

-1-

CRYSTALLINE FORMS OF 2-[3-(2,2,6,6-TETRAMETHYLPYPERIDIN-4-YL)-3H-[1,2,3]TRIAZOLO[4,5-C]PYRIDAZIN-6-YL]-5-(2H-1,2,3-TRIAZOL-2-YL)PHENOL

FIELD OF THE INVENTION

[0001] The present invention is directed to crystalline forms of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol, methods of making the same, pharmaceutical compositions comprising the same and methods using the same in treating Huntington's Disease.

BACKGROUND

[0002] Polymorphism denotes the existence of more than one crystalline form of a substance. Polymorphs (or crystalline modifications) have an identical chemical structure but often quite different physicochemical properties. Polymorphs include enantiotropic polymorphs and monotropic polymorphs. This ability of a chemical substance to crystallize in more than one crystalline form can have a profound effect on the shelf life, solubility, formulation properties, and processing properties of a drug. In addition, the action of a drug can be affected by the polymorphism of the drug molecule. Different polymorphs can have different rates of uptake in the body, leading to lower or higher biological activity than desired. In extreme cases, an undesired polymorph can even show toxicity. The occurrence of an unknown crystalline form during manufacture can have a significant impact.

[0003] Understanding and controlling polymorphism, then, gives a decided advantage in bringing new drugs to the marketplace. First and foremost, searching for any possible polymorphs for a drug product can be used to diminish the possibility of contamination during a drug's manufacture or storage by other polymorphic forms. Failure to catch contamination can have life-threatening consequences in some cases. Crystallizing an unintended polymorph during manufacture can mean weeks or even months of production downtime while scientists find and correct the cause of the new crystalline form or go through another round of testing to obtain approval for the new crystalline form.

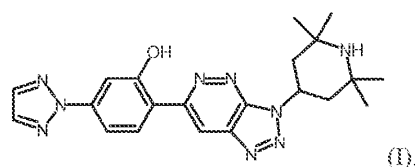
[0004] Second, understanding which crystalline forms of a drug are possible in certain cases allows researchers to maximize the desired properties of a compound, such as solubility, formulation properties, processing properties, and shelf life. Understanding these factors early

-2-

in the development of a new drug may mean a more active, more stable, or less expensively manufactured drug.

[0005] Huntington's Disease (HD) is a rare inherited neurodegenerative disorder caused by a mutation in the *huntingtin* (*HTT*) gene. The disorder results in behavioral, cognitive, and motor impairments. These symptoms progressively reduce an individual's quality of life, and ultimately lead to death within 15 to 25 years of overt clinical motoric onset. Each child of a parent with a mutation in the *huntingtin* gene has a 50% chance of inheriting the mutation. It is estimated that around one person in 10,000 carries the mutated huntingtin gene. Current HD therapies manage the severity of the symptoms, but there are currently no therapeutics approved that slow the progression of the disease.

[0006] An international application published as WO2020/005873 identified a genus of compounds that can be used in the treatment of Huntington's disease (HD), methods of making the same and pharmaceutical formulations of the same, which is incorporated herein by reference in its entirety. One such compound is 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol of the formula



[0007] Knowledge of potential polymorphic forms of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol is useful in the development of a suitable dosage form, because the failure to utilize a single polymorphic form during clinical or stability studies may result in the exact dosage form being used or studied not being comparable from one lot to another. Once chosen, it is important that a polymorphic form can be reproducibly prepared and remain unchanged for prolonged time periods in the dosage form developed.

[0008] WO2020/005873 A1 provides no information about possible crystal modifications of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol. Accordingly, new crystalline forms of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol can further drug product development of the compound in the treatment of Huntington's disease. The present invention provides such novel crystalline forms, for example, crystalline forms of 2-

-3-

[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol

SUMMARY OF THE INVENTION

[0009] The present invention is directed to crystalline forms of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol.

[0010] The present invention is also directed methods of making, isolating and/or characterizing various crystalline forms of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol.

[0011] The present invention also provides a pharmaceutical composition comprising: (a) a therapeutically effective amount of a crystalline form of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol of the present invention; and (b) at least one pharmaceutically acceptable carrier.

[0012] The present invention is also directed to a method for treating or ameliorating Huntington's Disease comprising the step of administering to a subject in need of such treatment a therapeutically effective amount of a crystalline form of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol of the present invention or a pharmaceutical composition comprising a therapeutically effective amount of a crystalline form of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol of the present invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] FIG. 1 depicts the X-ray powder diffraction (XRPD) pattern for crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to the present invention.

[0014] FIG. 2 depicts the differential scanning calorimetry (DSC) thermogram for crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to the present invention.

[0015] FIG. 3 depicts the thermogravimetry coupled fourier transform infrared spectroscopy (TG-FTIR) thermogram for crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-

-4-

[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to the present invention.

[0016] FIG. 4 depicts the fourier transform Raman spectroscopy (FT-Raman) spectrum for crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to the present invention.

[0017] FIG. 5 depicts the X-ray powder diffraction (XRPD) pattern for crystalline Form B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to the present invention.

[0018] FIG. 6 depicts the differential scanning calorimetry (DSC) thermogram for crystalline Form B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to the present invention.

[0019] FIG. 7 depicts the thermogravimetry coupled fourier transform infrared spectroscopy (TG-FTIR) thermogram for crystalline Form B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to the present invention.

[0020] FIG. 8 depicts the fourier transform Raman spectroscopy (FT-Raman) spectrum for crystalline Form B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to the present invention.

[0021] FIG. 9 depicts the X-ray powder diffraction (XRPD) pattern for crystalline Form C of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to the present invention.

[0022] FIG. 10 depicts the X-ray powder diffraction (XRPD) pattern for trihydrate crystalline form H_A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to the present invention.

[0023] FIG. 11 depicts the XRPD pattern for solvate form S_A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to the present invention.

[0024] FIG. 12 depicts the XRPD pattern for solvate form S_B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to the present invention.

-5-

[0025] FIG. 13 depicts the XRPD pattern for solvate form S_c of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to the present invention.

[0026] FIG. 14 depicts the XRPD pattern for solvate form S_D of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to the present invention.

DETAILED DESCRIPTION OF THE INVENTION

[0027] In the context of the present invention, the following definitions have the indicated meaning, unless explicitly stated otherwise:

[0028] Reference to “about” a value or parameter herein includes (and describes) variations that are directed to that value or parameter per se. For example, description referring to “about X” includes description of “X”.

[0029] The terms “a” or “an,” as used in herein means one or more, unless context clearly dictates otherwise.

[0030] As used herein the term “room temperature” or “RT” refers to a temperature in the range of from 20 to 30 °C.

[0031] The term “reflection” with regard to X-ray powder diffraction (XRPD) as used herein, means peaks in an X-ray diffractogram, which are caused at certain diffraction angles (Bragg angles) by constructive interference from X-rays scattered by parallel planes of atoms in solid material, which are distributed in an ordered and repetitive pattern in a long-range positional order. Such a solid material is classified as crystalline material, whereas amorphous material is defined as solid material, which lacks long-range order and only displays short-range order, thus resulting in broad scattering. According to literature, long-range order e.g. extends over approximately 100 to 1000 atoms, whereas short-range order is over a few atoms only (see “Fundamentals of Powder Diffraction and Structural Characterization of Materials” by Vitalij K. Pecharsky and Peter Y Zavalij, Kluwer Academic Publishers, 2003, page 3).

[0032] The crystalline forms of the present invention may be referred to herein as being characterized by graphical data “as shown in” a figure, for example, XRPD. The person skilled in the art understands that factors such as variations in instrument type, response and variations in sample directionality, sample concentration and sample purity may lead to small variations for such data when presented in graphical form, for example variations relating to the exact

-6-

peak positions and intensities. However, a comparison of the graphical data in the figures herein with the graphical data generated for another or an unknown solid form and the confirmation that two sets of graphical data relate to the same crystal form is well within the knowledge of a person skilled in the art.

[0033] The terms “solid form” or “solid state form” as used herein interchangeably refer to any crystalline and/or amorphous phase of a compound.

[0034] As used herein, the term “amorphous” refers to a solid form of a compound that is not crystalline. An amorphous compound possesses no long-range order and does not display a definitive XRPD pattern with reflections.

[0035] As used herein the term “polymorph” refers to crystalline forms having the same chemical composition but different spatial arrangements of the molecules, atoms, and/or ions forming the crystal.

[0036] The term “hydrate” as used herein, refers to a crystalline solid where either water is cooperated in or accommodated by the crystal structure, e.g., is part of the crystal structure or entrapped into the crystal (water inclusions). Thereby, water can be present in a stoichiometric or non-stoichiometric amount. When water is present in stoichiometric amount, the hydrate may be referred to by adding Greek numeral prefixes. For example, a hydrate may be referred to as a hemihydrate or as a monohydrate depending on the water/compound stoichiometry. The water content can be measured, for example, by Karl-Fischer-Coulometry.

[0037] The terms “dehydrating” or “dehydration” as used herein, describe the at least partial removal of water from the crystal structure of the host molecule.

[0038] The term “solvate” as used herein, refers to a crystalline solid where either one or more organic solvent(s) is/are cooperated in or accommodated by the crystal structure e.g. is/are part of the crystal structure or entrapped into the crystal (water inclusions). Thereby, the one or more organic solvent(s) can be present in a stoichiometric or non-stoichiometric amount. When the one or more organic solvent(s) is/are present in stoichiometric amount(s), the solvate may be referred to by adding Greek numeral prefixes. For example, a solvate may be referred to as a hemisolvate or as a monosolvate depending on the solvent(s)/compound stoichiometry. The solvent content can be measured, for example, by GC, NMR, SXRD and/or TGA/MS.

[0039] The term “pharmaceutically acceptable excipient” as used herein refers to substances, which do not show a significant pharmacological activity at the given dose and that are added to a pharmaceutical composition in addition to the active pharmaceutical ingredient. Excipients

-7-

may take the function of vehicle, diluent, release agent, disintegrating agent, dissolution modifying agent, absorption enhancer, stabilizer or a manufacturing aid among others.

[0040] Excipients may include fillers (diluent), binders, disintegrants, lubricants and glidants.

[0041] The terms "filler" or "diluent" as used herein refer to substances that are used to dilute the active pharmaceutical ingredient prior to delivery. Diluents and fillers can also serve as stabilizers.

[0042] As used herein the term "binder" refers to substances that bind the active pharmaceutical ingredient and pharmaceutically acceptable excipient together to maintain cohesive and discrete portions.

[0043] The terms "disintegrant" or "disintegrating agent" as used herein refers to substances which, upon addition to a solid pharmaceutical composition, facilitate its break-up or disintegration after administration and permits the release of the active pharmaceutical ingredient as efficiently as possible to allow for its rapid dissolution.

[0044] The term "lubricant" as used herein refers to substances that are added to a powder blend to prevent the compacted powder mass from sticking to the equipment during tableting or encapsulation process. They aid the ejection of the tablet from the dies and can improve powder flow.

[0045] The term "glidant" as used herein refers to substances that are used for tablet and capsule formulations in order to improve flow properties during tablet compression and to produce an anti-caking effect.

[0046] One aspect of the present invention provides distinct crystalline forms of the compound 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol. These "crystalline form(s)" (or "crystal forms" or "crystalline modification(s)" or "polymorphic form(s)" or "polymorph(s)", as the terms will be used interchangeably herein) differ with respect to thermodynamic stability, physical parameters, x-ray structure and methods of preparation.

[0047] Polymorphs exist in two main categories: enantiotropic or monotropic. "Enantiotropic" polymorphs are those that can interconvert depending upon the temperature at a given pressure or depending upon the pressure at a given temperature, called the transition temperature or pressure. The relative thermodynamic stability inverts above and below the transition temperature or pressure. If one polymorph is more stable independent of the temperature, it is

“monotropic.” While polymorphism classically refers to the ability of a compound to crystallize into more than one distinct crystal species (having identical chemical structure but quite different physicochemical properties), the term pseudopolymorphism is typically applied to solvate and hydrate crystalline forms. For purposes of this invention, however, both true polymorphs as well as pseudopolymorphs, i.e., hydrate and solvate forms, are included in the scope of “crystalline forms.” In addition, “amorphous” refers to a disordered solid state. It should be noted that different samples of a particular crystalline form will share the same major X-ray powder diffraction (XRPD) “peaks” or “reflections,” but that there can be variation in powder patterns with regard to minor peaks. In addition, the term “about” with regard to XRPD peak values (in degrees) generally means within 0.3°, more preferably within 0.2°, and most preferably within 0.1° of the given value. Alternatively, the term “about” means (in this and all contexts) within an accepted standard of error of the mean, when considered by one of ordinary skill in the art.

[0048] In one embodiment, a crystalline form of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol is provided, referred to as crystalline Form A.

[0049] In another embodiment, crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol is characterized by the XRPD pattern of FIG. 1. Angular positions of characteristic peaks in XRPD pattern for Form A are described in Table A.

TABLE A

Angle, 2-Theta °	d-value, Angstrom
4.5	19.6
8.1	11.0
9.0	9.9
11.9	7.5
12.2	7.2
13.2	6.7
13.5	6.6
14.2	6.2
14.6	6.1
15.0	5.89
15.3	5.79
15.7	5.64

-9-

16.6	5.33
17.0	5.23
17.2	5.16
17.7	4.99
18.0	4.92
19.0	4.67
19.8	4.48
20.0	4.43
20.2	4.38
20.4	4.34
21.1	4.21
22.8	3.91
23.3	3.82
23.8	3.73
24.3	3.66
24.9	3.57
25.3	3.51
25.8	3.44
26.3	3.39
27.1	3.28
27.3	3.26
27.7	3.22
28.0	3.19
28.4	3.14

[0050] In one embodiment, the invention relates to crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol characterized by 3, 4, 5, 6, 7, 8, 9, 10, or more angular positions as provided in Table A. In some embodiments, the angular positions may vary by ± 0.2 . In some embodiments, the angular positions may vary by ± 0.1 . In some embodiments, the angular positions may vary by ± 0.05 . In some embodiments, the angular positions may vary by ± 0.02 .

[0051] In one embodiment, the invention relates to crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol characterized by having a XRPD pattern comprising reflections at 2-Theta angles (2 theta values) of:

$4.5 \pm 0.2^\circ$, $9.0 \pm 0.2^\circ$ and $16.6 \pm 0.2^\circ$; or

$4.5 \pm 0.2^\circ$, $9.0 \pm 0.2^\circ$, $16.6 \pm 0.2^\circ$, $21.1 \pm 0.2^\circ$ and $25.3 \pm 0.2^\circ$; or

-10-

$4.5 \pm 0.2^\circ$, $9.0 \pm 0.2^\circ$, $13.2 \pm 0.2^\circ$, $13.5 \pm 0.2^\circ$, $14.2 \pm 0.2^\circ$, $15.3 \pm 0.2^\circ$, $16.6 \pm 0.2^\circ$, $18.0 \pm 0.2^\circ$, $19.8 \pm 0.2^\circ$, $21.1 \pm 0.2^\circ$, $25.3 \pm 0.2^\circ$, $25.8 \pm 0.2^\circ$ and $26.3 \pm 0.2^\circ$; measured using Cu-Kalpha radiation.

[0052] In another embodiment, crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol is characterized by having a XRPD pattern comprising at least three, or at least four, or at least five, or all, 2 theta values selected from the group consisting of $4.5 \pm 0.2^\circ$, $8.1 \pm 0.2^\circ$, $9.0 \pm 0.2^\circ$, $11.9 \pm 0.2^\circ$, $12.2 \pm 0.2^\circ$, $13.2 \pm 0.2^\circ$, $13.5 \pm 0.2^\circ$, $14.2 \pm 0.2^\circ$, $14.6 \pm 0.2^\circ$, $15.0 \pm 0.2^\circ$, $15.3 \pm 0.2^\circ$, $15.7 \pm 0.2^\circ$, $16.6 \pm 0.2^\circ$, $17.0 \pm 0.2^\circ$, $17.2 \pm 0.2^\circ$, $17.7 \pm 0.2^\circ$, $18.0 \pm 0.2^\circ$, $19.0 \pm 0.2^\circ$, $19.8 \pm 0.2^\circ$, $20.0 \pm 0.2^\circ$, $20.2 \pm 0.2^\circ$, $20.4 \pm 0.2^\circ$, $21.1 \pm 0.2^\circ$, $22.8 \pm 0.2^\circ$, $23.3 \pm 0.2^\circ$, $23.8 \pm 0.2^\circ$, $24.3 \pm 0.2^\circ$, $24.9 \pm 0.2^\circ$, $25.3 \pm 0.2^\circ$, $25.8 \pm 0.2^\circ$, $26.3 \pm 0.2^\circ$, $27.1 \pm 0.2^\circ$, $27.3 \pm 0.2^\circ$, $27.7 \pm 0.2^\circ$, $28.0 \pm 0.2^\circ$, and $28.4 \pm 0.2^\circ$, measured using Cu-Kalpha radiation.

[0053] Crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol may be characterized thermally. In one embodiment, Form A is characterized by a DSC thermogram exhibiting three endotherms, a small one at 193.4°C (onset at 189.4°C) and two large, overlapping ones at 261.2°C (onset at 260.6°C) and 261.7°C (onset at 260.6°C). In another embodiment, Form A is characterized by a DSC thermogram substantially as shown in FIG. 2. In one embodiment, Form A is characterized by a TG-FTIR thermogram exhibiting decomposition at temperatures of about 270°C . In another embodiment, Form A is characterized by a TG-FTIR thermogram substantially as shown in FIG. 3.

[0054] Crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol may also be characterized by raman spectroscopy. In one embodiment, Form A is characterized by an FT-RAMAN spectrum having at least one, more preferably at least two, still more preferably at least four, and most preferably all, of the RAMAN bands at about 3123, 3107, 3075, 2974, 1620, 1610, 1590, 1458, 1397, 1377, 1335, 1319, 1305, 1291, 1266, 1259, 1230, 1188, 1166, 1138, 1126, 1082, 1064, 1028, 971, 960, 900, 827, 770, 742, 713, 625, 580, 550, 531, 446, 377, 345, 330, 256, 241, 180, 163, 141, 108, 101 cm^{-1} . In another embodiment, Form A is characterized by a FT-RAMAN spectrum substantially as shown in FIG. 4.

[0055] In one embodiment, a crystalline form of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol is provided, referred to as crystalline Form B.

[0056] In another embodiment, crystalline Form B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol is characterized by the XRPD pattern of FIG. 5. Angular positions of characteristic peaks in XRPD pattern for Form B are described in Table B.

TABLE B

Angle, 2-Theta °	d-value, Angstrom
5.2	16.8
6.0	14.8
8.7	10.2
10.5	8.4
12.0	7.4
12.6	7.0
12.9	6.9
14.5	6.1
14.8	5.98
15.0	5.90
15.8	5.60
17.4	5.10
17.6	5.03
17.8	4.98
18.0	4.92
18.4	4.82
19.0	4.66
19.2	4.62
19.9	4.45
22.7	3.91
23.3	3.81
23.7	3.75
24.0	3.71
24.5	3.64
25.0	3.56
25.4	3.51
25.8	3.46
26.2	3.40
27.6	3.24

-12-

[0057] In one embodiment, the invention relates to crystalline Form B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol characterized by 3, 4, 5, 6, 7, 8, 9, 10, or more angular positions as provided in Table B. In some embodiments, the angular positions may vary by ± 0.2 . In some embodiments, the angular positions may vary by ± 0.1 . In some embodiments, the angular positions may vary by ± 0.05 . In some embodiments, the angular positions may vary by ± 0.02 .

[0058] In one embodiment, the invention relates to crystalline Form B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol characterized by having a XRPD pattern comprising reflections at 2-Theta angles (2 theta values) of:

$5.2 \pm 0.2^\circ$, $6.0 \pm 0.2^\circ$ and $15.8 \pm 0.2^\circ$; or

$5.2 \pm 0.2^\circ$, $6.0 \pm 0.2^\circ$, $10.5 \pm 0.2^\circ$, $12.6 \pm 0.2^\circ$ and $15.8 \pm 0.2^\circ$; or

$5.2 \pm 0.2^\circ$, $6.0 \pm 0.2^\circ$, $8.7 \pm 0.2^\circ$, $10.5 \pm 0.2^\circ$, $12.6 \pm 0.2^\circ$, $14.5 \pm 0.2^\circ$, and $15.8 \pm 0.2^\circ$; measured using Cu-Kalpha radiation.

[0059] In another embodiment, crystalline Form B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol is characterized by having a XRPD pattern comprising at least three, or at least four, or at least five, or all, 2 theta values selected from the group consisting of $5.2 \pm 0.2^\circ$, $6.0 \pm 0.2^\circ$, $8.7 \pm 0.2^\circ$, $10.5 \pm 0.2^\circ$, $12.0 \pm 0.2^\circ$, $12.6 \pm 0.2^\circ$, $12.9 \pm 0.2^\circ$, $14.5 \pm 0.2^\circ$, $14.8 \pm 0.2^\circ$, $15.0 \pm 0.2^\circ$, $15.8 \pm 0.2^\circ$, $17.4 \pm 0.2^\circ$, $17.6 \pm 0.2^\circ$, $17.8 \pm 0.2^\circ$, $18.0 \pm 0.2^\circ$, $18.4 \pm 0.2^\circ$, $19.0 \pm 0.2^\circ$, $19.2 \pm 0.2^\circ$, $19.9 \pm 0.2^\circ$, $22.7 \pm 0.2^\circ$, $23.3 \pm 0.2^\circ$, $23.7 \pm 0.2^\circ$, $24.0 \pm 0.2^\circ$, $24.5 \pm 0.2^\circ$, $25.0 \pm 0.2^\circ$, $25.4 \pm 0.2^\circ$, $25.8 \pm 0.2^\circ$, $26.2 \pm 0.2^\circ$, and $27.6 \pm 0.2^\circ$, measured using Cu-Kalpha radiation.

[0060] Crystalline Form B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol may be characterized thermally. In one embodiment, Form B is characterized by a DSC thermogram exhibiting a single melting endotherm at 260.3°C (onset at 259.5°C). In another embodiment, Form B is characterized by a DSC thermogram substantially as shown in FIG. 6. In one embodiment, Form A is characterized by a TG-FTIR thermogram exhibiting undergoes mass changes from 25°C to 140°C and 140°C to 210°C , followed by decomposition at higher temperatures. In another embodiment, Form B is characterized by a TG-FTIR thermogram substantially as shown in FIG. 7.

[0061] Crystalline Form B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol may also be characterized by raman spectroscopy. In one embodiment, Form B is characterized by an FT-RAMAN spectrum having at least one, more preferably at least two, still more preferably at least four, and most preferably all, of the RAMAN bands at about 3145, 2974, 2931, 1629, 1611, 1462, 1401, 1376, 1340, 1325, 1307, 1295, 1271, 1215, 1164, 1058, 996, 900, 836, and 706 cm^{-1} . In another embodiment, Form B is characterized by a FT-RAMAN spectrum substantially as shown in FIG. 8.

[0062] In one embodiment, a crystalline form of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol is provided, referred to as crystalline Form C. Form C was isolated by heating Form A to 225°C. Form C spontaneously converts back into Form A upon cooling to ambient temperature. In another embodiment, crystalline Form C of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol is characterized by the XRPD pattern of FIG. 9. Angular positions of characteristic peaks in XRPD pattern for Form C are described in Table C.

TABLE C

Angle, 2-Theta °	d-value, Angstrom
4.0	22.3
7.9	11.1
12.0	7.4
12.6	7.0
13.5	6.5
14.4	6.1
14.7	6.0
15.2	5.83
15.6	5.67
16.0	5.54
16.4	5.40
16.9	5.24
17.7	5.01
18.1	4.89
19.0	4.66
19.6	4.52
20.0	4.43
20.4	4.35
21.2	4.18
22.0	4.03

-14-

22.6	3.94
22.8	3.89
23.5	3.78
24.2	3.68
24.9	3.58
25.8	3.45
26.4	3.37
26.8	3.32

[0063] In one embodiment, the invention relates to crystalline Form C of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol characterized by 3, 4, 5, 6, 7, 8, 9, 10, or more angular positions as provided in Table C. In some embodiments, the angular positions may vary by ± 0.2 . In some embodiments, the angular positions may vary by ± 0.1 . In some embodiments, the angular positions may vary by ± 0.05 . In some embodiments, the angular positions may vary by ± 0.02 .

[0064] In one embodiment, the invention relates to crystalline Form C of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol characterized by having a XRPD pattern comprising reflections at 2-Theta angles (2 theta values) of:

$4.0 \pm 0.2^\circ$, $7.9 \pm 0.2^\circ$ and $13.5 \pm 0.2^\circ$; or

$4.0 \pm 0.2^\circ$, $7.9 \pm 0.2^\circ$, $13.5 \pm 0.2^\circ$, $14.4 \pm 0.2^\circ$ and $17.7 \pm 0.2^\circ$; or

$4.0 \pm 0.2^\circ$, $7.9 \pm 0.2^\circ$, $12.0 \pm 0.2^\circ$, $12.6 \pm 0.2^\circ$, $13.5 \pm 0.2^\circ$, $14.4 \pm 0.2^\circ$, $14.7 \pm 0.2^\circ$, $15.2 \pm 0.2^\circ$, $15.6 \pm 0.2^\circ$, $16.0 \pm 0.2^\circ$, $17.7 \pm 0.2^\circ$, $19.0 \pm 0.2^\circ$, $19.6 \pm 0.2^\circ$, $24.9 \pm 0.2^\circ$ and $25.8 \pm 0.2^\circ$; measured using Cu-Kalpha radiation.

[0065] In another embodiment, crystalline Form C of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol is characterized by having a XRPD pattern comprising at least three, or at least four, or at least five, or all, 2 theta values selected from the group consisting of $4.0 \pm 0.2^\circ$, $7.9 \pm 0.2^\circ$, $12.0 \pm 0.2^\circ$, $12.6 \pm 0.2^\circ$, $13.5 \pm 0.2^\circ$, $14.4 \pm 0.2^\circ$, $14.7 \pm 0.2^\circ$, $15.2 \pm 0.2^\circ$, $15.6 \pm 0.2^\circ$, $16.0 \pm 0.2^\circ$, $16.4 \pm 0.2^\circ$, $16.9 \pm 0.2^\circ$, $17.7 \pm 0.2^\circ$, $18.1 \pm 0.2^\circ$, $19.0 \pm 0.2^\circ$, $19.6 \pm 0.2^\circ$, $20.0 \pm 0.2^\circ$, $20.4 \pm 0.2^\circ$, $21.2 \pm 0.2^\circ$, $22.0 \pm 0.2^\circ$, $22.6 \pm 0.2^\circ$, $22.8 \pm 0.2^\circ$, $23.5 \pm 0.2^\circ$, $24.2 \pm 0.2^\circ$, $24.9 \pm 0.2^\circ$, $25.8 \pm 0.2^\circ$, $26.4 \pm 0.2^\circ$, and $26.8 \pm 0.2^\circ$, measured using Cu-Kalpha radiation.

[0066] In one embodiment, a crystalline form of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol is provided, referred to as

trihydrate crystalline form H_A. Form H_A was isolated in suspension equilibration study of Form A in a solvent mixture of 9:1 (v/v) tetrahydrofuran/ H₂O. In another embodiment, crystalline form H_A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol is characterized by the XRPD pattern of FIG. 10. Angular positions of characteristic peaks in XRPD pattern for Form H_A are described in Table D.

TABLE D

Angle, 2-Theta °	d-value, Angstrom
7.8	11.3
8.2	10.8
11.5	7.7
12.4	7.2
13.0	6.8
13.2	6.7
13.7	6.5
13.9	6.4
14.5	6.1
14.7	6.0
15.0	5.89
15.8	5.61
16.4	5.40
17.3	5.12
18.5	4.78
18.8	4.73
19.6	4.51
19.8	4.47
20.6	4.30
20.9	4.24
21.7	4.09
22.1	4.03
22.4	3.96
24.5	3.63
25.4	3.51
25.7	3.47
25.9	3.44
26.2	3.40
26.7	3.34
27.0	3.30
27.6	3.23
28.1	3.17
28.9	3.09
29.3	3.05
29.6	3.01

-16-

30.1	2.97
31.7	2.82
32.9	2.72
33.3	2.69
33.6	2.67

[0067] In one embodiment, the invention relates to crystalline Form H_A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol characterized by 3, 4, 5, 6, 7, 8, 9, 10, or more angular positions as provided in Table D. In some embodiments, the angular positions may vary by ± 0.2 . In some embodiments, the angular positions may vary by ± 0.1 . In some embodiments, the angular positions may vary by ± 0.05 . In some embodiments, the angular positions may vary by ± 0.02 .

[0068] In one embodiment, the invention relates to crystalline Form H_A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol characterized by having a XRPD pattern comprising reflections at 2-Theta angles (2 theta values) of:

$7.8 \pm 0.2^\circ$, $13.2 \pm 0.2^\circ$ and $25.4 \pm 0.2^\circ$; or

$7.8 \pm 0.2^\circ$, $13.2 \pm 0.2^\circ$, $14.5 \pm 0.2^\circ$, $25.4 \pm 0.2^\circ$ and $26.7 \pm 0.2^\circ$; or

$7.8 \pm 0.2^\circ$, $8.2 \pm 0.2^\circ$, $11.5 \pm 0.2^\circ$, $12.4 \pm 0.2^\circ$, $13.2 \pm 0.2^\circ$, $14.5 \pm 0.2^\circ$, $14.7 \pm 0.2^\circ$, $15.0 \pm 0.2^\circ$, $15.8 \pm 0.2^\circ$, $16.4 \pm 0.2^\circ$, $25.4 \pm 0.2^\circ$ and $26.7 \pm 0.2^\circ$; measured using Cu-Kalpha radiation.

[0069] In another embodiment, crystalline form H_A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol is characterized by having a XRPD pattern comprising at least three, or at least four, or at least five, or all, 2 theta values selected from the group consisting of $7.8 \pm 0.2^\circ$, $8.2 \pm 0.2^\circ$, $11.5 \pm 0.2^\circ$, $12.4 \pm 0.2^\circ$, $13.0 \pm 0.2^\circ$, $13.2 \pm 0.2^\circ$, $13.7 \pm 0.2^\circ$, $13.9 \pm 0.2^\circ$, $14.5 \pm 0.2^\circ$, $14.7 \pm 0.2^\circ$, $15.0 \pm 0.2^\circ$, $15.8 \pm 0.2^\circ$, $16.4 \pm 0.2^\circ$, $17.3 \pm 0.2^\circ$, $18.5 \pm 0.2^\circ$, $18.8 \pm 0.2^\circ$, $19.6 \pm 0.2^\circ$, $19.8 \pm 0.2^\circ$, $20.6 \pm 0.2^\circ$, $20.9 \pm 0.2^\circ$, $21.7 \pm 0.2^\circ$, $22.1 \pm 0.2^\circ$, $22.4 \pm 0.2^\circ$, $24.5 \pm 0.2^\circ$, $25.4 \pm 0.2^\circ$, $25.7 \pm 0.2^\circ$, $25.9 \pm 0.2^\circ$, $26.2 \pm 0.2^\circ$, $26.7 \pm 0.2^\circ$, $27.0 \pm 0.2^\circ$, $27.6 \pm 0.2^\circ$, $28.1 \pm 0.2^\circ$, $28.9 \pm 0.2^\circ$, $29.3 \pm 0.2^\circ$, $29.6 \pm 0.2^\circ$, $30.1 \pm 0.2^\circ$, $31.7 \pm 0.2^\circ$, $32.9 \pm 0.2^\circ$, $33.3 \pm 0.2^\circ$, and $33.6 \pm 0.2^\circ$, measured using Cu-Kalpha radiation.

[0070] In addition, several solvates were discovered during equilibration suspension and evaporation studies of crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-

[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol. A dioxane solvate Form S_A, and an acetic acid disolvate Form S_B was isolated in suspension equilibration studies with the respective solvents. A formic acid disolvate Form S_C was isolated in an evaporation study and a formic acid monosolvate Form S_D was obtained by drying form S_C. Solvate forms S_A, S_B, S_C, and S_D can be characterized by the XRPD patterns as shown in FIGs 11-14, respectively.

[0071] Angular positions of characteristic peaks in XRPD pattern for Solvate forms S_A, S_B, S_C, and S_D are described in Table S1, S2, S3, and S4, respectively.

TABLE S1

Angle, 2-Theta °	d-value, Angstrom
8.0	11.0
11.3	7.8
13.1	6.7
13.5	6.6
13.7	6.4
14.6	6.1
16.1	5.51
16.3	5.45
17.6	5.05
18.7	4.74
19.1	4.65
19.4	4.56
20.1	4.41
20.4	4.36
21.2	4.19
22.3	3.99
23.3	3.82
23.9	3.71
25.0	3.56

TABLE S2

Angle, 2-Theta °	d-value, Angstrom
4.1	21.5
4.3	20.7
4.7	18.9
8.3	10.7
8.5	10.3
9.3	9.5
9.6	9.2
10.5	8.4

-18-

11.0	8.0
11.3	7.8
11.6	7.6
11.8	7.5
12.0	7.4
12.3	7.2
12.8	6.9
13.1	6.7
13.5	6.6
14.2	6.3
14.4	6.1
14.8	5.98
14.9	5.95
14.9	5.93
15.2	5.81
15.5	5.70
15.8	5.60
16.2	5.48
16.3	5.43
16.6	5.33
16.8	5.28
17.2	5.16
17.7	5.02
18.5	4.79
18.7	4.74
19.0	4.67
19.4	4.58
19.5	4.54
19.8	4.49
20.0	4.43
20.4	4.35
20.6	4.31
21.0	4.22

TABLE S3

Angle, 2-Theta °	d-value, Angstrom
4.3	21
8.5	10
8.7	10
10.8	8
11.2	8
11.6	8
12.8	7

-19-

16.7	5.32
17.1	5.19
17.4	5.09
17.7	5.00
20.8	4.26
21.4	4.16
21.8	4.07

TABLE S4

Angle, 2-Theta °	d-value, Angstrom
4.6	19.3
5.5	16.2
6.3	14.1
9.1	9.7
9.4	9.4
10.9	8.1
11.4	7.7
11.8	7.5
12.5	7.1
12.7	6.9
13.5	6.6
13.8	6.4
14.4	6.1
15.4	5.75
15.9	5.59
16.5	5.35
16.9	5.25
17.8	4.98
18.3	4.85
18.5	4.78
19.5	4.55
19.8	4.49
20.5	4.32
22.0	4.03
23.0	3.87
23.8	3.73
24.5	3.63
25.3	3.51
25.8	3.44
26.7	3.33
27.1	3.29

-20-

[0072] In one embodiment, the invention relates to crystalline form S_A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol characterized by 3, 4, 5, 6, 7, 8, 9, 10, or more angular positions as provided in Table S1. In some embodiments, the angular positions may vary by ± 0.2 . In some embodiments, the angular positions may vary by ± 0.1 . In some embodiments, the angular positions may vary by ± 0.05 . In some embodiments, the angular positions may vary by ± 0.02 .

[0073] In one embodiment, the invention relates to crystalline form S_B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol characterized by 3, 4, 5, 6, 7, 8, 9, 10, or more angular positions as provided in Table S2. In some embodiments, the angular positions may vary by ± 0.2 . In some embodiments, the angular positions may vary by ± 0.1 . In some embodiments, the angular positions may vary by ± 0.05 . In some embodiments, the angular positions may vary by ± 0.02 .

[0074] In one embodiment, the invention relates to crystalline form S_C of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol characterized by 3, 4, 5, 6, 7, 8, 9, 10, or more angular positions as provided in Table S3. In some embodiments, the angular positions may vary by ± 0.2 . In some embodiments, the angular positions may vary by ± 0.1 . In some embodiments, the angular positions may vary by ± 0.05 . In some embodiments, the angular positions may vary by ± 0.02 .

[0075] In one embodiment, the invention relates to crystalline form S_D of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol characterized by 3, 4, 5, 6, 7, 8, 9, 10, or more angular positions as provided in Table S4. In some embodiments, the angular positions may vary by ± 0.2 . In some embodiments, the angular positions may vary by ± 0.1 . In some embodiments, the angular positions may vary by ± 0.05 . In some embodiments, the angular positions may vary by ± 0.02 .

[0076] Various methods can be used to achieve the crystalline forms of the 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol (forms A, B, C, H_A, S_A, S_B, S_C, and S_D). Such methods are as set forth above and as set forth in the below-presented examples and include equilibration with solvents, crystallization at room temperature, crystallization from hot saturated solutions, precipitation by addition of solvent, evaporation with solvent, vapor diffusion with solvent, and drying/desolvation.

-21-

[0077] Another embodiment of the present invention is directed to a pharmaceutical composition comprising: (a) a therapeutically effective amount of a crystalline form of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to one of the earlier embodiments of the present invention; and (b) at least one at least one pharmaceutically acceptable carrier, diluent, vehicle or excipient.

[0078] In one embodiment, the pharmaceutical composition comprises: (a) a therapeutically effective amount of crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to one of the earlier embodiments of the present invention; and (b) at least one at least one pharmaceutically acceptable carrier, diluent, vehicle or excipient.

[0079] The terms "a therapeutically effective amount" or "an effective amount" of Compound 1, as used herein, refer to an amount of the inventive crystalline form of the present invention that, when administered to a subject in need thereof, will elicit the biological or medical response of a subject. In another embodiment, the term refers to the amount of inventive crystalline form of the present invention that, when administered to a subject, is effective to at least partially ameliorate a condition, or a disorder or a disease. The amount of a given compound of the invention that will be therapeutically effective will vary depending upon factors such as the disease condition and the severity thereof, the identity of the subject in need thereof, etc., which amount may be routinely determined by artisans of ordinary skill in the art.

[0080] The "at least one pharmaceutically acceptable carrier, diluent, vehicle or excipient" can readily be selected by one of ordinary skill in the art and will be determined by the desired mode of administration. Illustrative examples of suitable modes of administration include oral, nasal, parenteral, topical, transdermal, and rectal. The pharmaceutical compositions of this invention may take any pharmaceutical form recognizable to the skilled artisan as being suitable. Suitable pharmaceutical forms include solid, semisolid, liquid, or lyophilized formulations, such as tablets, powders, capsules, suppositories, suspensions, liposomes, and aerosols.

[0081] Another aspect of the present invention is directed to a method of treating or ameliorating Huntington's Disease comprising the step of administering to a subject in need of such treatment a pharmaceutical composition comprising a therapeutically effective amount of a crystalline form of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol of the present invention or a pharmaceutical

-22-

composition comprising a therapeutically effective amount of a crystalline form of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol of the present invention.

[0082] The terms "treat" "treating" "treatment" or "therapy", as used herein, refer to obtaining beneficial or desired results, for example, clinical results. Beneficial or desired results can include, but are not limited to, stabilizing or improving progression of stage of HD (e.g. compared to placebo). One aspect of the treatment is, for example, that said treatment should have a minimal adverse effect on the patient, e.g. the agent used should have a high level of safety, for example without producing adverse side effects. In another aspect, the term "method for the treatment", as used herein, refers to "method to treat".

[0083] In one embodiment, the present invention is directed to a method of treating or ameliorating Huntington's Disease comprising the step of administering to a subject in need of such treatment a therapeutically effective amount of crystalline form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol of the present invention. In another embodiment, the present invention is directed to a method of treating or ameliorating Huntington's Disease comprising the step of administering to a subject in need of such treatment a pharmaceutical composition comprising a therapeutically effective amount of crystalline form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol of the present invention. As noted above, illustrative modes of administration include oral, nasal, parenteral, topical, transdermal, and rectal. Administration of the crystalline form may be accomplished by administration of a pharmaceutical composition of this invention or via any other effective means.

[0084] Specific embodiments of the invention will now be demonstrated by reference to the following examples. It should be understood that these examples are disclosed solely by way of illustrating the invention and should not be taken in any way to limit the scope of the present invention.

EXAMPLES

[0085] The following abbreviations are used throughout the present disclosure with respect to chemical and biological terminology:

DSC: Differential scanning calorimetry

FT-IR: Fourier transform-infrared

-23-

HPLC: High performance liquid chromatography

NMR: Nuclear magnetic resonance spectroscopy

RH: Relative humidity

RT: Room temperature

TGA: Thermo gravimetric analysis

XRPD: X-ray powder diffraction

The following examples include illustrations of aspects of the invention. The examples are not to be construed as limitations.

General Test Conditions

The following procedures were employed under each test condition.

Differential Scanning Calorimetry (DSC)

[0086] The DSC instrument used to test the crystalline forms was the Thermal Analysis Q2000 in closed (hermetically sealed) gold or aluminum crucibles. Samples were filled either under ambient conditions or under nitrogen flow (for 3 to 10 minutes), heating rate of 10 K. min⁻¹, and -50°C to 285°C temperature range.

Fourier Transform-Raman (FT-Raman) Spectroscopy

[0087] Instrument: Bruker MultiRAM (with OPUS 7.0 software); Nd:YAG 1064-nm excitation, 100–300 mW nominal laser power, Ge detector, 64–256 scans, 3500–100 cm⁻¹ spectral range, 2 cm⁻¹ resolution. Samples were measured using aluminum sample holders.

Thermogravimetry coupled Fourier Transform Infrared (TG-FTIR) Spectroscopy

[0088] The TG-FTIR spectral range used of samples were recorded with the Netzsch Thermo-Microbalance TG 209 with Bruker FT-IR Spectrometer IFS28 or Vector 22 in an Al crucible, nitrogen atmosphere, 10 K. min⁻¹ heating rate, and a 25°C to 300°C or 350°C temperature range.

X-Ray Powder Diffraction

[0089] The X-ray powder diffraction (XRPD) patterns described herein, with the exception of Form C, were recorded on a Bruker D8 Advance diffractometer using CuK α radiation (wavelength of 1.5406 Å), 40 kV/40 mA, LynxEye detector, Bragg-Brentano reflection geometry, 0.02°2 θ step size, 37-s step time, 2.5–50°2 θ range, at room temperature, . The

-24-

powder samples were measured in 0.1-mm deep silicon single-crystal sample holders. No special treatment was used in preparing the samples other than the application of slight pressure to get a flat surface. An ambient air atmosphere was used for all measurements.

[0090] The X-ray powder diffraction (XRPD) patterns described for Form C was recorded on a PANalytical X'Pert PRO-MPD using CuK α radiation (wavelength of 1.5406 Å), 45 kV/40 mA, PIXCEL detector, Bragg-Brentano reflection geometry, 0.0131° 2 θ step size, 87.72 s step time, 3.0-33.0° 2 θ range, at 225°C. The powder sample was measured in a 0.4-mm deep, nickel-coated copper sample holders without any special treatment other than the application of slight pressure to get a flat surface. The sample was measured in a Parr TTK-450 chamber, and an ambient air atmosphere was used. The sample was not rotated during the measurement. Variable divergent and anti-scatter slits were used at a distance of 9.0 mm on either side of the sample, and the Soller slits were 0.04 radians on both sides. A heating rate of 2 K min⁻¹ was used, and the temperature was held constant during the 15 min required for each measurement.

[0091] One of ordinary skill in the art will appreciate that an XRPD pattern may be obtained with a measurement error that is dependent upon the measurement conditions employed. In particular, it is generally known that intensities in an XRPD pattern may fluctuate depending upon measurement conditions employed. It should be further understood that relative intensities may also vary depending upon experimental conditions and wavelength of X-ray radiation used. The agreement in the 2-theta-diffraction angles between specimen and reference is within 0.2° for the same crystal form and such degree of measurement error should be taken into account as pertaining to the aforementioned diffraction angles. Consequently, it is to be understood that the crystal forms of the instant invention are not limited to the crystal forms that provide X-ray diffraction patterns completely identical to the XRPD patterns depicted in the accompanying Figures disclosed herein. Any crystal forms that provide XRPD patterns substantially identical to those disclosed in the accompanying Figures fall within the scope of the present invention. The ability to ascertain substantial identities of XRPD patterns is within the purview of one of ordinary skill in the art.

Example 1

Preparation of crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol

[0092] The starting material, 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol, is prepared in accordance to Example 37 of WO 2020/005873. A vial was charged with the starting material (245 mg) and N,N-dimethylformamide (10 mL). After warming to 90 °C, a clear solution was obtained. The mixture was cooled to 60 °C, then water (5 mL) was added dropwise. The resulting suspension was stirred for 15 min at 60 °C and 1 h at room temperature, then filtered. The solid cake was washed with 20 mL of water, dried at room temperature under full vacuum to give 228 mg of the product as yellow solid identified as Form A upon XRPD analysis.

[0093] The XRPD pattern and FT-Raman spectrum for Form A are shown in FIGs 1 and 4, respectively. The DSC thermogram indicates that Form A exhibits three endotherms, a small one at 193.4°C (onset at 189.4°C) and two large, overlapping ones at 261.2°C (onset at 260.6°C) and 261.7°C (onset at 260.6°C) as shown in FIG. 2. The TG-FTIR thermogram indicates that Form A starts to decompose at a temperature of about 270°C as shown in FIG. 3.

Example 2

Solid State Stability

[0094] In the solid state, samples of crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol was subjected to accelerated temperature and humidity conditions (25°C/60% RH open, 40°C/75% RH closed, and 40°C/75% RH open) for up to 6 months. The HPLC conditions used for chemical stability are described in Table 1.

TABLE 1

Column:	Supelco Ascentis Express C8, 150mm × 4.6mm, 2.7µm particle size		
Column Temperature:	40°C		
Mobile Phase A:	100% water +0.1%TFA		
Mobile Phase B:	100% acetonitrile +0.1%TFA		
Flow Rate:	1.0 mL/min		
Injection Volume:	2.0 µL		
Detection:	UV at 282 nm		
Run Time:	12 min		
Typical Retention time:	~ 5.4 minutes		
Gradient:	Time (min)	%mobile phase A	%mobile phase B
	0	95	5
	8	5	95
	10	5	95
	10.01	95	5
	12	95	5

[0095] The HPLC results (as in Tables 2 and 3) show that Form A is chemically stable for up to 6 months at accelerated conditions of temperature and humidity without any significant growth in process impurities (RRTs 0.89, 0.98, 1.02, 1.04 and 1.17) or generation of degradants.

TABLE 2

Chemical Stability at Accelerated Conditions of Temperature and Humidity at 1 Month

Sample ID	HPLC area percent at Relative Retention Time (RRT)						
	0.89	0.98	1 (Form A)	1.02	1.04	1.17	1.31
T0	0.01	-	99.76	0.04	0.17	0.02	-
40°C/75% RH (1 month)	0.01	0.03	99.74	0.04	0.16	0.02	-
65°C (22 days)	0.01	0.02	99.74	0.04	0.15	0.03	0.01

TABLE 3

Chemical Stability at Accelerated Conditions of Temperature and Humidity at 6 Months

		HPLC % Area
--	--	-------------

-27-

Sample ID	Assay	RRT 1.0 (Form A)	RRT 1.043	RRT 1.175
25°C/60% RH Open (6 months)	102.14	99.78	0.18	0.04
40°C/75% RH Closed (6 months)	101.38	99.78	0.17	0.04
40°C/75% RH Open (6 months)	100.67	99.78	0.18	0.04
Standard	100.0	99.78	0.18	0.04

[0096] Form A was also found by DSC, TGA, and XRPD to be physically stable for 6 months under accelerated conditions of temperature and humidity (25°C/60% RH open, 40°C/75% RH closed, and 40°C/75% RH open) with no change from initial.

Example 3

Preparation of crystalline Form B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol

[0097] The starting material, 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol, is prepared in accordance to Example 37 of WO 2020/005873. A vial was charged with the starting material (118 mg) and ethyl acetate (40 mL). After warming to reflux, a clear solution was obtained. The mixture was cooled to room temperature and stirred for 2 h, then filtered. The solid was dried at room temperature under a full vacuum to give 86 mg of the product as yellow solid identified as Form B upon XRPD analysis.

[0098] Alternatively, Form B was obtained by suspension equilibration of Form A from Example 1 with a variety of solvents: methyl acetate at 25°C for 15 days, pyridine at 25°C for 15 days, dichloromethane at 10°C for 12 days, ethyl acetate at 40°C for 7 days, methyl ethyl ketone at 40°C for 7 days, 2-methyltetrahydrofuran at 40°C for 7 days, toluene at 40°C for 7 days, acetone at 5°C for 12 days, isopropyl acetate at 60°C for 4 days, and 2-methyltetrahydrofuran at 60°C for 4 days.

[0099] The XRPD pattern and FT-Raman spectrum for Form B are shown in FIGs 5 and 8, respectively. The DSC thermogram indicates that Form B exhibits a single melting endotherm at 260.3°C (onset at 259.5°C) as shown in FIG. 6. The TG-FTIR thermogram indicates that Form A undergoes mass changes from 25°C to 140°C and 140°C to 210°C, followed by decomposition at higher temperatures as shown in FIG. 7.

-28-

Example 4

Preparation of crystalline Form C of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol

[0100] Form C was obtained by heating Form A from Example 1 to 225°C. Form C spontaneously converts back into Form A upon cooling to ambient temperature. The XRPD pattern for Form C is shown in FIG. 9.

Example 5

Preparation of crystalline Form H_A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol

[0101] Trihydrate Form H_A was obtained by suspension equilibration of Form A from Example 1 in a solvent mixture of 9:1 (v/v) tetrahydrofuran /H₂O at 25°C for 5 to 15 days. The XRPD pattern for Form H_A is shown in FIG. 10.

Example 6

Preparation of crystalline Form S_A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol

[0102] Dioxane solvate Form S_A was obtained by suspension equilibration of Form A from Example 1 in a solvent mixture of 97:3 (v/v) dioxane/H₂O at 25°C for 15 days. The XRPD pattern for Form S_A is shown in FIG. 11.

Example 7

Preparation of crystalline Form S_B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol

[0103] Acetic acid disolvate Form S_B was obtained by suspension equilibration of Form A from Example 1 in acetic acid at 25°C for 14 days. The XRPD pattern for Form S_B is shown in FIG. 12.

Example 8

Preparation of crystalline Form S_C of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol

[0104] Formic acid disolvate Form S_C was obtained by evaporation of Form A from Example 1 in formic acid under ambient conditions. The XRPD pattern for Form S_C is shown in FIG. 13.

-29-

Example 9

Preparation of crystalline Form S_D of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol

[0105] Formic acid monosolvate Form S_D was obtained by drying Form S_C from Example 7 under vacuum at 40°C for five hours. The XRPD pattern for Form S_D is shown in FIG. 14.

CLAIMS

We claim:

1. A crystalline form of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol.
2. A crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol.
3. The crystalline form according to claims 1 or 2 characterized by having an x-ray powder diffraction pattern comprising reflections at 2-Theta angles of $4.5 \pm 0.2^\circ$, $9.0 \pm 0.2^\circ$ and $16.6 \pm 0.2^\circ$, when measured with Cu-Kalpha radiation.
4. The crystalline form according to claims 1 to 3, characterized by having an x-ray powder diffraction pattern comprises reflections at 2-Theta angles of $4.5 \pm 0.2^\circ$, $9.0 \pm 0.2^\circ$, $16.6 \pm 0.2^\circ$, $21.1 \pm 0.2^\circ$ and $25.3 \pm 0.2^\circ$ when measured with Cu-Kalpha radiation.
5. A crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol characterized by having an x-ray powder diffraction pattern comprising three, four, five or more 2 theta values selected from the group consisting of $4.5 \pm 0.2^\circ$, $8.1 \pm 0.2^\circ$, $9.0 \pm 0.2^\circ$, $11.9 \pm 0.2^\circ$, $12.2 \pm 0.2^\circ$, $13.2 \pm 0.2^\circ$, $13.5 \pm 0.2^\circ$, $14.2 \pm 0.2^\circ$, $14.6 \pm 0.2^\circ$, $15.0 \pm 0.2^\circ$, $15.3 \pm 0.2^\circ$, $15.7 \pm 0.2^\circ$, $16.6 \pm 0.2^\circ$, $17.0 \pm 0.2^\circ$, $17.2 \pm 0.2^\circ$, $17.7 \pm 0.2^\circ$, $18.0 \pm 0.2^\circ$, $19.0 \pm 0.2^\circ$, $19.8 \pm 0.2^\circ$, $20.0 \pm 0.2^\circ$, $20.2 \pm 0.2^\circ$, $20.4 \pm 0.2^\circ$, $21.1 \pm 0.2^\circ$, $22.8 \pm 0.2^\circ$, $23.3 \pm 0.2^\circ$, $23.8 \pm 0.2^\circ$, $24.3 \pm 0.2^\circ$, $24.9 \pm 0.2^\circ$, $25.3 \pm 0.2^\circ$, $25.8 \pm 0.2^\circ$, $26.3 \pm 0.2^\circ$, $27.1 \pm 0.2^\circ$, $27.3 \pm 0.2^\circ$, $27.7 \pm 0.2^\circ$, $28.0 \pm 0.2^\circ$, and $28.4 \pm 0.2^\circ$, when measured with Cu-Kalpha radiation.
6. A crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol characterized by the x-ray powder diffraction pattern shown in FIG. 1.
7. The crystalline form according to any one of claims 1 to 6 characterized by having endothermic events at about 193°C and at about 261°C in differential scanning calorimetry (DSC) thermogram profile.
8. The crystalline form according to any one of claims 1 to 7 characterized by having a thermogravimetry coupled fourier transform infrared (TG-FTIR) spectroscopy thermogram showing decomposition occurring at temperatures of about 270°C .

-31-

9. The crystalline form according to any one of claims 1 to 8 characterized by having an FT-RAMAN spectrum at least one, more preferably at least two, still more preferably at least four, and most preferably all, of the RAMAN bands at about 3123, 3107, 3075, 2974, 1620, 1610, 1590, 1458, 1397, 1377, 1335, 1319, 1305, 1291, 1266, 1259, 1230, 1188, 1166, 1138, 1126, 1082, 1064, 1028, 971, 960, 900, 827, 770, 742, 713, 625, 580, 550, 531, 446, 377, 345, 330, 256, 241, 180, 163, 141, 108, 101 cm^{-1} .
10. A crystalline Form B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol.
11. The crystalline form according to claims 1 and 10 characterized by having an x-ray powder diffraction pattern comprising reflections at 2-Theta angles of $5.2 \pm 0.2^\circ$, $6.0 \pm 0.2^\circ$ and $15.8 \pm 0.2^\circ$, when measured with Cu-Kalpha radiation.
12. The crystalline form according to claims 1, 10, and 11, characterized by having an x-ray powder diffraction pattern comprises reflections at 2-Theta angles of $5.2 \pm 0.2^\circ$, $6.0 \pm 0.2^\circ$, $10.5 \pm 0.2^\circ$, $12.6 \pm 0.2^\circ$ and $15.8 \pm 0.2^\circ$, when measured with Cu-Kalpha radiation.
13. A crystalline Form B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol characterized by having an x-ray powder diffraction pattern comprising three, four, five or more 2 theta values selected from the group consisting of $5.2 \pm 0.2^\circ$, $6.0 \pm 0.2^\circ$, $8.7 \pm 0.2^\circ$, $10.5 \pm 0.2^\circ$, $12.0 \pm 0.2^\circ$, $12.6 \pm 0.2^\circ$, $12.9 \pm 0.2^\circ$, $14.5 \pm 0.2^\circ$, $14.8 \pm 0.2^\circ$, $15.0 \pm 0.2^\circ$, $15.8 \pm 0.2^\circ$, $17.4 \pm 0.2^\circ$, $17.6 \pm 0.2^\circ$, $17.8 \pm 0.2^\circ$, $18.0 \pm 0.2^\circ$, $18.4 \pm 0.2^\circ$, $19.0 \pm 0.2^\circ$, $19.2 \pm 0.2^\circ$, $19.9 \pm 0.2^\circ$, $22.7 \pm 0.2^\circ$, $23.3 \pm 0.2^\circ$, $23.7 \pm 0.2^\circ$, $24.0 \pm 0.2^\circ$, $24.5 \pm 0.2^\circ$, $25.0 \pm 0.2^\circ$, $25.4 \pm 0.2^\circ$, $25.8 \pm 0.2^\circ$, $26.2 \pm 0.2^\circ$, and $27.6 \pm 0.2^\circ$, when measured with Cu-Kalpha radiation.
14. A crystalline Form B of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol characterized by the x-ray powder diffraction pattern shown in FIG. 5.
15. The crystalline form according to any one of claims 1, 10 to 14 characterized by having an endothermic event at about 260°C in differential scanning calorimetry (DSC) thermogram profile.
16. The crystalline form according to any one of claims 1, 10 to 15 characterized by having a thermogravimetry coupled fourier transform infrared (TG-FTIR) spectroscopy thermogram showing mass changes from about 25°C to about 140°C and from about 140°C to about 210°C .

-32-

17. The crystalline form according to any one of claims 1, 10 to 16 characterized by having an FT-RAMAN spectrum at least one, more preferably at least two, still more preferably at least four, and most preferably all, of the RAMAN bands at about 3145, 2974, 2931, 1629, 1611, 1462, 1401, 1376, 1340, 1325, 1307, 1295, 1271, 1215, 1164, 1058, 996, 900, 836, and 706 cm^{-1} .
18. A pharmaceutical composition comprising a crystalline form of claims 1-17, and a pharmaceutically acceptable carrier.
19. A process for the preparation of crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol comprising: (a) dissolving 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol in N,N-dimethylformamide; (b) adding water; and optionally (c) isolating crystalline Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol.
20. A pharmaceutical composition comprising: (a) a therapeutically effective amount of a crystalline form of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to any one of Claims 1-19; and (b) at least one pharmaceutically acceptable carrier, diluent, vehicle or excipient.
21. The pharmaceutical composition of Claim 20, wherein the crystalline form is Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol.
22. A method of treating or ameliorating Huntington's Disease comprising the step of administering to a subject in need of such treatment a therapeutically effective amount of a crystalline form of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol according to any one of Claims 1-17 or the pharmaceutical composition of claims 20-21.
23. The method of claim 22, wherein the crystalline form is Form A of 2-[3-(2,2,6,6-tetramethylpiperidin-4-yl)-3H-[1,2,3]triazolo[4,5-c]pyridazin-6-yl]-5-(2H-1,2,3-triazol-2-yl)phenol.