Gum	N/A
7	Acetone/heptane (1:1)	5	Gum	Gum	Gum	N/A
8	EtOH/heptane (1:1)	5	Emulsion	Gum	Gum	N/A
9	THF/heptane (1:1)	5	Gum	Gum	Gum	N/A
10	Water	5	Clear	Gum	Gum	N/A
11	2-Me-1-PrOH	10	Suspension	Suspension	Suspension	Form 6
12	1,4-dioxane/heptane (1:1)	5	Gum	Gum	Gum	N/A
13	(10% water/IPA) / heptane (1:1)	5	Emulsion	Suspension	Suspension	Dissolved on filter block
14	(10% water/acetone) / heptane (1:1)	5	Emulsion	Clear	Clear	N/A

Key: Vol. – volumes used; N/A not applicable; mixtures are prepared as v/v ratios

[0590] The higher solubility in the selected solvents at 50 °C was taken into consideration in the solvent preparation for RT/50 °C maturation cycling. To modulate the solubility and avoid full dissolution in the higher temperature window solvent/heptane mixtures at 9:1 v/v ratios were prepared.

[0591] The observations in Table S show that full dissolution was circumvented and suspensions observed from heptane, Heptane/IPA, Heptane/EtOH and Heptane/2-Me-1-PrOH (9:1), however, after extended maturation the latter three systems gummed on the vessel walls. In addition, all the other solvent mixtures (except neat water) became gums. Despite the gumming, this material could be extracted and was analysed by XRPD and Form 4 was observed again from heptane/IPA, a Form 7 from heptane/EtOH, Form 3 from heptane/1,4-dioxane and heptane/(10%water/acetone), and Form 8 was isolated from heptane/2-Me-1-PrOH.

[0592] The maturation in water resulted in a beige suspension which was poorly crystalline by XRPD. Due to the colour change of the compound the sample was checked for purity by HPLC a significant drop in purity with 61.0 % purity noted.

Table S Observations and XRPD Analysis for RT/50 °C Maturation Cycling

ID	Solvent	Vol	Observation after 24 hrs	Observation after 7 days	XRPD
1	Heptane	10	Suspension	Suspension	Amorphous
2	Heptane/EtOAc (9:1)	10	Gum	Gum on wall	Amorphous
3	Heptane/IPAc (9:1)	10	Gum	Gum on wall	Amorphous
4	Heptane/MIBK (9:1)	10	Gum	Gum on wall	Amorphous
5	Heptane/IPA (9:1)	10	Suspension	Gum on wall	Form 4
6	Heptane/MEK (9:1)	10	Gum	Gum on wall	Amorphous
7	Heptane/Acetone (9:1)	10	Gum	Gum on wall	Amorphous
8	Heptane/EtOH (9:1)	10	Suspension	Gum on wall	Form 7
9	Heptane/THF (9:1)	10	Gum	Gum on wall	Amorphous w/crystalline signals
10	Water	10	Clear	Beige suspension	Poorly crystalline
11	Heptane/2-Me-1-PrOH (9:1)	10	Suspension	Gum on wall	Form 8
12	Heptane/1,4-dioxane (9:1)	10	Gum	Gum on wall	Form 3
13	Heptane/(10% water/IPA) (9:1)	10	Gum	Gum	N/A
14	Heptane/(10% water/acetone) (9:1)	10	Gum	Gum on wall	Form 3

Key: Vol. – volumes used; any solvent mixtures were prepared as v/v ratios

[0593] The liquid-assisted grinding (Table T) screen was completed using the neat solvent under the knowledge that a small aliquot (0.25 volumes only) would be used. Despite the small solvent volumes all solvent (except heptane) yielded gums. To maximise output, these were sonicated for 4 hours but was unsuccessful in converting the gums to solids. Following vacuum during overnight at room temperature powders were successfully observed, however, these were amorphous except where Form 4 was identified from IPA, Form 2 (dihydrate) from water and Form 6 from 2-Me-1-PrOH.

Table T Observations and XRPD Analysis from Liquid-Assisted Grinding Screening

ID	Solvent	Observation milling	Observation after ultrasound	Observation after vacuum oven	XRPD
1	Heptane	Powder	N/A	N/A	Amorphous
2	EtOAc	Gum	Gum	Powder	Amorphous
3	IPAc	Gum	Gum	Powder	Amorphous
4	MIBK	Gum	Gum	Powder	Amorphous
5	IPA	Gum	Gum	Powder	Form 4
6	MEK	Gum	Gum	Powder	Amorphous
7	Acetone	Gum	Gum	Powder	Amorphous
8	EtOH	Gum	Gum	Powder	Amorphous
9	THF	Gum	Gum	Powder	Amorphous
10	Water	Gum	Gum	Powder	Form 2
11	2-Me-1-PrOH	Gum	Gum	Powder	Form 6
12	1,4-dioxane	Gum	Gum	Powder	Amorphous
13	10% water/IPA	Gum	Gum	Powder	Amorphous
14	10% water/Acetone	Gum	Gum	Powder	Amorphous

Key: N/A – not applicable

Example 13. Focused Hydrate Screen

[0594] **Storage at Elevated Temperature/Humidity:** Amorphous Compound A (35 mg) was weighed into HPLC vials and placed in a sealed container with a saturated salt solution to generate the required humidity, then placed in an incubator at the required temperature. Samples were stored for 1 week before XRPD analysis.

[0595] **5 °C Isothermal Slurry:** Amorphous Compound A (35 mg) was weighed into HPLC vials. The stated solvent (3 Vol. 105 µl) and a stirrer bar was added. Samples were stirred for at 5 °C for 7 days. Any solids were analysed by XRPD, clear samples were left to evaporate.

[0596] **RT/50 °C Maturation Cycling:** Compound A (35 mg) was weighed into HPLC vials. The stated solvent (3 Vol., 105 µl) and a stirrer bar was added. Samples were placed in a shaker with temperature cycling between 25 and 50 °C with 4 hours hold at each temperature for 7 days. Clear solutions after 24 hrs were placed in the freezer then left to evaporate. Slurries were smeared and dried under nitrogen onto XRPD flat place for analysis.

[0597] **Liquid-assisted Grinding:** Compound A (35 mg), stated solvent 10 µl was added and two steel grinding beads were added and milled at 500 rpm for 2 hours. Gums were then placed in an ultrasound bath for 4 hrs but remained gums. The gums were then placed in a vacuum oven overnight. All solids were analysed by XRPD.

[0598] A matrix of twelve temperature and humidity conditions were investigated covering 25 °C, 40 °C and 60 °C at increments in relative humidity from 30 % up to 97 % RH. The observations and XRPD analysis are summarised in Table U. At 97% RH, the amorphous input deliquesced at all temperatures and at 60 °C/97% RH the material became a brown gel which had 69.0% purity by HPLC.

[0599] At the lower humidity range (30 % and 50 % RH) most recovered solids were amorphous except those from 40 °C/30% RH which was poorly crystalline Form 2 (dihydrate).

[0600] The main region of activity occurred at 75 % RH where Form 2 was recovered from 25 °C/75% RH (poorly crystalline) and 40 °C/75% RH. The solids recovered from 60 °C/75% RH were Form 3 (monohydrate). There was no evidence of additional forms from this elevated storage study.

Table U Observations and XRPD Analysis Following Elevated Storage Conditions

XX	RH %	Temp °C	Observation	XRPD
1	30	25	Powder	Amorphous
2	30	40	Glass	Amorphous/poorly crystalline Form 2
3	30	60	Glass	Amorphous
4	50	25	Glass	Amorphous
5	50	40	Glass	Amorphous
6	50	60	Powder	Amorphous
7	75	25	Glass/Gum	Amorphous/poorly crystalline Form 2
8	75	40	Glass	Form 2
9	75	60	Glass	Form 3
10	97	25	Deliquesced/gel	N/A
11	97	40	Deliquesced/gel	N/A
12	97	60	Brown Gel	Suspected degradation – HPLC Purity 69.0%

25 °C/30% RH, 40 °C/30% RH, 60 °C/30% RH = saturated MgCl₂

25 °C/50% RH = saturated Mg(NO₃)₂, 40 °C/50% RH, 60 °C/50% RH = saturated NaBr

25 °C/75% RH, 40 °C/75% RH, 60 °C/75% RH = saturated NaCl

25 °C/97% RH, 40 °C/97% RH, 60 °C/97% RH = saturated K₂SO₄

[0601] For screening by solution methods, the water activity range was investigated from $a_w = 0.3 - 0.9$, and solvents were selected that avoided known solvate formation where possible. As it was known that Compound A was highly soluble in water and in aiming to avoid full dissolution and possible gumming previously observed, only 3 volumes of solvent were used for the 5 °C isothermal maturation (Table V). Despite lowering the solvent volumes, material could only be recovered from EtOAc/water (99.5:0.5 v/v) and was Form 2 (dihydrate). The remaining solutions were evaporated; however, this gave gums.

Table V Observations and XRPD Analysis Following 5 °C Isothermal Maturation

XX	Solvent	Water activity	Observation after 24 hrs	Observation 7 days	XRPD
1	5% water/MeOH	0.2	Clear solution	Clear solution	Evaporation#
2	0.5% water/EtOAc	0.3	Clear solution	Powder round the top of vial	Form 2
3	15%water/MeOH	0.4	Clear solution	Clear solution	Evaporation#
4	3.5% water/1,4-dioxane	0.5	Clear solution	Clear solution	Evaporation#
5	7% water/ACN	0.7	Clear solution	Clear solution	Evaporation#
6	7% water/THF	0.9	Clear solution	Clear solution	Evaporation#

= gums on evaporation

[0602] After the RT/50 °C maturation cycling there were 4 separate slurries observed. The recovery from EtOAc/water (99.5:0.5 v/v) was Form 3 (monohydrate) and in isolating the three slurries from $a_w = 0.5, 0.7$ and 0.9 , the samples all deliquesced on the filter frit and could not be analysed further (Table W).

Table W Observations and XRPD Analysis Following RT/50 °C Maturation Cycling

XX	Solvent	Water activity	Observation after 24 hrs	Treatment	Observation after 7 days	XRPD
1	5% water/MeOH	0.2	Clear	Freezer	Clear	Evaporation#
2	0.5% water/EtOAc	0.3	Thick slurry	Slurry	Thick Slurry	Form 3
3	15%water/MeOH	0.4	Clear	Freezer	Clear	Evaporation#
4	3.5% water/1,4-	0.5	Hazy suspension	Slurry	Slurry	Deliquesced *

XX	Solvent	Water activity	Observation after 24 hrs	Treatment	Observation after 7 days	XRPD
	dioxane					
5	7% water/ACN	0.7	Hazy suspension	Slurry	Slurry	Deliquesced *
6	7% water/THF	0.9	Hazy suspension	Slurry	Slurry	Deliquesced *

Key: * – The samples were prepared onto an XRPD slide for characterisation, on preparation the samples deliquesced and turned into a gum # = gums on evaporation

[0603] In the final screen liquid-assisted grinding was used with ~ a third of a volume of solvent. Two powders were recovered from two MeOH/water mixtures ($a_w = 0.2, 0.4$) and were Form 7 by XRPD which had been previously observed from EtOH. Gels were observed from the other solvent mixtures which were sonicated and then dried in a vacuum oven. These gave amorphous solids on removal (Table X).

Table X Observations and XRPD Analysis Following Liquid-Assisted Grinding

XX	Solvent	Water activity	Observation after milling	Further treatment	XRPD
01	5% water/MeOH	0.2	Powder	N/A	Form 7
02	0.5% water/EtOAc	0.3	Gel	Sonication/vac oven	Amorphous
03	15% water/MeOH	0.4	Powder	N/A	Form 7
04	3.5% water/1,4-dioxane	0.5	Gel	Sonication/vac oven	Amorphous
05	7% water/ACN	0.7	Gel	Sonication/vac oven	Amorphous
06	7% water/THF	0.9	Gel	Sonication/vac oven	Amorphous

Key: N/A – not applicable

[0604] A focused hydrate screen was undertaken using elevated temperature/humidity conditions to force form conversion in the solid-state in addition to solution screening. From the screening, no new hydrate forms were identified. However, Form 7 was observed again from MeOH/water, a different solvent to when it was first observed. This seems to suggest that Form 7 forms a family of structurally related solvates or mixed hydrate/solvate forms. In addition, an analysis of the thermal behaviour of Form 7 could suggest that the metastable anhydrous forms are enantiotropically related.

[0605] As Form 2 (dihydrate) and Form 3 (monohydrate) still appeared to be the most promising solid forms, these were recommended for scale-up.

Example 14. Solubility Determination Study.

[0606] Thermodynamic solubility was conducted in 3 different buffered pH levels (i.e., 1.2, 6, and 8) to allow for comparison of Compound A (amorphous material) with the two hydrated forms. Residual solids after the solubility assessment were analysed by XRPD. Results of the solubility assessment are summarised in Table Y.

[0607] The measured solubility was similar for the amorphous, Form 2 (dihydrate) and Form 3 (monohydrate) in the three pH values tested. Highest solubility was observed at pH 8 (≥ 10 mg/ml). XRPD on the residues showed that Form 2 and the amorphous material converted to Form 11.

Table Y Comparison of Thermodynamic Solubility Data for amorphous Compound A, Dihydrate Form 2 and Monohydrate Form 3

	Compound A	Test 1	Test 2
Condition	As-supplied	40 °C/75% RH	60 °C/75% RH
XRPD	Amorphous	Form 2	Form 3
Assignment	Amorphous	Dihydrate	Monohydrate
Solubility (mg/ml)	pH 1.2: 0.07 pH 6.0: 0.30 pH 8.0: >10	pH 1.2: 0.07 pH 6.0: 0.32 pH 8.0: >10	pH 1.2: 0.06 pH 6.0: 0.33 pH 8.0: 10.2
XRPD for solubility residues	pH 1.2: Form 11 pH 6.0: Form 11 pH 8.0: Form 11	pH 1.2: Form 11 pH 6.0: Form 11 pH 8.0: Form 11	pH 1.2: n/a pH 6.0: n/a pH 8.0: n/a

Example 15. Thermodynamic Solubility Study.

[0608] Saturated solution was prepared by slurring Compound A (200 mg) in 4 ml EtOAc/water 1% (v/v) at 50 °C for 24 hrs, giving a thick white suspension. Forms 2 and 3 (20 mg of each) were weighed into a HPLC vial 500 µl was filtered through a nylon syringe filter (0.45 µm pore size) into the HPLC vial. The saturated solution was then cooled to the stated temperature and held for 1 hour. Another 500 µl of suspension was filtered through a nylon syringe filter. This process was repeated for each of the stated temperatures (50 °C, 25 °C, 15 °C and 5 °C). Samples were slurried at the stated temperature for 24 hours when an aliquot was

taken and analysed by XRPD. If conversion to a single form was not achieved after 24 hrs a second aliquot was taken after 48 hrs and analysed by XRPD. Summary of these experiments is provided in Table Z.

Table Z XRPD analysis for competitive slurries in EtOAc/water (99:1 v/v)

Temp	Observation	XRPD after 24 hrs	XRPD after 48 hrs
50	White suspension	Form 3 only	N/A
25	White suspension	Form 2 and 3	Form 2 and 3
15	White suspension	Form 2 only	N/A
5	White suspension	Form 2 only	N/A

[0609] It was found that at 50 °C, after 24 hrs the sample had converted to Form 3 only, whereas experiments at 15 °C and below converted to Form 2 only. The competitive slurry at 25 °C showed the presence of both Form 2 and 3 up to 48 hrs. These experiments show that relative form stability in suspension is temperature dependent, and it would be possible to isolate either form depending on the isolation temperature.

[0610] At 50 °C Form 3 (monohydrate) was the most stable while at 15 °C and 5 °C Form 2 (dihydrate) was most stable. A mixture for Form 2 and Form 3 was obtained at 25 °C indicating that 25 °C is close to the transition temperature where the relative stability of the respective hydrates changes in this solvent mixture ($a_w \sim 0.5$).

Example 16. Crystal Structure of Compound A (Form 3)

[0611] Crystals of Compound A Na salt monohydrate, Form 3, were obtained by cooling from an ethyl acetate and water solution. A crystal of sufficient size and quality for analysis by single crystal X-ray diffraction was cut from a larger rod-type crystal and isolated, with approximate dimensions $0.15 \times 0.10 \times 0.10$ mm.

[0612] The crystal structure of Compound A Na salt monohydrate was determined at 100(2) K and a summary of all the structural data can be found in Table AA. The Compound A Na salt monohydrate crystallises in the monoclinic, space group $P2_1$ with the final $R1 [I > 2\sigma(I)] = 4.28$ %. The structure was identified and the asymmetric unit found to contain two molecules of Compound A, one which is fully ordered and the other which contains the 1-methyl-N-{(2S)-oxolan-2-yl)methyl}-1H-pyrazol-4-amine group disordered over two positions with an occupancy ratio of 0.63:0.37. Each Compound A is bound to a sodium ion through the sulfonate groups and both sodium ions are coordinated to a water molecule. Both coordinated water

molecules are disordered over two positions (O1A and O1B occupancy ratio of 0.70:0.30; O10A and O10B occupancy ratio of 0.74:0.26).

Table AA Sample and Crystal Data for Compound A (Form 3)

Compound number	Compound A Na salt monohydrate	
Crystallisation solvents	EtOAc and water	
Crystallisation method	Cooling	
Empirical formula	$C_{22}H_{30}N_5NaO_5S$	
Formula weight	499.56	
Temperature	100(2) K	
Wavelength	1.54184 Å	
Crystal size	0.300 x 0.250 x 0.200 mm	
Crystal habit	colourless cut rod	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	$a = 10.17100(10)$ Å	$a = 90^\circ$
	$b = 12.04740(10)$ Å	$b = 89.8050(10)^\circ$
	$c = 20.0561(2)$ Å	$c = 90^\circ$
Volume	$2457.54(4)$ Å ³	
Z	4	
Density (calculated)	1.350 Mg/m ³	
Absorption coefficient	1.708 mm^{-1}	
$F(000)$	1056	

Overall structure quality factor: 2

[0613] The absolute stereochemistry of Compound A Na Salt (Form 3) is in the S configuration.

[0614] The simulated XRPD pattern of Compound A Na salt monohydrate, Form 3 at 100(2) K is shown in FIG. 32. An overlay with the experimental diffractogram at RT confirms that the simulated diffractogram from the single crystal structure is consistent with the experimental diffractogram of Compound A Na salt monohydrate, Form 3 (FIG. 33). Slight differences in the simulated and experimental diffractograms are attributable to lattice vibrations with temperature and specified orientation.

Example 17. Exemplary Preparation of Form 12 – Anhydrous.

[0615] To generate Form 12, 2.0 g of Form 4 was dissolved in EtOAc (40 mL, 20 vol) and water (0.20 mL), then heated to 45 °C forming a clear solution, and seeded (~20 mg, 1 wt%). A hazy

solution was formed which was cooled to 30 °C after 30 min and aged at 30 °C for 65 h. The hazy solution was magnetically stirred (4.5 mg/mL), to obtain crystalline Form 12. Form 12 was filtered and dried under vacuum at 20 °C to provide a solid having greater than 99.9% HPLC purity. The sample collected had 99.7 wt% Form 12 and 0.3 wt% H₂O.

[0616] Characterization data of Form 12 are provided in FIGs. 34A-38B.

[0617] The XRPD diffractogram of anhydrous Form 12 is provided in FIG. 34A. Further, the XRPD diffractogram of anhydrous Form 12 was compared to the XRPD diffractogram of Form 3 monohydrate (FIG. 34B). TGA of anhydrous Form 12 exhibited substantially no weight loss up to 150 °C followed by thermal degradation. The DSC showed single endothermic melt transition with an onset temperature of *ca.* 178 °C. Thermal analysis showed that Form 12 is anhydrous (FIG. 35). DVS analysis at 25 °C showed a weight change of *ca.* 1% from 0-80% RH, indicating that anhydrous Form 12 was slightly hygroscopic (Ph.Eur.) as shown in FIG. 36. DVS analysis at varying humidity showed that anhydrous Form 12 was stable up to 80% RH at 25 °C. A weight gain of more than 30% after 80% RH was observed (FIG. 37), and conversion to monohydrate was observed by XRPD post DVS. Crystals of anhydrous Form 12 had needle shaped crystal morphology with particle size of up to 30 µm as shown in FIGs. 38A and 38B.

Example 18. Competitive Slurry of Anhydrous Form 12 and Form 3 Monohydrate

[0618] About 10 mg of each anhydrous Form 12 and Form 3 monohydrate were weighed out in 2 mL clear glass vials. 0.5 mL of EtOAc and water mixture with different level of water from 0.1, 0.25, 0.5, and 1% was added. Each slurry was left to stir at 25 °C and 50 °C for 4 days (FIGs. 39 and 40, respectively). XRPD was performed on slurries after 4 days. Anhydrous Form 12 was dominant up to 0.5% water in the solvent system. Form 3 monohydrate was formed with 1% water in the solvent system.

EQUIVALENTS

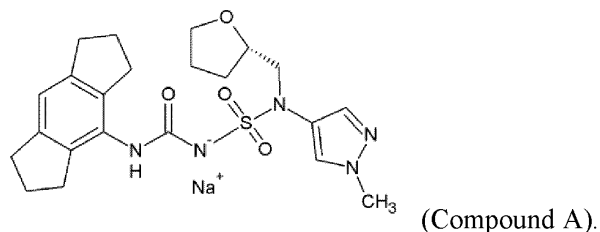
[0619] The details of one or more embodiments of the disclosure are set forth in the accompanying description above. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present disclosure, the preferred methods and materials are now described. Other features, objects, and advantages of the disclosure will be apparent from the description and from the claims. In the specification and

the appended claims, the singular forms may include plural referents unless the context clearly dictates otherwise. Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. All patents and publications cited in this specification are incorporated by reference.

[0620] The foregoing description has been presented only for the purposes of illustration and is not intended to limit the disclosure to the precise form disclosed, but by the claims appended hereto.

What is claimed is:

1. A morphic form of Compound A:



2. The morphic form of claim 1, being a crystalline form of Compound A.
3. The morphic form of any one of the preceding claims, being anhydrous Form 1 of Compound A.
4. The morphic form of any one of the preceding claims, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.5 ± 0.5 , 18.1 ± 0.5 , and 18.3 ± 0.5 °2 θ using Cu K α radiation.
5. The morphic form of any one of the preceding claims, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.5 ± 0.5 , 18.1 ± 0.5 , 18.3 ± 0.5 , and 22.7 ± 0.5 °2 θ using Cu K α radiation.
6. The morphic form of any one of the preceding claims, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.5 ± 0.5 , 18.1 ± 0.5 , 18.3 ± 0.5 , 19.0 ± 0.5 , and 22.7 ± 0.5 °2 θ using Cu K α radiation.
7. The morphic form of any one of the preceding claims, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.5 ± 0.5 , 18.1 ± 0.5 , 18.3 ± 0.5 , 19.0 ± 0.5 , 22.7 ± 0.5 , and 23.4 ± 0.5 °2 θ using Cu K α radiation.

8. The morphic form of any one of the preceding claims, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.5 ± 0.5 , 13.3 ± 0.5 , 18.1 ± 0.5 , 18.3 ± 0.5 , 19.0 ± 0.5 , 22.7 ± 0.5 , and 23.4 ± 0.5 $^{\circ}2\theta$ using Cu K α radiation.
9. The morphic form of any one of the preceding claims, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.5 ± 0.5 , 13.3 ± 0.5 , 16.2 ± 0.5 , 18.1 ± 0.5 , 18.3 ± 0.5 , 19.0 ± 0.5 , 22.7 ± 0.5 , and 23.4 ± 0.5 $^{\circ}2\theta$ using Cu K α radiation.
10. The morphic form of any one of the preceding claims, wherein the morphic form is characterized by an XRPD pattern comprising one or more signals as described in Table 1.
11. The morphic form of any one of the preceding claims, wherein the morphic form is characterized by an XRPD pattern substantially similar to that set forth in FIG. 2.
12. The morphic form of claim 1 or claim 2, being dihydrate Form 2 of Compound A.
13. The morphic form of claim 1, 2 or 12, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.2 ± 0.5 , 16.7 ± 0.5 , and 16.8 ± 0.5 $^{\circ}2\theta$ using Cu K α radiation.
14. The morphic form of claim 1, 2, 12 or 13, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.2 ± 0.5 , 16.7 ± 0.5 , 16.8 ± 0.5 , and 18.2 ± 0.5 $^{\circ}2\theta$ using Cu K α radiation.
15. The morphic form of any one of claims 1, 2, and 12-14, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.2 ± 0.5 , 10.4 ± 0.5 , 16.7 ± 0.5 , 16.8 ± 0.5 , and 18.2 ± 0.5 $^{\circ}2\theta$ using Cu K α radiation.
16. The morphic form of any one of claims 1, 2, and 12-15, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.2 ± 0.5 , 8.4 ± 0.5 , 10.4 ± 0.5 , 16.7 ± 0.5 , 16.8 ± 0.5 , and 18.2 ± 0.5 $^{\circ}2\theta$ using Cu K α radiation.

17. The morphic form of any one of claims 1, 2, and 12-16, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.2 ± 0.5 , 8.4 ± 0.5 , 10.4 ± 0.5 , 16.7 ± 0.5 , 16.8 ± 0.5 , 18.2 ± 0.5 , and 20.8 ± 0.5 °2 θ using Cu K α radiation.
18. The morphic form of any one of claims 1, 2, and 12-17, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.2 ± 0.5 , 8.4 ± 0.5 , 10.4 ± 0.5 , 16.7 ± 0.5 , 16.8 ± 0.5 , 18.2 ± 0.5 , 20.8 ± 0.5 , and 21.1 ± 0.5 °2 θ using Cu K α radiation.
19. The morphic form of any one of claims 1, 2, and 12-18, wherein the morphic form is characterized by an XRPD pattern comprising one or more signals as described in Table 2.
20. The morphic form of any one of claims 1, 2, and 12-19, wherein the morphic form is characterized by an XRPD pattern substantially similar to that set forth in FIG. 4.
21. The morphic form of claim 1 or claim 2, being Form 3 of Compound A.
22. The morphic form of claim 1, 2 or 21, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.4 ± 0.5 , and 17.8 ± 0.5 °2 θ using Cu K α radiation.
23. The morphic form of claim 1, 2, 21 or 22, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.4 ± 0.5 , 17.8 ± 0.5 , and 19.0 ± 0.5 °2 θ using Cu K α radiation.
24. The morphic form of any one of claims 1, 2, and 21-23, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.4 ± 0.5 , 17.8 ± 0.5 , 19.0 ± 0.5 , and 22.3 ± 0.5 °2 θ using Cu K α radiation.
25. The morphic form of any one of claims 1, 2, and 21-24, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.4 ± 0.5 , 17.8 ± 0.5 , 19.0 ± 0.5 , 19.6 ± 0.5 , and 22.3 ± 0.5 °2 θ using Cu K α radiation.

26. The morphic form of any one of claims 1, 2, and 21-25, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.4 ± 0.5 , 17.8 ± 0.5 , 19.0 ± 0.5 , 19.6 ± 0.5 , 20.9 ± 0.5 , and 22.3 ± 0.5 $^{\circ}2\theta$ using Cu K α radiation.
27. The morphic form of any one of claims 1, 2, and 21-26, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.4 ± 0.5 , 14.3 ± 0.5 , 17.8 ± 0.5 , 19.0 ± 0.5 , 19.6 ± 0.5 , 20.9 ± 0.5 , and 22.3 ± 0.5 $^{\circ}2\theta$ using Cu K α radiation.
28. The morphic form of any one of claims 1, 2, and 21-27, wherein the morphic form is characterized by an XRPD pattern comprising one or more signals as described in Table 3.
29. The morphic form of any one of claims 1, 2, and 21-28, wherein the morphic form is characterized by an XRPD pattern substantially similar to that set forth in FIG. 10.
30. The morphic form of any one of claims 1, 2, and 21-29, wherein the morphic form is a crystalline solid having crystal data as provided in Table AA.
31. The morphic form of claim 1 or claim 2, wherein the morphic form is characterized by an XRPD pattern substantially similar to that set forth in FIG. 32.
32. The morphic form of claim 1 or claim 2, being Form 4 of Compound A.
33. The morphic form of claim 1 or claim 2, being Form 5 of Compound A.
34. The morphic form of claim 1 or claim 2, being Form 6 of Compound A.
35. The morphic form of any one of claims 1, 2, or 34, wherein the morphic form is characterized by an XRPD pattern substantially similar to that set forth in FIG. 20.
36. The morphic form of claim 1 or claim 2, being Form 7 of Compound A.

37. The morphic form of claim 1 or claim 2, being Form 8 of Compound A.
38. The morphic form of claim 1 or claim 2, being Form 9 of Compound A.
39. The morphic form of claim 1, 2 or 38, wherein the morphic form is characterized by an XRPD pattern comprising signals at 8.0 ± 0.5 , 21.3 ± 0.5 , and 22.1 ± 0.5 °2 θ using Cu K α radiation.
40. The morphic form of claim 1, 2, 38 or 39, wherein the morphic form is characterized by an XRPD pattern comprising signals at 8.0 ± 0.5 , 21.3 ± 0.5 , 22.1 ± 0.5 , and 22.9 ± 0.5 °2 θ using Cu K α radiation.
41. The morphic form of any one of claims 1, 2, and 38-40, wherein the morphic form is characterized by an XRPD pattern comprising signals at 8.0 ± 0.5 , 18.2 ± 0.5 , 21.3 ± 0.5 , 22.1 ± 0.5 , and 22.9 ± 0.5 °2 θ using Cu K α radiation.
42. The morphic form of any one of claims 1, 2, and 38-41, wherein the morphic form is characterized by an XRPD pattern comprising signals at 8.0 ± 0.5 , 18.2 ± 0.5 , 19.7 ± 0.5 , 21.3 ± 0.5 , 22.1 ± 0.5 , and 22.9 ± 0.5 °2 θ using Cu K α radiation.
43. The morphic form of any one of claims 1, 2, and 38-42, wherein the morphic form is characterized by an XRPD pattern comprising signals at 8.0 ± 0.5 , 18.2 ± 0.5 , 19.7 ± 0.5 , 21.3 ± 0.5 , 22.1 ± 0.5 , 22.9 ± 0.5 , and 25.3 ± 0.5 °2 θ using Cu K α radiation.
44. The morphic form of any one of claims 1, 2, and 38-43, wherein the morphic form is characterized by an XRPD pattern comprising signals at 8.0 ± 0.5 , 18.2 ± 0.5 , 19.7 ± 0.5 , 21.3 ± 0.5 , 22.1 ± 0.5 , 22.9 ± 0.5 , 24.6 ± 0.5 , and 25.3 ± 0.5 °2 θ using Cu K α radiation.
45. The morphic form of any one of claims 1, 2, and 38-44, wherein the morphic form is characterized by an XRPD pattern comprising one or more signals as described in Table 4.

46. The morphic form of any one of claims 1, 2, and 38-45, wherein the morphic form is characterized by an XRPD pattern substantially similar to that set forth in FIG. 25.
47. The morphic form of claim 1 or claim 2, being Form 10 of Compound A.
48. The morphic form of claim 1, 2 or 47, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.3 ± 0.5 , and 17.5 ± 0.5 $^{\circ}2\theta$ using Cu K α radiation.
49. The morphic form of claim 1, 2, 47 or 48, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.3 ± 0.5 , 17.5 ± 0.5 , and 19.2 ± 0.5 $^{\circ}2\theta$ using Cu K α radiation.
50. The morphic form of any one of claims 1, 2, and 47-49, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 8.3 ± 0.5 , 14.9 ± 0.5 , 17.5 ± 0.5 , and 19.2 ± 0.5 $^{\circ}2\theta$ using Cu K α radiation.
51. The morphic form of any one of claims 1, 2, and 47-50, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 4.7 ± 0.5 , 8.3 ± 0.5 , 14.9 ± 0.5 , 17.5 ± 0.5 , and 19.2 ± 0.5 $^{\circ}2\theta$ using Cu K α radiation.
52. The morphic form of any one of claims 1, 2, and 47-51, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 4.7 ± 0.5 , 7.4 ± 0.5 , 8.3 ± 0.5 , 14.9 ± 0.5 , 17.5 ± 0.5 , and 19.2 ± 0.5 $^{\circ}2\theta$ using Cu K α radiation.
53. The morphic form of any one of claims 1, 2, and 47-52, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.4 ± 0.5 , 4.7 ± 0.5 , 7.4 ± 0.5 , 8.3 ± 0.5 , 14.9 ± 0.5 , 17.5 ± 0.5 , 19.2 ± 0.5 , and 23.3 ± 0.5 $^{\circ}2\theta$ using Cu K α radiation.
54. The morphic form of any one of claims 1, 2, and 47-53, wherein the morphic form is characterized by an XRPD pattern comprising one or more signals as described in Table 5.

55. The morphic form of any one of claims 1, 2, and 47-54, wherein the morphic form is characterized by an XRPD pattern substantially similar to that set forth in FIG. 27.
56. The morphic form of claim 1 or claim 2, being Form 12 of Compound A.
57. The morphic form of claim 1, 2, or 56, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.1 ± 0.5 , 4.7 ± 0.5 , and 8.2 ± 0.5 °2 θ using Cu K α radiation.
58. The morphic form of any one of claims 1, 2, 56, and 57, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.1 ± 0.5 , 4.7 ± 0.5 , 8.2 ± 0.5 , and 8.7 ± 0.5 °2 θ using Cu K α radiation).
59. The morphic form of any one of claims 1, 2, and 56-58, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.1 ± 0.5 , 4.7 ± 0.5 , 8.2 ± 0.5 , 8.7 ± 0.5 , and 12.4 ± 0.5 °2 θ using Cu K α radiation.
60. The morphic form of any one of claims 1, 2, and 56-59, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.1 ± 0.5 , 4.7 ± 0.5 , 8.2 ± 0.5 , 8.7 ± 0.5 , 10.2 ± 0.5 , and 12.4 ± 0.5 °2 θ using Cu K α radiation.
61. The morphic form of any one of claims 1, 2, and 56-60, wherein the morphic form is characterized by an XRPD pattern comprising signals at 4.1 ± 0.5 , 4.7 ± 0.5 , 8.2 ± 0.5 , 8.7 ± 0.5 , 10.2 ± 0.5 , 11.3 ± 0.5 , and 12.4 ± 0.5 °2 θ using Cu K α radiation.
62. The morphic form of any one of claims 1, 2, and 56-61, wherein the morphic form is characterized by an XRPD pattern comprising one or more signals as described in Table 5-1.
63. The morphic form of any one of claims 1, 2, and 56-62, wherein the morphic form is characterized by an XRPD pattern substantially similar to that set forth in FIG. 34A.
64. The morphic form of claim 1 or claim 2, prepared using one of the methods provided in FIG. 1.

65. A method of preparing a morphic form of Compound A of any one of the preceding claims.
66. A pharmaceutical composition comprising a morphic form of Compound A of any one of the preceding claims, and one or more pharmaceutically acceptable carrier or excipient.
67. A method of preventing or treating a disease or disorder in a subject, comprising administering to the subject a morphic form of Compound A of any one of the preceding claims.
68. A morphic form of Compound A of any one of the preceding claims for use in preventing or treating a disease or disorder in a subject.
69. Use of a morphic form of Compound A of any one of the preceding claims in the manufacture of a medicament for preventing or treating a disease or disorder in a subject.
70. A method of inhibiting inflammasome activity in a subject, comprising contacting a cell with a morphic form of Compound A of any one of the preceding claims.
71. A morphic form of Compound A of any one of the preceding claims for use in inhibiting inflammasome activity in a subject.
72. Use of a morphic form of Compound A in the manufacture of a medicament for inhibiting inflammasome activity in a subject.
73. The method, morphic form, or use of any one of the preceding claims, wherein the subject is human.