CRYSTAL FORM OF ACID SALT OF SULFOXIMINE COMPOUND, PREPARATION METHOD THEREFOR, AND USE THEREOF

Technical Field

The present invention relates to the field of medicinal development, specifically to a crystal form of an acid salt of a sulfoximine compound, preparation method therefor, and a use thereof.

Background

Fibroblast growth factor receptors (FGFRs) are receptors for fibroblast growth factor (FGF) signaling, and its family consists of four members (FGFR1, FGFR2, FGFR3, and FGFR4). Each FGFR is a glycoprotein composed of an extracellular immunoglobulin (Ig)-like domain, a hydrophobic transmembrane region, and an intracellular domain that includes a tyrosine kinase domain. Binding of FGF ligands induces receptor dimerization and conformational changes in the intracellular domain, leading to intermolecular phosphorylation in the kinase domain and the intracellular tail. Phosphorylated residues serve as docking sites for adaptor proteins, which facilitate downstream signaling cascades, resulting in cellular behaviors including proliferation, survival, differentiation, migration, and angiogenesis. Abnormal FGFR signaling is implicated in various cancer types, including hepatocellular carcinoma, intrahepatic cholangiocarcinoma, bladder cancer, endometrial cancer, breast cancer, and lung cancer, and contributes to disease progression through overexpression, point mutations, and/or chromosomal translocations.

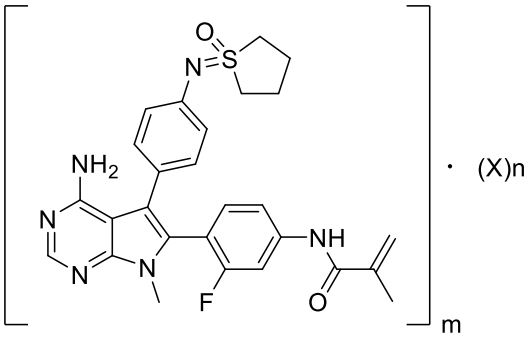
As research progresses, pan-FGFR1-3 inhibitors have demonstrated clinical responses in various FGFR-altered cancers, however, they also exhibit target-limited toxicities, leading to adverse side effects such as hyperphosphatemia and tissue mineralization, as the regulation of phosphate reabsorption is mediated by FGFR1 and FGFR3. Some studies have reported FGFR2 translocations in 14% of intrahepatic cholangiocarcinomas; FGFR2 mutations occur in 12–14% of endometrial cancers and 5% of squamous non-small cell lung cancers; FGFR2 is amplified in 12–14% of gastric cancers and 4% of breast cancers. FGFR2 contributes to the development of acquired resistance to human epidermal growth factor receptor 2 (HER2)-targeted therapy by indirectly overactivating FGFR2 in tumor-associated fibroblasts.

Therefore, given the unmet clinical needs, the development of FGFR2-selective inhibitors for treatment holds significant value and promising prospects.

Summary of the Invention

The objective of the present invention is to develop pharmaceutically acceptable salt forms and crystal forms of a sulfoximine FGFR inhibitor compound, and a preparation method therefor.

In one aspect of the present invention, provided is a compound of formula (I),



(I)

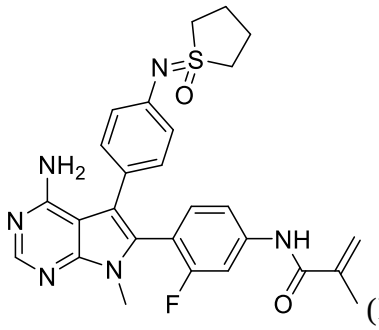
in an amorphous form or a crystal form or a solvate thereof;

wherein m is 1, 2, 3, 4, 5, 6, 7, 8, or 9;

n is 0, 0.5, 1, 1.5, 2, 2.5, or 3; and X is selected from the group consisting of: hydrochloric acid, hydrobromic acid, hydrofluoric acid, sulfuric acid, nitric acid or phosphoric acid, formic

acid, acetic acid, trifluoroacetic acid, propionic acid, oxalic acid, malonic acid, succinic acid, fumaric acid, maleic acid, lactic acid, malic acid, tartaric acid, citric acid, picric acid, benzoic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, benzenesulfonic acid, naphthalenesulfonic acid, hippuric acid, glycolic acid, or glutaric acid.

In another preferred embodiment, the structure of the compound of Formula I-1 is as follows:



(I-1).

the present invention provides a crystal form A of the compound of Formula I-1, the X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 11.59±0.2°, 12.00±0.2°, 14.16±0.2°, 15.50±0.2°, 16.74±0.2°, 18.38±0.2°, 18.81±0.2°, 21.32 ± 0.2°, 21.80 ± 0.2 °, 23.01 ± 0.2°, 24.37 ± 0.2°, 26.50 ± 0.2°, 28.90 ± 0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the crystal form A of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 8.44±0.2°, 11.59±0.2°, 12.00±0.2°, 12.34±0.2°, 14.16 ± 0.2°, 15.50 ± 0.2°, 16.50 ± 0.2°, 16.74 ± 0.2°, 18.38 ± 0.2°, 18.81 ± 0.2°, 19.79 ± 0.2°, 20.44±0.2°, 21.32±0.2°, 21.53±0.2°, 21.80±0.2°, 22.24±0.2°, 23.01±0.2°, 24.37±0.2°, 25.43±0.2°, 26.50±0.2°, 27.13±0.2°, 27.74±0.2°, 28.90±0.2°, 29.72±0.2°, 29.93±0.2°, 30.83±0.2°, 31.56±0.2°, 32.47±0.2°, 33.64±0.2°, 34.12±0.2°, 35.03±0.2°, 36.17±0.2°.

In another preferred embodiment, the crystal form A further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the crystal form A further has one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) 2θ angles selected from the group consisting of: 8.44±0.2°, 11.59±0.2°, 12.00±0.2°, 12.34 ± 0.2°, 15.50 ± 0.2°, 16.50 ± 0.2°, 18.38 ± 0.2°, 18.81 ± 0.2°, 19.79 ± 0.2 °, 20.44 ± 0.2°, 21.32±0.2°, 21.53±0.2°, 21.80±0.2°, 22.24±0.2°, 24.37±0.2°, 25.43±0.2°, 26.50±0.2°, 27.13±0.2°, 27.74±0.2°, 28.90±0.2°, 29.72±0.2°, 29.93±0.2°, 30.83±0.2°, 31.56 ± 0.2 °, 32.47 ± 0.2°, 33.64 ± 0.2°, 34.12 ± 0.2 °, 35.03 ± 0.2°, 36.17 ± 0.2°;

b. the differential scanning calorimetry curve of the crystal form A has the onsets of the endothermic peaks at 26.10°C ± 2°C and 223.34°C ± 2°C;

c. the thermogravimetric analysis curve of the crystal form A has three small weight loss steps at 24.00°C ± 2°C, 110.00°C ± 2°C, and 200.00°C ± 2°C, and decomposition begins above 250.00°C ± 2°C.

In another preferred embodiment, the crystal form A has an X-ray powder diffraction pattern substantially as shown in Figure 1.

In another preferred embodiment, the crystal form A has a differential scanning calorimetry pattern substantially as shown in Figure 2.

In another preferred embodiment, the crystal form A has a thermogravimetric analysis pattern substantially as shown in Figure 3.

In some embodiments of the present invention, the XRPD pattern of the crystal form A of the compound of Formula I-1 is shown in Figure 1.

Table 1 XRPD analysis data for the crystal form A of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak#1	8.443401	10.46377	465.3955	776.6761	0.02581691	0.100

Peak#2	11.59481	7.625884	1981.868	2352.141	0.1099402	0.100
Peak#3	12.00092	7.368722	2054.35	2439.293	0.113961	0.100
Peak#4	12.33819	7.168041	863.7459	1256.884	0.04791462	0.100
Peak#5	14.16416	6.247813	16,581.67	17,117.91	0.9198356	0.100
Peak#6	15.49514	5.714016	11,020.04	11,669.23	0.6113151	0.100
Peak#7	16.50191	5.367605	3768.419	4467.886	0.2090457	0.121
Peak#8	16.74475	5.290301	15,225.11	15,931.87	0.8445831	0.100
Peak#9	18.3777	4.823748	3973.455	4712.12	0.2204197	0.133
Peak#10	18.81417	4.712814	4317.971	5066.824	0.239531	0.100
Peak#11	19.79016	4.482541	3621.8	4405.136	0.2009123	0.100
Peak#12	20.44199	4.341054	784.3597	1607.157	0.04351082	0.100
Peak#13	21.32422	4.163405	6370.541	7270.211	0.3533933	0.102
Peak#14	21.52857	4.124347	4452.761	5370.366	0.2470082	0.102
Peak#15	21.79978	4.073646	10,626.56	11,565.94	0.5894879	0.100
Peak#16	22.24138	3.99375	2008.293	2978.074	0.1114061	0.100
Peak#17	23.00732	3.862497	18,026.77	19,034.55	1	0.100
Peak#18	24.37473	3.648822	13,513.07	14,542.2	0.749611	0.132
Peak#19	25.43489	3.499086	2514.506	3519.17	0.1394873	0.151
Peak#20	26.50102	3.360687	3923.504	4867.41	0.2176488	0.104
Peak#21	27.13202	3.283944	634.6851	1535.413	0.03520792	0.100
Peak#22	27.73726	3.213646	1539.967	2427.688	0.08542667	0.100
Peak#23	28.89928	3.087016	3747.38	4612.75	0.2078786	0.110
Peak#24	29.72192	3.00342	798.2333	1621.757	0.04428044	0.228
Peak#25	29.92524	2.983475	708.6496	1518.506	0.03931096	0.228
Peak#26	30.83398	2.897586	1476.005	2267.967	0.08187852	0.106
Peak#27	31.55616	2.832901	1184.099	1972.253	0.06568556	0.127
Peak#28	32.46742	2.75544	834.8455	1614.822	0.04631143	0.123
Peak#29	33.63531	2.662387	408.7598	1182.296	0.02267515	0.176
Peak#30	34.12203	2.625516	495.4477	1258.51	0.02748399	0.109
Peak#31	35.03429	2.559211	678.4774	1427.322	0.03763721	0.196
Peak#32	36.17301	2.481217	667.2708	1389.91	0.03701555	0.124

In some embodiments of the present invention, the differential scanning calorimetry (DSC) curve of the crystal form A of the compound of Formula I-1 has the onsets of the endothermic peaks at 26.10°C ± 2°C and 223.34°C ± 2°C.

In some embodiments of the present invention, the crystal form A of the compound of Formula I-1 has a DSC pattern as shown in Figure 2.

In some embodiments of the present invention, the thermogravimetric analysis (TGA)

curve of crystal form A of the compound of Formula I-1 has three small weight loss steps at 24.00°C ± 2°C, 110.00°C ± 2°C, and 200.00°C ± 2°C, and decomposition begins above 250.00°C ± 2°C.

In some embodiments of the present invention, the TGA pattern of the crystal form A of the compound of Formula I-1 is as shown in Figure 3.

The present invention also provides a method for preparing the crystal form A of the compound of Formula I-1, which includes adding the compound of Formula I-1 to acetonitrile, an alcoholic solvent, an ester solvent, an ether solvent, or a mixed solvent of an alcoholic solvent and water, and then performing recrystallization or slurrying to obtain it, wherein the alcoholic solvent is selected from methanol, ethanol, isopropanol, etc., the ester solvent is selected from ethyl acetate, isopropyl acetate, methyl formate, ethyl formate, isopropyl formate, etc., the ether solvent is selected from methyl tert-butyl ether, tetrahydrofuran, ethylene glycol dimethyl ether, etc, and the mixed solvent of an alcoholic solvent and water is selected from a mixture of methanol and water, a mixture of ethanol and water, or a mixture of isopropanol and water, and in the mixed solvent of an alcoholic solvent and water, the volume ratio of the alcoholic solvent to water is selected from 1:0.1 to 1.5.

The present invention also provides the maleate crystal form A of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 5.82±0.2°, 9.86±0.2°, 11.29±0.2°, 12.72 ± 0.2°, 13.04 ± 0.2°, 15.17 ± 0.2°, 17.88 ± 0.2°, 18.11 ± 0.2 °, 22.28 ± 0.2°, 23.02 ± 0.2°, 24.42 ± 0.2°, 25.34 ± 0.2°, 26.77 ± 0.2°.

In some embodiments of the present invention, the maleate crystal form A of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles in its X-ray powder diffraction pattern: 8.44±0.2°, 11.59±0.2°, 12.00±0.2°, 12.34±0.2°, 14.16 ± 0.2°, 15.50 ± 0.2°, 16.50 ± 0.2°, 16.74 ± 0.2°, 18.38 ± 0.2°, 18.81 ± 0.2°, 19.79 ± 0.2°, 20.44±0.2°, 21.32±0.2°, 21.53±0.2°, 21.80±0.2°, 22.24±0.2°, 23.01±0.2°, 24.37±0.2°, 25.43±0.2°, 26.50±0.2°, 27.13±0.2°, 27.74±0.2°, 28.90±0.2°, 29.72±0.2°, 29.93±0.2°, 30.83±0.2°, 31.56±0.2°, 32.47±0.2°, 33.64±0.2°, 34.12 ±0.2°, 35.03±0.2° , 36.17±0.2°.

In another preferred embodiment, the maleate crystal form A has an X-ray powder diffraction pattern substantially as shown in Figure 4.

In some embodiments of the present invention, the XRPD pattern of the maleate crystal form A of the compound of Formula I-1 is shown in Figure 4.

Table 2 XRPD analysis data for the maleate crystal form A of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak#1	5.816485	15.18233	49.66369	65.44668	0.2465863	0.100
Peak#2	9.859919	8.96345	73.92227	91.99165	0.3670331	0.101
Peak#3	11.06471	7.990012	33.00455	54.12584	0.1638716	0.142
Peak#4	11.29159	7.829976	71.99976	93.48729	0.3574875	0.129
Peak#5	11.64355	7.594069	28.69745	50.38568	0.1424863	0.133
Peak#6	11.90079	7.430491	53.98288	75.53851	0.2680315	0.100
Peak#7	12.72461	6.951217	49.88066	70.707	0.2476635	0.148
Peak#8	13.0453	6.781051	55.81887	75.97722	0.2771474	0.168
Peak#9	15.16811	5.836466	162.1551	178.0625	0.8051198	0.100
Peak#10	15.66005	5.65421	60.71101	77.37029	0.3014376	0.100

Peak#11	16.36081	5.413575	29.68445	47.71005	0.1473869	0.132
Peak#12	17.70085	5.006646	96.75628	119.5969	0.4804066	0.122
Peak#13	17.87988	4.956915	66.58391	89.8793	0.3305972	0.217
Peak#14	18.1084	4.894873	88.23072	111.9404	0.4380763	0.215
Peak#15	18.35028	4.830894	79.95369	103.8986	0.3969797	0.220
Peak#16	18.61376	4.763102	50.00529	73.96861	0.2482823	0.100
Peak#17	19.40942	4.569603	61.80075	86.36585	0.3068482	0.100
Peak#18	20.15778	4.401615	61.40547	87.72269	0.3048856	0.134
Peak#19	20.38478	4.353108	57.58932	84.15148	0.285938	0.162
Peak#20	20.68509	4.290583	29.13599	55.74016	0.1446637	0.222
Peak#21	21.32064	4.164098	69.45016	95.71144	0.3448285	0.100
Peak#22	21.6195	4.107205	29.40524	56.03273	0.1460006	0.150
Peak#23	22.28023	3.986875	117.0337	144.4462	0.5810865	0.100
Peak#24	22.70711	3.912881	56.87783	84.4616	0.2824053	0.102
Peak#25	23.02009	3.860384	201.405	228.6998	1	0.100
Peak#26	24.42011	3.642144	192.9104	220.1278	0.9578236	0.110
Peak#27	24.99754	3.559304	38.4386	65.54317	0.1908523	0.100
Peak#28	25.33689	3.512397	60.09032	86.57373	0.2983557	0.100
Peak#29	26.24092	3.393405	39.44109	63.79497	0.1958298	0.164
Peak#30	26.77359	3.327089	56.9196	80.2638	0.2826127	0.100
Peak#31	29.85257	2.990573	36.64283	61.98938	0.1819361	0.268
Peak#32	34.08594	2.628213	27.72369	53.10707	0.1376515	0.100

The present invention also provides a method for preparing crystal form A of the compound of formula I-1, comprising adding the compound of formula I-1 and maleic acid to acetonitrile and dichloromethane, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to maleic acid is selected from 0.8 to 1.2.

The present invention also provides monomaleate crystal form B of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 7.98±0.2°, 8.29 ± 0.2°, 11.61 ± 0.2°, 13.21 ± 0.2° , 13.99 ± 0.2 °, 15.25 ± 0.2 °, 15.95 ± 0.2°, 16.57 ± 0.2°, 17.38 ± 0.2°, 18.06 ± 0.2°, 20.39 ± 0.2° , 21.25 ± 0.2°, 21.61 ± 0.2°, 22.17 ± 0.2°, 23.54±0.2°, 24.70±0.2°, 25.91±0.2°, 27.24±0.2°, 29.47±0.2°, 29.71±0.2°, 32.64±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the monomaleate crystal form B of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 7.98±0.2°, 8.29±0.2°, 10.27±0.2°, 11.61±0.2°, 13.21±0.2°, 13.99±0.2°, 14.52±0.2°, 15.25±0.2°, 15.95±0.2°, 16.57±0.2°, 16.89±0.2°, 17.38±0.2°, 18.06±0.2°, 20.39±0.2°, 20.61±0.2°, 21.25±0.2°, 21.61±0.2°, 22.17±0.2°, 23.31±0.2°, 23.54±0.2°, 23.98±0.2°, 24.70±0.2°, 24.93±0.2°, 25.32±0.2°, 25.91±0.2°, 26.55±0.2°, 27.24±0.2°, 28.23±0.2°, 28.54±0.2°, 29.00±0.2°, 29.47±0.2°, 29.71±0.2°, 32.64±0.2°, 35.12±0.2°.

In another preferred embodiment, the maleate crystal form B has an X-ray powder

diffraction pattern substantially as shown in Figure 5.

In some embodiments of the present invention, the XRPD pattern of the monomaleate crystal form B of the compound of Formula I-1 is shown in Figure 5.

Table 3 X-ray diffraction data for the monomaleate crystal form B of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak#1	7.981822	11.06781	1723.857	1994.387	0.1169017	0.149
Peak#2	8.291428	10.65522	1137.191	1412.092	0.07711747	0.164
Peak#3	10.26916	8.607141	529.8829	820.8134	0.03593348	0.100
Peak#4	11.61435	7.613101	2756.817	3085.549	0.1869509	0.100
Peak#5	13.21075	6.696494	2119.543	2516.378	0.1437347	0.100
Peak#6	13.98848	6.325882	11811.49	12269.85	0.8009846	0.100
Peak#7	14.5199	6.095533	1061.446	1551.665	0.0719809	0.100
Peak#8	15.25275	5.804268	6038.434	6581.751	0.4094904	0.100
Peak#9	15.94566	5.553574	11989.22	12576.86	0.8130369	0.100
Peak#10	16.57134	5.34527	14746.21	15361.82	1	0.100
Peak#11	16.89114	5.244782	1575.195	2200.658	0.1068203	0.100
Peak#12	17.37723	5.099149	13942.37	14577.09	0.9454884	0.100
Peak#13	18.05592	4.908983	13096.95	13733.03	0.888157	0.100
Peak#14	20.39062	4.351873	14023.45	14713.4	0.9509865	0.100
Peak#15	20.61231	4.305566	5244.903	5947.155	0.355678	0.100
Peak#16	21.24602	4.178554	7214.775	7944.283	0.4892629	0.100
Peak#17	21.60538	4.109857	7723.3	8463.026	0.523748	0.175
Peak#18	22.17168	4.006149	3996.755	4744.93	0.271036	0.100
Peak#19	23.30505	3.813822	2970.041	3761.162	0.2014104	0.178
Peak#20	23.53755	3.776674	6206.884	7010.807	0.4209137	0.108
Peak#21	23.98418	3.707347	1311.471	2135.541	0.08893615	0.100
Peak#22	24.70086	3.601379	9470.771	10314.98	0.642251	0.100
Peak#23	24.92502	3.569496	3107.844	3955.256	0.2107554	0.100
Peak#24	25.31763	3.515025	1042.744	1892.22	0.07071263	0.167
Peak#25	25.91234	3.435686	10856.43	11700.45	0.736218	0.100
Peak#26	26.54931	3.354684	685.3824	1512.089	0.04647854	0.205
Peak#27	27.2363	3.271608	3106.794	3914.549	0.2106842	0.100
Peak#28	28.22876	3.1588	2131.622	2937.217	0.1445538	0.224
Peak#29	28.53832	3.125235	2016.763	2825.172	0.1367648	0.240
Peak#30	28.99892	3.076636	1532.671	2340.075	0.1039366	0.100

Peak#31	29.46878	3.028641	2286.111	3086.088	0.1550303	0.168
Peak#32	29.7058	3.005013	3049.359	3843.141	0.2067892	0.153
Peak#33	32.63929	2.741322	4630.014	5344.848	0.3139799	0.100
Peak#34	35.11711	2.553365	1318.593	1961.014	0.08941906	0.213

In some embodiments of the present invention, the monomaleate crystal form B of the compound of Formula I-1 has the onset of the endothermic peak at 213.92°C ± 2°C in its differential scanning calorimetry (DSC) curve.

In another preferred embodiment, the maleate crystal form B has a differential scanning calorimetry pattern substantially as shown in Figure 6.

In some embodiments of the present invention, the monomaleate crystal form B of the compound of Formula I-1 has a DSC pattern as shown in Figure 6.

In some embodiments of the present invention, the monomaleate crystal form B of the compound of Formula I-1 has two weight loss steps at 24.00°C ± 2°C and 180.00°C ± 2°C in its thermogravimetric analysis (TGA) curve, and decomposition begins above 250.00°C ± 2°C.

In another preferred embodiment, the maleate crystal form B has a thermogravimetric analysis pattern substantially as shown in Figure 7.

In some embodiments of the present invention, the TGA pattern of the monomaleate crystal form B of the compound of Formula I-1 is shown in Figure 7.

The present invention also provides a method for preparing the monomaleate crystal form B of the compound of Formula I-1, comprising adding the compound of Formula I-1 and maleic acid to tetrahydrofuran, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to maleic acid is selected from 0.8 to 1.2.

The present invention also provides the fumarate crystal form A of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 5.11±0.2°, 10.20±0.2°, 14.23±0.2°, 17.03±0.2°, 18.79 ± 0.2°, 28.85 ± 0.2 °, and 29.46 ± 0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the fumarate crystal form A of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 5.11±0.2°, 7.26±0.2°, 10.20±0.2°, 10.51±0.2°, 14.23 ± 0.2°, 14.47 ± 0.2°, 14.93 ± 0.2°, 16.17 ± 0.2°, 17.03 ± 0.2°, 17.90 ± 0.2 °, 18.79 ± 0.2°, 19.44±0.2°, 20.19±0.2°, 20.80±0.2°, 22.48±0.2°, 23.07±0.2°, 23.74±0.2°, 24.07±0.2°, 27.06±0.2°, 27.85±0.2°, 28.30±0.2°, 28.85±0.2°, 29.46±0.2°, 38.24±0.2°.

In another preferred embodiment, the fumarate crystal form A has an X-ray powder diffraction pattern substantially as shown in Figure 8.

In some embodiments of the present invention, the X-ray powder diffraction (XRPD) pattern of the fumarate crystal form A of the compound of Formula I-1 is shown in Figure 8.

Table 4 XRPD analysis data for the fumarate crystal form A of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak#1	5.106943	17.29001	66.02386	80.74232	0.6328462	0.100
Peak#2	7.257269	12.17109	15.48998	32.61639	0.1484732	0.123
Peak#3	10.20005	8.665302	44.82843	61.36366	0.4296856	0.171
Peak#4	10.50647	8.413257	25.31782	41.40717	0.2426742	0.100
Peak#5	14.22988	6.219109	94.52111	109.7326	0.9059956	0.138
Peak#6	14.46519	6.118463	44.95081	60.22918	0.4308586	0.153
Peak#7	14.93302	5.927817	26.26917	41.2175	0.251793	0.100

Peak#8	16.16592	5.478399	35.9365	51.60095	0.3444554	0.117
Peak#9	17.02807	5.202913	44.72762	61.55038	0.4287193	0.100
Peak#10	17.90158	4.950956	21.9525	40.30973	0.2104172	0.178
Peak#11	18.78968	4.718902	49.85003	67.55918	0.4778182	0.107
Peak#12	19.44071	4.562319	28.59071	45.95156	0.2740452	0.100
Peak#13	20.19247	4.394129	33.90914	52.76979	0.325023	0.149
Peak#14	20.79758	4.267629	33.02869	51.93834	0.3165837	0.201
Peak#15	22.48454	3.951108	11.28123	28.946	0.1081319	0.169
Peak#16	23.06632	3.852751	12.43236	31.23554	0.1191656	0.167
Peak#17	23.73916	3.745054	18.25035	37.17823	0.1749317	0.152
Peak#18	24.07149	3.694097	20.07611	38.59465	0.1924318	0.207
Peak#19	27.06206	3.292275	40.86212	66.92372	0.3916681	0.119
Peak#20	27.84687	3.201246	20.41484	49.1985	0.1956785	0.160
Peak#21	28.29739	3.151295	22.67108	52.42942	0.2173048	0.199
Peak#22	28.84687	3.092505	104.3285	134.4994	1	0.101
Peak#23	29.46212	3.02931	23.97766	53.60007	0.2298286	0.138
Peak#24	38.24442	2.351456	16.4544	35.48725	0.1577173	0.165

The present invention also provides a method for preparing the fumarate crystal form A of the compound of Formula I-1, comprising adding the compound of Formula I-1 and fumaric acid to acetonitrile and dichloromethane, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to fumaric acid is selected from 0.8 to 1.2.

The present invention also provides the hemifumarate crystal form B of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 5.12±0.2°, 10.20±0.2°, 10.53±0.2°, 14.24±0.2°, 16.99 ± 0.2°, 18.81 ± 0.2°, 19.45 ± 0.2°, 20.22 ± 0.2°, 20.43 ± 0.2°, 20.84 ± 0.2°, 27.04 ± 0.2°, 27.904±0.2°, 28.254±0.2° , 28.754±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hemifumarate crystal form B of the compound of formula I-1 has characteristic diffraction peaks at the following 2θ angles: 5.12±0.2°, 7.27±0.2°, 7.48±0.2°, 8.77 ± 0.2°, 9.18 ± 0.2°, 9.74 ± 0·2°, 10.20 ± 0.2°, 10.53 ± 0.2°, 14.24 ± 0.2°, 14.96 ± 0.2°, 16.09±0.2°, 16.99±0.2°, 17.61±0.2° , 17.95±0.2°, 18.81±0.2°, 19.45±0.2°, 20.22±0.2°, 20.43±0.2°, 20.84±0.2°, 22.51±0.2°, 23.11±0.2°, 23.76±0.2°, 24.19±0.2°, 25.24±0.2°, 27.04±0.2°, 27.90±0.2°, 28.25±0.2°, 28.75±0.2°, 29.73±0.2°, 30.14±0.2°, 30.77±0.2°, 31.28±0.2°, 33.95±0.2°, 34.52±0.2°, 37.07±0.2°, 38.26±0.2°.

In another preferred embodiment, the hemifumarate crystal form B has an X-ray powder diffraction pattern substantially as shown in Figure 9.

In some embodiments of the present invention, the XRPD pattern of the hemifumarate crystal form B of the compound of Formula I-1 is shown in Figure 9.

Table 5 XRPD analysis data for the hemifumarate crystal form B of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM

Peak#1	5.12113	17.24215	4647.751	4910.723	0.8420983	0.100
Peak#2	7.273411	12.14412	623.8793	910.8909	0.113037	0.142
Peak#3	7.477666	11.81285	412.141	704.9915	0.07467337	0.142
Peak#4	8.774699	10.06943	198.996	518.1956	0.03605491	0.129
Peak#5	9.180456	9.62527	368.1948	696.2799	0.06671103	0.133
Peak#6	9.736835	9.076479	448.8479	784.1718	0.08132408	0.128
Peak#7	10.19865	8.666491	2325.105	2662.089	0.421272	0.188
Peak#8	10.53449	8.390942	2150.306	2486.023	0.3896012	0.100
Peak#9	14.24094	6.214301	5519.25	6023.346	1	0.100
Peak#10	14.9559	5.918799	899.1369	1478.035	0.1629093	0.106
Peak#11	16.09258	5.503201	1338.067	2023.104	0.2424364	0.154
Peak#12	16.99405	5.213253	2242.453	3003.123	0.4062966	0.122
Peak#13	17.60838	5.03273	547.075	1350.681	0.09912127	0.100
Peak#14	17.95021	4.937653	762.8884	1587.368	0.1382232	0.100
Peak#15	18.80551	4.714965	2077.941	2945.17	0.3764898	0.133
Peak#16	19.45143	4.55983	1987.91	2878.464	0.3601776	0.100
Peak#17	20.2158	4.389112	1462.113	2370.312	0.2649115	0.315
Peak#18	20.42854	4.343882	1577.348	2488.53	0.2857904	0.310
Peak#19	20.84079	4.258877	1320.896	2235.486	0.2393253	0.176
Peak#20	22.50678	3.947253	631.9739	1528.338	0.1145036	0.100
Peak#21	23.11194	3.84525	710.6365	1587.676	0.128756	0.189
Peak#22	23.75574	3.742477	1328.016	2177.066	0.2406154	0.100
Peak#23	24.18724	3.676679	635.7908	1461.799	0.1151951	0.100
Peak#24	25.23851	3.525865	378.4447	1133.886	0.06856815	0.100
Peak#25	27.04291	3.294563	1310.952	2070.533	0.2375235	0.253
Peak#26	27.90105	3.195153	1727.994	2515.479	0.313085	0.100
Peak#27	28.25099	3.156364	1116.084	1911.047	0.2022166	0.100
Peak#28	28.74762	3.102957	1000.29	1801.975	0.1812366	0.100
Peak#29	29.73267	3.002359	710.9998	1512.519	0.1288218	0.100
Peak#30	30.14065	2.962642	604.3896	1400.594	0.1095058	0.211
Peak#31	30.76595	2.903837	492.9324	1275.009	0.08931148	0.161
Peak#32	31.27625	2.857613	378.292	1143.485	0.06854048	0.140
Peak#33	33.94976	2.638443	415.4766	1098.577	0.07527773	0.125
Peak#34	34.52381	2.595875	324.9706	1017.928	0.05887949	0.115
Peak#35	37.06812	2.423331	331.5999	994.89	0.06008062	0.178
Peak#36	38.25865	2.350615	330.8221	950.937	0.05993968	0.142

In some embodiments of the present invention, the hemifumarate crystal form B of the compound of Formula I-1 has the onsets of the endothermic peaks at 21.34°C ± 2°C, 172.21°C ± 2°C, and 234.34°C ± 2°C in its differential scanning calorimetry (DSC) curve.

In another preferred embodiment, the hemifumarate crystal form B has a differential scanning calorimetry pattern substantially as shown in Figure 10.

In some embodiments of the present invention, the hemifumarate crystal form B of the compound of Formula I-1 has a DSC pattern as shown in Figure 10.

In some embodiments of the present invention, the hemifumarate crystal form B of the compound of Formula I-1 has three weight loss steps at 31.90°C ± 2°C, 90.00°C ± 2°C, and 190.00°C ± 2°C in its thermogravimetric analysis (TGA) curve, and decomposition begins above 270.00°C ± 2°C.

In another preferred embodiment, the hemifumarate crystal form B has a thermogravimetric analysis pattern substantially as shown in Figure 11.

In some embodiments of the present invention, the TGA pattern of the hemifumarate crystal form B of the compound of Formula I-1 is shown in Figure 11.

The present invention also provides a method for preparing the hemifumarate crystal form B of the compound of Formula I-1, comprising adding the compound of Formula I-1 and fumaric acid to tetrahydrofuran, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to fumaric acid is selected from 1.6 to 2.4.

The present invention also provides the monoglycolate crystal form A of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 6.37 ± 0.2°, 10.37 ± 0.2°, 12.69 ± 0.2°, 13.55 ± 0.2°, 14.06 ± 0.2°, 18.22 ± 0.2°, 18.47 ± 0.2°, 21.25 ± 0.2°, 22.83 ± 0.2°, 23.49 ± 0.2°, 26.41 ± 0.2°, 30.96 ± 0.2°.

In some embodiments of the present invention, the monoglycolate crystal form A of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 6.37±0.2°, 10.37±0.2°, 11.09±0.2°, 11.70±0.2°, 12.69 ± 0.2°, 13.55 ± 0.2 °, 14.06 ± 0.2°, 15.97 ± 0.2°, 17.34 ± 0.2°, 18.22 ± 0.2°, 18.47±0.2°, 19.09±0.2°, 20.41±0.2°, 20.71±0.2°, 21.25±0.2°, 22.06±0.2°, 22.43±0.2°, 22.83±0.2°, 23.49±0.2°, 24.09±0.2°, 24.79±0.2°, 25.21±0.2°, 26.41±0.2°, 27.23±0.2°, 28.00±0.2°, 29.59±0.2°, 30.44±0.2°, 30.96±0.2°, 38.67±0.2°.

In another preferred embodiment, the monoglycolate crystal form A has an X-ray powder diffraction pattern substantially as shown in Figure 12.

In some embodiments of the present invention, the XRPD pattern of the monoglycolate crystal form A of the compound of Formula I-1 is shown in Figure 12.

Table 6 XRPD analysis data for the monoglycolate crystal form A of the compound of Formula I-1

Name	Angle	dValue	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak#1	6.367303	13.87013	2029.288	2272.519	0.07434029	0.100
Peak#2	10.37207	8.521972	6470.729	6785.768	0.2370466	0.100
Peak#3	11.09208	7.970361	1010.483	1340.449	0.0370177	0.100
Peak#4	11.70461	7.55459	1500.982	1841.876	0.05498648	0.100
Peak#5	12.69449	6.967646	3589.622	3976.064	0.131501	0.100
Peak#6	13.55449	6.527435	10232.45	10650.02	0.3748523	0.100
Peak#7	14.05714	6.29514	10135.51	10557.75	0.3713008	0.100
Peak#8	15.97294	5.544148	3536.131	4003.394	0.1295415	0.100
Peak#9	17.33713	5.110852	2288.859	2836.97	0.0838493	0.100

Peak#10	18.21904	4.865397	27297.29	27912.26	1	0.100
Peak#11	18.46709	4.800599	12375.91	13004.16	0.453375	0.138
Peak#12	19.08811	4.645792	4405.293	5056.107	0.1613821	0.100
Peak#13	20.40513	4.348813	1117.151	1859.68	0.04092536	0.179
Peak#14	20.71391	4.284677	1886.923	2660.549	0.06912491	0.165
Peak#15	21.2549	4.176828	9592.014	10411.04	0.3513907	0.100
Peak#16	22.05512	4.027056	1278.383	2158.564	0.04683188	0.127
Peak#17	22.43277	3.960109	1131.067	2042.437	0.04143513	0.131
Peak#18	22.83447	3.891343	14043.22	14981.57	0.5144547	0.100
Peak#19	23.48801	3.784526	9793.021	10761.67	0.3587543	0.157
Peak#20	24.09406	3.690687	3140.149	4121.826	0.1150352	0.108
Peak#21	24.78808	3.588905	6995.654	7974.427	0.2562765	0.100
Peak#22	25.21228	3.529473	3274.032	4241.681	0.1199398	0.108
Peak#23	26.41114	3.37192	15344.24	16294.99	0.5621157	0.100
Peak#24	27.22701	3.272703	1465.29	2397.752	0.05367895	0.114
Peak#25	27.99766	3.184346	3541.794	4432.819	0.1297489	0.100
Peak#26	29.59053	3.016456	1490.567	2310.24	0.05460494	0.100
Peak#27	30.43898	2.934282	1485.749	2333.618	0.05442845	0.100
Peak#28	30.96021	2.886059	7547.225	8398.33	0.2764826	0.100
Peak#29	38.66922	2.326597	1355.032	1979.99	0.04963982	0.100

In some embodiments of the present invention, the monoglycolate crystal form A of the compound of Formula I-1 has the onsets of the endothermic peaks at 109.66°C ± 2°C and 198.83°C ± 2°C in its differential scanning calorimetry (DSC) curve.

In another preferred embodiment, the monoglycolate crystal form A has a differential scanning calorimetry pattern substantially as shown in Figure 13.

In some embodiments of the present invention, the monoglycolate crystal form A of the compound of Formula I-1 has a DSC pattern as shown in Figure 13.

In some embodiments of the present invention, the monoglycolate crystal form A of the compound of Formula I-1 has three weight loss steps at 33.00°C ± 2°C, 100.00°C ± 2°C, and 165.00°C ± 2°C in its thermogravimetric analysis (TGA) curve, and decomposition begins above 200.00°C ± 2°C.

In another preferred embodiment, the monoglycolate crystal form A has a thermogravimetric analysis pattern substantially as shown in Figure 14.

In some embodiments of the present invention, the TGA pattern of the monoglycolate crystal form A of the compound of Formula I-1 is shown in Figure 14.

The present invention also provides a method for preparing the monoglycolate crystal form A of the compound of Formula I-1, comprising adding the compound of Formula I-1 and glycolic acid to acetonitrile, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to glycolic acid is selected from 0.8 to 1.2.

The present invention also provides the glycolate crystal form B of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 5.95±0.2°, 12.20 ± 0.2°, 13.87 ± 0.2°, 15.79 ± 0.2°, 15.97 ± 0.2°, 16.44 ± 0.2°, 16.63 ± 0.2°, 16.79 ± 0.2°, 17.30 ± 0.2°, 19.49 ± 0.2°, 23.50 ± 0.2°, 26.68 ± 0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the glycolate crystal form B of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 5.95±0.2°, 11.06±0.2°, 12.20±0.2°, 13.87±0.2°, 15.01±0.2°, 15.79±0.2°, 15.97±0.2°, 16.44±0.2°, 16.63±0.2°, 16.79±0.2°, 17.30±0.2°, 17.90±0.2°, 18.33±0.2°, 18.91±0.2°, 19.49±0.2°, 21.59±0.2°, 22.18±0.2°, 22.80±0.2°, 23.16±0.2°, 23.50±0.2°, 23.93±0.2°, 24.49±0.2° , 25.13±0.2°, 26.68±0.2°, 27.95±0.2°, 30.49±0.2°, 31.62±0.2°, 32.27±0.2°.

In another preferred embodiment, the glycolate crystal form B has an X-ray powder diffraction pattern substantially as shown in Figure 15.

In some embodiments of the present invention, the XRPD pattern of the glycolate crystal form B of the compound of Formula I-1 is shown in Figure 15.

Table 7 XRPD analysis data for the glycolate crystal form B of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak#1	5.94826	14.84628	47.21226	62.80721	0.2820042	0.100
Peak#2	11.05959	7.993703	27.85228	46.52969	0.1663649	0.100
Peak#3	12.19964	7.249135	42.98131	61.03759	0.2567323	0.100
Peak#4	13.8704	6.379468	111.6527	128.6609	0.6669146	0.100
Peak#5	15.01254	5.896596	26.83811	41.78902	0.1603071	0.100
Peak#6	15.78903	5.60831	44.40633	61.01559	0.2652441	0.100
Peak#7	15.97478	5.543516	34.20984	51.4254	0.2043393	0.100
Peak#8	16.43714	5.388608	14.20148	32.83326	0.08482705	0.166
Peak#9	16.6293	5.326771	22.48186	41.62296	0.1342867	0.166
Peak#10	16.79174	5.275602	31.88576	51.36475	0.1904573	0.100
Peak#11	17.30051	5.12159	142.7281	162.7214	0.8525316	0.100
Peak#12	17.89638	4.952384	43.38684	63.59336	0.2591546	0.100
Peak#13	18.32724	4.836915	84.93102	104.8279	0.5073028	0.100
Peak#14	18.91279	4.688461	18.65536	37.72074	0.1114306	0.100
Peak#15	19.48954	4.550999	167.4168	186.2042	1	0.100
Peak#16	21.58975	4.112796	17.46467	35.08154	0.1043185	0.100
Peak#17	22.18036	4.0046	52.74449	72.09505	0.3150489	0.100
Peak#18	22.80481	3.896337	60.85134	82.53977	0.363472	0.173
Peak#19	23.15596	3.83804	45.15902	67.61517	0.26974	0.125
Peak#20	23.49665	3.783154	107.6953	130.5205	0.6432761	0.100
Peak#21	23.92768	3.715973	15.04318	37.80346	0.08985461	0.191
Peak#22	24.49098	3.631765	17.92286	39.70282	0.1070553	0.161
Peak#23	25.12531	3.541494	38.13791	58.55093	0.2278021	0.119
Peak#24	26.67703	3.338912	82.84576	102.2695	0.4948473	0.100
Peak#25	27.94708	3.189994	33.99763	54.5564	0.2030717	0.107
Peak#26	30.48514	2.929944	31.34254	53.22852	0.1872126	0.100

Peak#27	31.62302	2.827063	15.2675	32.42916	0.09119453	0.100
Peak#28	32.26844	2.771976	22.99334	38.4986	0.1373419	0.192

The present invention also provides a method for preparing the glycolate crystal form B of the compound of Fomular I-1, comprising adding the compound of Formula I-1 and glycolic acid to tetrahydrofuran and dichloromethane, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to glycolic acid is selected from 0.8 to 1.2.

The present invention also provides the mono-L-malate crystal form A of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 6.01±0.2°, 15.15±0.2°, 17.27±0.2°, 17.99±0.2°, 18.58 ± 0.2°, 22.58 ± 0.2 °, 24.00 ± 0.2°, 24.50 ± 0.2°, 25.00 ± 0·2°, 29.40 ± 0.2°, 30.53 ± 0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the mono-L-malate crystal form A of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 6.01±0.2°, 10.06±0.2°, 11.04±0.2°, 11.98±0.2°, 12.66 ± 0.2° , 12.86 ± 0.2°, 13.39 ± 0.2° , 15.15 ± 0.2°, 15.62 ± 0·2°, 16.46 ± 0.2°, 17.27 ± 0.2°, 17.99±0.2°, 18.58±0.2°, 19.53±0.2°, 19.77±0.2°, 20.25±0.2°, 21.01±0.2°, 21.57±0.2°, 22.04±0.2°, 22.58±0.2°, 23.67±0.2°, 24.00±0.2°, 24.50±0.2°, 25.00±0.2°, 27.34±0.2°, 28.54±0.2°, 28.91±0.2°, 29.40±0.2°, 29.89±0.2°, 30.53±0.2°, 31.33±0.2°, 33.67±0.2°, 36.16±0.2°.

In another preferred embodiment, the mono-L-malate crystal form A has an X-ray powder diffraction pattern substantially as shown in Figure 16.

In some embodiments of the present invention, the XRPD pattern of the mono-L-malate crystal form A of the compound of Formula I-1 is shown in Figure 16.

Table 8. XRPD analysis data for the mono-L-malate crystal form A of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak#1	6.005817	14.70413	3458.47	3698.186	0.1756963	0.100
Peak#2	10.05991	8.785703	1235.219	1524.838	0.06275127	0.100
Peak#3	11.04048	8.007493	1010.378	1324.343	0.05132898	0.100
Peak#4	11.98007	7.381497	1546.43	1893.062	0.07856131	0.100
Peak#5	12.65977	6.986674	1564.73	1932.612	0.07949098	0.141
Peak#6	12.86478	6.875793	1744.169	2115.445	0.0886068	0.133
Peak#7	13.39037	6.607066	1748.559	2122.191	0.08882982	0.100
Peak#8	15.15275	5.842348	6447.348	6874.498	0.3275365	0.100
Peak#9	15.61757	5.669495	415.1237	858.8148	0.021089	0.100
Peak#10	16.46146	5.3807	1753.405	2260.688	0.08907603	0.100
Peak#11	17.27465	5.129198	9650.521	10,238.98	0.4902632	0.100
Peak#12	17.99119	4.926498	11,219.57	11,861.34	0.5699735	0.109
Peak#13	18.57705	4.772433	10,433.66	11,106.38	0.5300483	0.108
Peak#14	19.52605	4.542572	1184.517	1891.812	0.06017552	0.222
Peak#15	19.77436	4.486085	3155.73	3872.169	0.1603165	0.130
Peak#16	20.24735	4.382343	3376.988	4105.192	0.1715568	0.121
Peak#17	21.0078	4.225396	2453.564	3206.388	0.1246453	0.100

Peak#18	21.5734	4.115878	3826.304	4620.834	0.1943829	0.100
Peak#19	22.04117	4.029573	2859.582	3680.584	0.1452717	0.100
Peak#20	22.58438	3.933865	15,035.12	15,877.77	0.7638101	0.100
Peak#21	23.67221	3.755494	3964.6	4821.112	0.2014086	0.100
Peak#22	24.00331	3.704436	19,684.37	20,537.32	1	0.100
Peak#23	24.50464	3.629771	6524.69	7365.307	0.3314656	0.100
Peak#24	24.99671	3.559421	4225.784	5046.185	0.2146772	0.104
Peak#25	27.33987	3.259448	1009.065	1702.707	0.05126226	0.100
Peak#26	28.53714	3.125362	2079.627	2806.331	0.1056487	0.100
Peak#27	28.90615	3.086298	1564.794	2296.025	0.07949425	0.100
Peak#28	29.4012	3.035449	2180.341	2910.555	0.1107651	0.142
Peak#29	29.89372	2.986549	849.0558	1570.18	0.04313351	0.153
Peak#30	30.52674	2.926045	1898.222	2595.839	0.09643298	0.163
Peak#31	31.33463	2.852422	933.9003	1606.439	0.04744376	0.120
Peak#32	33.66905	2.659796	1560.925	2238.357	0.07929768	0.183
Peak#33	36.16417	2.481803	1357.96	2054.411	0.06898671	0.100

In some embodiments of the present invention, the mono-L-malate crystal form A of the compound of Formula I-1 has the onset of endothermic peak at 204.74°C ± 2°C in its differential scanning calorimetry (DSC) curve.

In another preferred embodiment, the mono-L-malate crystal form A has a differential scanning calorimetry pattern substantially as shown in Figure 17.

In some embodiments of the present invention, the DSC pattern of the mono-L-malate crystal form A of the compound of Formula I-1 is shown in Figure 17.

In some embodiments of the present invention, the mono-L-malate crystal form A of the compound of Formula I-1 has two weight loss steps at 33.00°C ± 2°C and 185.00°C ± 2°C in its thermogravimetric analysis (TGA) curve, and decomposition begins above 250.00°C ± 2°C.

In another preferred embodiment, the mono-L-malate crystal form A has a thermogravimetric analysis pattern substantially as shown in Figure 18.

In some embodiments of the present invention, the TGA pattern of mono-L-malate crystal form A of the compound of Formula I-1 is shown in Figure 18.

The present invention also provides a method for preparing the mono-L-malate crystal form A of the compound of Formula I-1, comprising adding the compound of Formula I-1 and L-malic acid to acetonitrile, tetrahydrofuran, and dichloromethane, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to L-malic acid is selected from 0.8 to 1.2.

The present invention also provides the monosuccinate crystal form A of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 6.15±0.2°, 12.26 ± 0.2°, 17.59 ± 0.2°, 18.40 ± 0.2°, 18.89 ± 0.2°, 19.11 ± 0.2°, 19.73 ± 0.2°, 20.90 ± 0.2°, 23.12±0.2°, 23.83±0.2°, 24.09±0.2°, 24.35±0.2°, 24.62±0.2°, 24.93±0.2°, 25.17±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the monosuccinate crystal form A of the compound of formula I-1 has characteristic diffraction peaks at the following 2θ angles: 6.15±0.2°, 9.64±0.2°, 9.95±0.2°, 11.19±0.2°, 12.26 ± 0.2°, 12.70 ± 0.2°, 13.30 ± 0.2°, 14.95 ± 0.2°, 15.25 ± 0.2°, 16.18 ± 0.2°, 17.59 ± 0.2°,

18.40±0.2°, 18.89±0.2°, 19.11±0.2°, 19.73±0.2°, 20.28±0.2°, 20.90±0.2°, 21.27±0.2°, 21.64±0.2°, 22.12±0.2°, 23.12±0.2°, 23.83±0.2°, 24.09±0.2°, 24.35±0.2°, 24.62±0.2°, 24.93±0.2°, 25.17±0.2°, 26.05±0.2°, 27.00±0.2°, 28.27±0.2°, 28.72±0.2°, 30.12±0.2°, 31.20±0.2°, 33.57±0.2°, 34.13±0.2°, 34.58±0.2°, 35.60±0.2°, 38.23±0.2°.

In another preferred embodiment, the monosuccinate crystal form A has an X-ray powder diffraction pattern substantially as shown in Figure 19.

In some embodiments of the present invention, the XRPD pattern of the monosuccinate crystal form A of the compound of Formula I-1 is shown in Figure 19.

Table 9: XRPD analysis data for the monosuccinate crystal form A of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	6.150476	14.35861	1079.754	1326.613	0.07385032	0.100
Peak #2	9.639017	9.168368	507.5315	837.8813	0.03471289	0.100
Peak #3	9.947687	8.884562	756.1947	1093.582	0.05172034	0.193
Peak #4	11.19269	7.898941	418.548	786.0864	0.02862681	0.104
Peak #5	12.26293	7.211865	5643.144	6055.72	0.3859659	0.100
Peak #6	12.69721	6.966156	1808.497	2238.503	0.1236932	0.183
Peak #7	13.30472	6.649406	441.7258	886.793	0.03021207	0.170
Peak #8	14.94649	5.922504	2066.371	2623.71	0.1413305	0.100
Peak #9	15.25239	5.804404	2862.093	3448.346	0.1957544	0.100
Peak #10	16.17555	5.475159	3974.573	4631.365	0.271843	0.100
Peak #11	17.58521	5.039309	9714.239	10,581.19	0.6644106	0.178
Peak #12	18.40139	4.817592	12,708.81	13,696.54	0.8692256	0.109
Peak #13	18.8852	4.69525	3,885.743	4935.811	0.2657675	0.275
Peak #14	19.10943	4.640657	3969.688	5046.307	0.271509	0.284
Peak #15	19.73177	4.495673	5384.054	6526.596	0.3682452	0.100
Peak #16	20.28191	4.374954	2270.541	3461.857	0.1552948	0.126
Peak #17	20.90259	4.246425	3615.605	4851.244	0.2472912	0.100
Peak #18	21.27065	4.173772	3046.671	4303.229	0.2083787	0.102
Peak #19	21.63627	4.10406	1379.22	2652.606	0.0943325	0.100
Peak #20	22.1207	4.015265	1392.721	2682.337	0.0952559	0.100
Peak #21	23.11513	3.844727	6964.299	8265.567	0.476327	0.234
Peak #22	23.83111	3.730811	7252.805	8544.42	0.4960595	0.101
Peak #23	24.0942	3.690666	12,167.04	13,451.31	0.832171	0.100
Peak #24	24.35121	3.652293	10,144.41	11,419.54	0.6938321	0.100
Peak #25	24.61575	3.613639	14,620.84	15,884.53	1	0.130
Peak #26	24.93286	3.568392	5294.415	6541.669	0.3621143	0.100
Peak #27	25.16802	3.535581	5032.057	6265.21	0.3441702	0.100

Peak #28	26.0534	3.417403	778.8174	1944.266	0.05326763	0.100
Peak #29	27.00305	3.299335	1246.342	2313.507	0.08524425	0.216
Peak #30	28.26834	3.154467	725.8612	1800.543	0.04964567	0.228
Peak #31	28.7181	3.106079	1720.941	2828.181	0.1177047	0.111
Peak #32	30.12463	2.964181	1318.532	2489.126	0.09018173	0.343
Peak #33	31.20475	2.863997	646.1497	1825.823	0.04419375	0.353
Peak #34	33.56967	2.667443	732.0571	1829.258	0.05006944	0.187
Peak #35	34.12764	2.625098	1220.828	2279.93	0.08349918	0.114
Peak #36	34.58483	2.591435	594.5156	1615.563	0.04066221	0.137
Peak #37	35.60008	2.519824	551.2985	1542.296	0.03770636	0.154
Peak #38	38.23304	2.352131	558.504	1479.673	0.03819918	0.162

In some embodiments of the present invention, the monosuccinate crystal form A of the compound of Formula I-1 has the onsets of the endothermic peaks at 72.75°C ± 2°C, 146.41°C ± 2°C, and 175.72°C ± 2°C in its differential scanning calorimetry (DSC) curve.

In another preferred embodiment, the monosuccinate crystal form A has a differential scanning calorimetry pattern substantially as shown in Figure 20.

In some embodiments of the present invention, the DSC pattern of the monosuccinate crystal form A of the compound of Formula I-1 is shown in Figure 20.

In some embodiments of the present invention, the monosuccinate crystal form A of the compound of Formula I-1 has three weight loss steps at 33.00°C ± 2°C, 90.00°C ± 2°C, and 160.00°C ± 2°C in its thermogravimetric analysis (TGA) curve, and decomposition begins above 260.00°C ± 2°C.

In another preferred embodiment, the monosuccinate crystal form A has a thermogravimetric analysis pattern substantially as shown in Figure 21.

In some embodiments of the present invention, the TGA pattern of the monosuccinate crystal form A of the compound of Formula I-1 is shown in Figure 21.

The present invention also provides a method for preparing the monosuccinate crystal form A of the compound of Formula I-1, comprising adding the compound of Formula I-1 and succinic acid to acetonitrile, tetrahydrofuran, dichloromethane, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to succinic acid is selected from 0.8 to 1.2.

The present invention also provides the sulfate crystal form A of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 6.74±0.2°, 9.56±0.2°, 12.89±0.2°, 13.78 ± 0.2°, 14.97 ± 0.2 °, 15.70 ± 0.2 °, 18.68 ± 0.2 °, 19.87 ± 0.2 °, 20.21 ± 0.2 °, 21.54 ± 0.2°, 21.76±0.2°, 22.58±0.2°, 23.75±0.2°, 24.11±0.2°, 24.50±0.2°, 25.25±0.2°, 25.86±0.2°, 27.73±0.2°, 28.41±0.2°, 29.70±0.2°, 30.21±0.2°, 30.99±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the sulfate crystal form A of the compound of formula I-1 has characteristic diffraction peaks at the following 2θ angles: 6.74±0.2°, 9.56±0.2°, 12.89 ± 0.2°, 13.78 ± 0.2 ° , 14.68 ± 0.2°, 14.97 ± 0.2°, 15.49 ± 0.2 °, 15.70 ± 0.2 °, 16.41 ± 0.2°, 16.90±0.2°, 18.47±0.2°, 18.68±0.2°, 18.86±0.2°, 19.33±0.2°, 19.87±0.2°, 20.21±0.2°, 20.70±0.2°, 21.54±0.2°, 21.76±0.2°, 22.25±0.2°, 22.58±0.2°, 23.75±0.2°, 24.11±0.2°, 24.50±0.2°, 25.25±0.2°, 25.86±0.2°, 26.10±0.2°, 26.71±0.2°, 26.96±0.2°, 27.73±0.2°, 28.41±0.2°, 28.90±0.2°, 29.70±0.2°, 30.21±0.2°, 30.99±0.2°.

In another preferred embodiment, the sulfate crystal form A has an X-ray powder

diffraction pattern substantially as shown in Figure 22.

In some embodiments of the present invention, the XRPD pattern of sulfate crystal form A of the compound of Formula I-1 is shown in Figure 22.

Table 10 XRPD analysis data for the sulfate crystal form A of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	6.744119	13.09598	35.65135	52.09074	0.07305558	0.100
Peak #2	9.561178	9.242833	46.10621	65.47356	0.09447933	0.100
Peak #3	12.8933	6.860647	63.02497	82.15709	0.1291487	0.100
Peak #4	13.78205	6.420164	125.4007	141.7527	0.256967	0.100
Peak #5	14.67751	6.03043	43.68357	60.03772	0.08951494	0.120
Peak #6	14.9725	5.912276	162.9075	180.921	0.3338248	0.100
Peak #7	15.48903	5.716255	33.8544	53.65991	0.06937333	0.137
Peak #8	15.70464	5.638256	75.82063	95.95579	0.1553692	0.107
Peak #9	16.40931	5.397684	27.52728	46.81891	0.056408	0.122
Peak #10	16.89674	5.243056	26.01051	42.90306	0.05329987	0.137
Peak #11	18.46692	4.800645	66.26648	87.1077	0.1357911	0.100
Peak #12	18.68092	4.74613	150.3831	172.4377	0.3081601	0.100
Peak #13	18.85655	4.702318	68.76389	91.63316	0.1409087	0.100
Peak #14	19.32761	4.58876	43.94986	68.19607	0.09006061	0.100
Peak #15	19.86924	4.464878	73.86705	99.83997	0.1513659	0.100
Peak #16	20.2137	4.389563	488.0031	514.8398	1	0.100
Peak #17	20.70499	4.286504	63.89549	90.87065	0.1309325	0.100
Peak #18	21.54397	4.121434	97.47784	125.4785	0.1997484	0.159
Peak #19	21.76018	4.080969	98.40488	127.1933	0.2016481	0.180
Peak #20	22.24623	3.992892	67.09114	96.74156	0.137481	0.122
Peak #21	22.57571	3.935357	161.0002	190.5227	0.3299163	0.100
Peak #22	23.74843	3.743612	56.21038	83.58575	0.1151845	0.100
Peak #23	24.11135	3.68808	61.4445	89.07555	0.1259101	0.193
Peak #24	24.4972	3.630857	66.60504	93.7385	0.1364849	0.117
Peak #25	25.25065	3.524197	48.23406	75.23211	0.09883966	0.100
Peak #26	25.8563	3.443004	47.72845	74.68002	0.09780359	0.197
Peak #27	26.09526	3.412015	76.15202	102.5496	0.1560482	0.133
Peak #28	26.70874	3.33502	23.33187	50.96179	0.04781092	0.168
Peak #29	26.96348	3.304087	15.27831	43.83334	0.03130781	0.168
Peak #30	27.73352	3.214072	36.22639	65.48412	0.07423393	0.100
Peak #31	28.40891	3.139177	73.84084	101.121	0.1513122	0.100
Peak #32	28.90162	3.086772	32.87369	60.11243	0.06736368	0.171

Peak #33	29.6984	3.005745	44.70893	73.78767	0.09161608	0.101
Peak #34	30.20773	2.956216	44.79463	73.28409	0.09179169	0.100
Peak #35	30.98633	2.883686	44.91674	71.77048	0.09204191	0.100

The present invention also provides a method for preparing the sulfate crystal form A of the compound of Formula I-1, comprising adding the compound of Formula I-1 and sulfuric acid to acetonitrile, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to sulfuric acid is selected from 0.8 to 1.2.

The present invention also provides the L-tartarate crystral form A of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 5.53±0.2°, 8.90±0.2°, 9.35±0.2°, 11.05±0.2°, 12.54 ± 0.2 °, 12.90 ± 0.2 °, 14.35 ± 0.2 °, 14.64 ± 0.2 °, 16.95 ± 0.2°, 18.70±0.2°, 19.45±0.2°, 19.74±0.2°, 20.38±0.2°, 20.79±0.2°, 21.45±0.2°, 21.94±0.2°, 22.88±0.2°, 23.80±0.2°, 25.01±0.2°, 25.77±0.2°, 27.33±0.2°, 27.80±0.2°, 28.65±0.2°, 29.41±0.2°, 30.00±0.2°, 31.09±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the L-tartarate crystal form A of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 5.53±0.2°, 8.90±0.2°, 9.35±0.2°, 11.05±0.2°, 12.54 ± 0.2°, 12.90 ± 0.2°, 14.35 ± 0.2°, 14.64 ± 0.2°, 16.95 ± 0.2°, 18.70 ± 0.2°, 19.45 ± 0.2°, 19.74±0.2°, 20.38±0.2°, 20.79±0.2°, 21.45±0.2°, 21.94±0.2°, 22.88±0.2°, 23.80±0.2°, 25.01±0.2°, 25.77±0.2°, 27.33±0.2°, 27.80±0.2°, 28.65±0.2°, 29.41±0.2°, 30.00±0.2°, 31.09±0.2°.

In another preferred embodiment, the L-tartarate crystal form A has an X-ray powder diffraction pattern substantially as shown in Figure 23.

In some embodiments of the present invention, the XRPD pattern of the L-tartrate crystal form A of the compound of Formula I-1 is shown in Figure 23.

Table 11 XRPD analysis data for the L-tartrate crystal form A of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	5.532435	15.96118	109.1809	126.6481	0.7936769	0.100
Peak #2	8.902002	9.925714	17.76301	34.91975	0.129126	0.100
Peak #3	9.347501	9.453633	20.67122	38.23275	0.1502669	0.107
Peak #4	11.05106	7.999851	40.37062	57.19987	0.2934692	0.100
Peak #5	12.53919	7.053588	73.71306	91.06278	0.5358478	0.100
Peak #6	12.8953	6.859589	31.62126	49.20035	0.2298668	0.106
Peak #7	14.3487	6.167873	24.90215	41.21078	0.1810231	0.181
Peak #8	14.63806	6.046594	38.96151	55.6525	0.2832258	0.169
Peak #9	16.94772	5.227398	113.6682	132.2339	0.8262969	0.100
Peak #10	18.69887	4.741615	16.89806	36.56548	0.1228383	0.100
Peak #11	19.44714	4.560826	31.79594	53.59855	0.2311366	0.134
Peak #12	19.74014	4.493786	40.01748	62.17728	0.290902	0.139
Peak #13	20.37972	4.354178	102.8208	125.9592	0.7474431	0.112
Peak #14	20.79081	4.269002	137.5634	161.0057	1	0.100
Peak #15	21.45161	4.138969	104.2521	127.0696	0.7578474	0.100
Peak #16	21.942	4.047562	66.40536	87.87263	0.4827255	0.118

Peak #17	22.88227	3.883322	13.39118	34.40554	0.09734552	0.175
Peak #18	23.79606	3.736227	26.73411	47.92166	0.1943403	0.100
Peak #19	25.01189	3.557295	31.7189	53.23115	0.2305766	0.117
Peak #20	25.77077	3.454237	53.50304	75.36505	0.3889337	0.121
Peak #21	27.33488	3.260032	22.88951	45.80283	0.1663924	0.213
Peak #22	27.80017	3.206517	29.94634	54.00067	0.2176912	0.141
Peak #23	28.65149	3.113149	48.81897	74.25991	0.3548834	0.140
Peak #24	29.40593	3.034971	65.22767	90.68871	0.4741644	0.100
Peak #25	30.00085	2.976129	29.92109	54.13644	0.2175076	0.149
Peak #26	31.09079	2.874235	31.22145	54.13402	0.2269605	0.100

The present invention also provides a method for preparing the L-tartarate crystal form A of the compound of Formula I-1, comprising adding the compound of Formula I-1 and L-tartaric acid to acetonitrile, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to L-tartaric acid is selected from 0.8 to 1.2.

The present invention also provides the hippurate crystal form A of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 6.17±0.2°, 6.52±0.2°, 12.30±0.2°, 14.18±0.2°, 15.62±0.2°, 16.06±0.2°, 16.78±0.2°, 17.64±0.2°, 18.78±0.2°, 20.42±0.2°, 21.15±0.2°, 21.29±0.2°, 21.79±0.2°, 24.42±0.2°, 26.45±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hippurate crystal form A of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 6.17±0.2°, 6.52±0.2°, 8.77±0.2°, 10.74±0.2°, 11.16±0.2°, 12.30±0.2°, 14.18±0.2°, 14.70±0.2°, 15.62±0.2°, 16.06±0.2°, 16.78±0.2°, 17.64±0.2°, 18.78±0.2°, 20.42±0.2°, 21.15±0.2°, 21.29±0.2°, 21.79±0.2°, 23.03±0.2°, 24.05±0.2°, 24.42±0.2°, 25.32±0.2°, 26.45±0.2°, 26.87±0.2°, 28.85±0.2°.

In another preferred embodiment, the hippurate crystal form A has an X-ray powder diffraction pattern substantially as shown in Figure 24.

In some embodiments of the present invention, the XRPD pattern of the hippurate crystal form A of the compound of Formula I-1 is shown in Figure 24.

Table 12 XRPD analysis data for the hippurate crystal form A of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	6.165727	14.32313	46.84962	63.97629	0.3607576	0.100
Peak #2	6.518609	13.54852	37.30031	54.89573	0.2872247	0.183
Peak #3	8.770015	10.07479	10.25155	31.52564	0.07894034	0.100
Peak #4	10.73528	8.23445	17.72863	43.06414	0.1365163	0.199
Peak #5	11.15514	7.925448	11.28448	37.4897	0.08689421	0.131
Peak #6	12.30332	7.188276	107.018	134.0704	0.8240739	0.100
Peak #7	14.18347	6.239351	32.73286	58.3698	0.2520539	0.100
Peak #8	14.69591	6.022922	13.75151	40.19582	0.1058912	0.226
Peak #9	15.6192	5.668907	24.5425	53.66223	0.1889853	0.216
Peak #10	16.064	5.512926	40.11842	71.12805	0.3089251	0.160

Peak #11	16.78293	5.278353	30.71124	63.47039	0.2364867	0.100
Peak #12	17.64042	5.02366	38.97564	76.05798	0.3001254	0.146
Peak #13	18.78433	4.720233	129.8645	172.2274	1	0.106
Peak #14	20.41602	4.346517	36.85044	83.07684	0.2837606	0.194
Peak #15	21.14778	4.197742	32.82731	78.65607	0.2527812	0.181
Peak #16	21.29136	4.169756	29.05938	74.61411	0.2237668	0.155
Peak #17	21.79278	4.074936	27.59339	71.68633	0.2124783	0.186
Peak #18	23.02744	3.859168	22.89831	60.05222	0.1763246	0.100
Peak #19	24.05033	3.697299	16.04067	52.94743	0.1235185	0.171
Peak #20	24.42373	3.641612	21.46288	58.33859	0.1652713	0.230
Peak #21	25.32431	3.514113	21.20499	56.21917	0.1632854	0.182
Peak #22	26.44801	3.367302	20.40374	50.96436	0.1571156	0.203
Peak #23	26.8689	3.315503	12.99294	41.55479	0.1000499	0.117
Peak #24	28.85276	3.091887	14.44897	46.59393	0.1112619	0.138

The present invention also provides a method for preparing the hippurate crystal form A of compound of Formula I-1, comprising adding the compound of Formula I-1 and hippuric acid to tetrahydrofuran, and then performing recrystallization or slurrying to obtain it, wherein the ratio of compound of Formula I-1 to hippuric acid is selected from 0.8 to 1.2.

The present invention also provides the glutarate crystal form A of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 11.82±0.2°, 12.75±0.2°, 13.19±0.2°, 14.87±0.2°, 15.10±0.2°, 17.10±0.2°, 17.82±0.2°, 18.35±0.2°, 19.75±0.2°, 20.14±0.2°, 20.70±0.2°, 22.23±0.2°, 23.20±0.2°, 24.26±0.2°, 24.47±0.2°, 29.92±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the glutarate crystal form A of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 9.86±0.2°, 10.97±0.2°, 11.82±0.2°, 12.29±0.2°, 12.75 ± 0.2°, 13.19 ± 0.2°, 14.87 ± 0.2°, 15.10 ± 0.2°, 15.37 ± 0.2°, 16.33 ± 0.2°, 17.10 ± 0.2°, 17.82±0.2°, 18.35±0.2°, 19.17±0.2°, 19.75±0.2°, 20.14±0.2°, 20.70±0.2°, 21.14±0.2°, 22.23±0.2°, 23.20±0.2°, 24.26±0.2°, 24.47±0.2°, 24.86±0.2°, 25.28±0.2°, 29.92±0.2°.

In another preferred embodiment, the glutarate crystal form A has an X-ray powder diffraction pattern substantially as shown in Figure 25.

In some embodiments of the present invention, the XRPD pattern of the glutarate crystal form A of the compound of Formula I-1 is shown in Figure 25.

Table 13 XRPD analysis data for the glutarate crystal form A of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	9.863811	8.959923	12.85162	32.81104	0.08830153	0.172
Peak #2	10.98613	8.046987	10.89521	32.04998	0.07485931	0.116
Peak #3	11.82328	7.479033	49.71856	70.34775	0.3416087	0.100
Peak #4	12.28926	7.196469	17.15315	37.49989	0.1178567	0.218
Peak #5	12.74523	6.94002	19.68536	39.10459	0.1352551	0.100
Peak #6	13.18652	6.708745	33.55265	51.90237	0.2305351	0.100

Peak #7	14.8743	5.951086	39.69448	53.88385	0.2727347	0.129
Peak #8	15.09693	5.863826	34.88612	49.31273	0.2396972	0.216
Peak #9	15.37447	5.758588	31.72464	46.23314	0.2179752	0.115
Peak #10	16.33454	5.422222	16.56744	32.81384	0.1138324	0.100
Peak #11	17.103	5.180287	40.75071	60.68394	0.2799919	0.100
Peak #12	17.81628	4.974467	117.4363	139.108	0.8068871	0.142
Peak #13	18.34729	4.831675	68.64827	90.59112	0.4716718	0.100
Peak #14	19.17292	4.625432	24.33756	46.22366	0.1672196	0.100
Peak #15	19.7465	4.492352	38.56743	60.27261	0.2649909	0.156
Peak #16	20.14022	4.405412	21.05011	42.03999	0.1446321	0.236
Peak #17	20.69634	4.288275	50.58425	69.74656	0.3475567	0.100
Peak #18	21.13538	4.200177	21.00321	38.04622	0.1443098	0.128
Peak #19	22.23299	3.99524	31.02705	52.27459	0.2131821	0.116
Peak #20	23.19805	3.83117	145.5424	170.8203	1	0.110
Peak #21	24.25913	3.665946	52.19791	78.5784	0.3586439	0.282
Peak #22	24.47135	3.634633	118.7159	144.8973	0.8156791	0.263
Peak #23	24.86463	3.578029	53.22074	78.66595	0.3656716	0.103
Peak #24	25.28382	3.519649	25.77899	49.91108	0.1771235	0.100
Peak #25	29.92096	2.983892	13.18526	36.99868	0.09059394	0.107

The present invention also provides a method for preparing the glutarate crystal form A of the compound of Formula I-1, comprising adding the compound of Formula I-1 and glutaric acid to acetonitrile and dichloromethane, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to glutaric acid is selected from 0.8 to 1.2.

The present invention also provides the p-toluenesulfonate crystal form A of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 7.08±0.2°, 10.23±0.2°, 13.36±0.2°, 14.16±0.2°, 17.77 ± 0.2°, 18.10 ± 0.2°, 18.90 ± 0.2 °, 19.12 ± 0.2°, 20.11 ± 0.2°, 20.53 ± 0.2°, 20.91 ± 0.2°, 24.41±0.2°, 25.51±0.2°, 28.28±0.2°, 29.95±0.2°, 30.98±0.2°, 35.22±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the p-toluenesulfonate crystal form A of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 7.08±0.2°, 8.00±0.2°, 9.39±0.2°, 10.23±0.2°, 13.36 ± 0.2°, 14.16 ± 0.2°, 14.81 ± 0.2°, 15.77 ± 0.2°, 16.21 ± 0.2°, 17.77 ± 0.2°, 18.10 ± 0.2°, 18.90±0.2°, 19.12±0.2°, 20.11±0.2°, 20.53±0.2°, 20.91±0.2°, 21.29±0.2°, 22.49±0.2°, 23.11±0.2°, 24.41±0.2°, 25.51±0.2°, 26.77±0.2°, 28.28±0.2°, 28.81±0.2°, 29.22±0.2°, 29.95±0.2°, 30.98±0.2°, 35.22±0.2°.

In another preferred embodiment, the p-toluenesulfonate crystal form A has an X-ray powder diffraction pattern substantially as shown in Figure 26.

In some embodiments of the present invention, the X-ray powder diffraction (XRPD) pattern of the p-toluenesulfonate crystal form A of the compound of Formula I-1 is shown in Figure 26.

Table 14 XRPD analysis data for the p-toluenesulfonate crystal form A of the compound of

Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	7.079945	12.47553	85.42383	101.1101	0.2852689	0.100
Peak #2	7.997392	11.0463	13.96909	31.70288	0.04664912	0.102
Peak #3	9.390173	9.410768	23.25926	45.09923	0.07767321	0.100
Peak #4	10.22862	8.641167	147.574	170.6116	0.4928164	0.100
Peak #5	13.36138	6.621338	128.1409	150.1271	0.4279206	0.106
Peak #6	14.15906	6.250054	101.5931	123.0315	0.3392653	0.100
Peak #7	14.81465	5.974915	18.95654	40.14683	0.06330448	0.100
Peak #8	15.77269	5.614086	40.74862	62.03128	0.1360781	0.148
Peak #9	16.20564	5.46506	21.01715	41.812	0.07018578	0.100
Peak #10	17.76859	4.98771	130.6191	157.9745	0.4361964	0.159
Peak #11	18.10162	4.896693	89.64201	119.1474	0.2993553	0.175
Peak #12	18.89753	4.692213	123.9464	156.6549	0.4139133	0.146
Peak #13	19.11654	4.638949	299.4503	332.5616	1	0.100
Peak #14	20.11447	4.410995	277.3101	311.3669	0.9260639	0.100
Peak #15	20.52951	4.322745	236.2305	269.9984	0.7888807	0.164
Peak #16	20.90733	4.245474	119.2478	152.1095	0.3982224	0.239
Peak #17	21.2862	4.170756	69.93179	101.2655	0.2335339	0.129
Peak #18	22.49223	3.949774	43.0219	68.77164	0.1436696	0.100
Peak #19	23.11408	3.844899	30.92543	55.90915	0.103274	0.101
Peak #20	24.4086	3.643835	70.81258	94.66067	0.2364753	0.125
Peak #21	25.51375	3.488449	44.21862	66.18475	0.147666	0.100
Peak #22	26.77312	3.327147	28.30337	54.19617	0.09451779	0.228
Peak #23	28.28136	3.153044	122.5069	156.2957	0.409106	0.100
Peak #24	28.80565	3.096838	18.56351	52.80252	0.06199198	0.183
Peak #25	29.21899	3.053962	27.92734	61.68496	0.09326204	0.145
Peak #26	29.94764	2.981295	30.47235	61.59036	0.101761	0.100
Peak #27	30.98179	2.884098	24.56855	53.25895	0.0820455	0.117
Peak #28	35.21519	2.546478	18.38519	46.0497	0.06139646	0.100

The present invention also provides a method for preparing the p-toluenesulfonate crystal form A of the compound of Formula I-1, comprising adding the compound of Formula I-1 and p-toluenesulfonic acid to acetonitrile, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to p-toluenesulfonic acid is selected from 0.8 to 1.2.

The present invention also provides the p-toluenesulfonate crystal form B of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 8.27 ± 0.2°, 13.69 ± 0.2°, 13.95 ± 0.2°, 16.15 ±

0.2°, 17.72 ± 0.2°, 19.52 ± 0.2°, 21.05 ± 0.2°, 22.45 ± 0.2°, 23.91 ± 0·2°, 25.40 ± 0.2°, 27.33 ± 0.2°, 29.25 ± 0. °.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the p-toluenesulfonate crystal form B of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 8.27±0.2°, 12.59±0.2°, 13.69±0.2°, 13.95±0.2°, 14.63 ± 0.2 °, 16.15 ± 0.2°, 17.72 ± 0.2 °, 18.68 ± 0.2 °, 19.52 ± 0.2°, 20.75 ± 0.2°, 21.05 ± 0.2°, 21.92±0.2°, 22.45±0.2°, 23.23±0.2°, 23.91±0.2°, 25.40±0.2°, 27.33±0.2°, 29.25±0.2°.

In another preferred embodiment, the p-toluenesulfonate crystal form B has an X-ray powder diffraction pattern substantially as shown in Figure 27.

In some embodiments of the present invention, the XRPD pattern of the p-toluenesulfonate crystal form B of the compound of Formula I-1 is shown in Figure 27.

Table 15 XRPD analysis data for the p-toluenesulfonate crystal form B of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	8.269233	10.68376	66.65063	82.69354	0.205002	0.100
Peak #2	12.58982	7.025336	25.67633	42.4886	0.07897448	0.113
Peak #3	13.68799	6.464071	66.10264	84.78497	0.2033165	0.100
Peak #4	13.95157	6.342537	205.2721	224.0923	0.6313697	0.100
Peak #5	14.63412	6.048212	56.90355	74.64372	0.1750222	0.100
Peak #6	16.14528	5.485354	75.07107	90.46928	0.2309013	0.100
Peak #7	17.7228	5.000495	52.54952	70.41904	0.1616302	0.161
Peak #8	18.68129	4.746037	24.92735	44.40676	0.0766708	0.106
Peak #9	19.51727	4.544596	325.1219	346.1157	1	0.100
Peak #10	20.74879	4.277555	39.79155	64.27892	0.1223896	0.131
Peak #11	21.04592	4.217828	131.2454	156.5197	0.4036806	0.142
Peak #12	21.91903	4.051752	33.07592	58.38848	0.1017339	0.100
Peak #13	22.4462	3.95777	89.58733	113.2832	0.27555	0.104
Peak #14	23.22516	3.82676	15.41252	37.83067	0.04740537	0.159
Peak #15	23.9116	3.718435	104.2562	125.6726	0.3206681	0.176
Peak #16	25.40249	3.503475	177.7236	200.8911	0.5466368	0.100
Peak #17	27.3258	3.261095	60.00591	86.0919	0.1845644	0.141
Peak #18	29.24715	3.051085	41.28314	68.31211	0.1269774	0.100

The present invention also provides a method for preparing the p-toluenesulfonate crystal form B of the compound of Formula I-1, comprising adding the compound of Formula I-1 and p-toluenesulfonic acid to tetrahydrofuran, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to p-toluenesulfonic acid is selected from the 0.8 to 1.2.

The present invention also provides the methanesulfonate crystal form A of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 6.70 ± 0.2°, 9.10 ± 0.2°, 9.81 ± 0.2°, 10.16 ± 0.2°, 13.34 ± 0.2°, 13.87 ± 0.2°, 14.27 ± 0.2°, 15.37 ± 0.2°, 17.21 ± 0.2°, 19.57 ± 0.2°, 21.16 ± 0.2°, 22.09 ± 0.2°, 23.86 ± 0.2°, 24.30 ± 0.2°, 24.99 ± 0.2° , 27.18 ± 0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the methanesulfonate crystal form A of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 6.70±0.2°, 9.10±0.2°, 9.81±0.2°, 10.16±0.2°, 13.34±0.2°, 13.87±0.2°, 14.27±0.2°, 15.37±0.2°, 15.79±0.2°, 17.21±0.2°, 18.75±0.2°, 19.57±0.2°, 21.16±0.2°, 22.09±0.2°, 23.31±0.2°, 23.86±0.2°, 24.30±0.2°, 24.99±0.2°, 27.18±0.2°, 28.04±0.2°, 28.83±0.2°.

In another preferred embodiment, the methanesulfonate crystal form A has an X-ray powder diffraction pattern substantially as shown in Figure 28.

In some embodiments of the present invention, the XRPD pattern of methanesulfonate crystal form A of the compound of Formula I-1 is shown in Figure 28.

Table 16 XRPD analysis data for the methanesulfonate crystal form A of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	6.697615	13.18681	29.2205	44.84843	0.1374156	0.100
Peak #2	9.102916	9.707085	21.63046	38.52872	0.1017218	0.100
Peak #3	9.807705	9.011051	21.38057	39.66219	0.1005466	0.143
Peak #4	10.16039	8.699037	29.45585	47.7616	0.1385223	0.161
Peak #5	13.34429	6.629781	27.07287	46.42973	0.1273159	0.100
Peak #6	13.87172	6.378866	29.43882	48.18745	0.1384423	0.100
Peak #7	14.27292	6.20045	66.19603	83.79364	0.3113008	0.100
Peak #8	15.36627	5.761644	37.38631	53.25999	0.175817	0.100
Peak #9	15.78599	5.609385	17.09895	33.88383	0.0804114	0.134
Peak #10	17.21072	5.148107	48.49517	67.62392	0.2280588	0.100
Peak #11	18.75375	4.727863	28.35833	51.94065	0.133361	0.100
Peak #12	19.57472	4.531386	212.6433	239.0555	1	0.110
Peak #13	21.16175	4.195003	37.02691	62.74215	0.1741268	0.160
Peak #14	22.09032	4.020719	46.08796	67.99896	0.2167384	0.100
Peak #15	23.31411	3.81236	19.21252	40.88506	0.09035092	0.173
Peak #16	23.85573	3.727016	34.5036	58.00617	0.1622605	0.100
Peak #17	24.30463	3.659186	33.63316	57.83051	0.158167	0.190
Peak #18	24.98785	3.560663	65.20639	89.03184	0.3066468	0.106
Peak #19	27.18207	3.278012	31.54118	56.58994	0.148329	0.104
Peak #20	28.04009	3.179624	18.07375	44.88169	0.08499562	0.164
Peak #21	28.8345	3.093804	24.47278	50.48177	0.1150884	0.249

The present invention also provides a method for preparing methanesulfonate crystal form A of the compound of Formula I-1, comprising adding the compound of Formula I-1 and methanesulfonic acid to tetrahydrofuran, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to methanesulfonic acid is selected from 0.8 to 1.2.

The present invention also provides the hydrochloride crystal form C1 of the compound

of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 7.47±0.2°, 7.73±0.2°, 12.25±0.2°, 13.18±0.2°, 13.51 ± 0.2 °, 14.96 ± 0.2°, 15.46 ± 0.2°, 17.31 ± 0.2° , 18.56 ± 0.2°, 19.34 ± 0.2°, 19.57 ± 0.2°, 19.78±0.2°, 20.01±0.2°, 20.41±0.2°, 20.76±0.2°, 24.36±0.2°, 25.63±0.2°, 26.47±0.2°, 27.51±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hydrochloride crystal form C1 of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 7.47±0.2°, 7.73±0.2°, 9.63±0.2°, 11.46±0.2°, 12.25 ± 0.2°, 13.18 ± 0.2°, 13.51 ± 0.2°, 14.96 ± 0.2°, 15.46 ± 0.2°, 16.79 ± 0.2°, 17.04 ± 0.2°, 17.31±0.2°, 17.72±0.2°, 18.56±0.2°, 19.34±0.2°, 19.57±0.2°, 19.78±0.2°, 20.01±0.2°, 20.41±0.2°, 20.76±0.2°, 22.60±0.2°, 23.09±0.2°, 23.80±0.2°, 24.36±0.2°, 25.63±0.2°, 26.47±0.2°, 27.51±0.2°, 29.09±0.2°, 30.76±0.2°, 31.99±0.2°, 36.24±0.2°.

In another preferred embodiment, the hydrochloride crystal form C1 has an X-ray powder diffraction pattern substantially as shown in Figure 29.

In some embodiments of the present invention, the X-ray diffraction (XRPD) pattern of the hydrochloride crystal form C1 of the compound of Formula I-1 is shown in Figure 29.

Table 17 XRPD analysis data for the hydrochloride crystal form C1 of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	7.469565	11.82564	170.3781	233.8982	0.3741632	0.165
Peak # 2	7.727614	11.43132	288.2178	351.6654	0.6329481	0.135
Peak # 3	9.625598	9.181119	30.23456	95.12409	0.06639738	0.154
Peak # 4	11.46039	7.715022	35.40674	99.13931	0.07775588	0.100
Peak # 5	12.25008	7.219398	187.329	254.1297	0.4113886	0.100
Peak # 6	13.18162	6.711229	176.609	244.8173	0.3878468	0.165
Peak # 7	13.50989	6.548882	101.0302	168.6256	0.22187	0.120
Peak # 8	14.96371	5.915727	130.4177	199.7892	0.2864071	0.106
Peak # 9	15.46443	5.725291	145.8036	215.9147	0.3201957	0.100
Peak # 10	16.79406	5.27488	51.23669	120.018	0.1125197	0.134
Peak # 11	17.03815	5.199857	68.14204	136.5628	0.1496451	0.220
Peak # 12	17.31437	5.117519	68.7573	136.3839	0.1509962	0.143
Peak # 13	17.72217	5.000671	20.89011	88.21156	0.04587625	0.100
Peak # 14	18.56032	4.776697	158.9897	234.8893	0.3491534	0.100
Peak # 15	19.33619	4.586743	193.7012	275.9999	0.4253825	0.106
Peak # 16	19.57052	4.532349	243.5362	327.1351	0.5348239	0.151
Peak # 17	19.78009	4.4848	455.3577	539.8668	1	0.100
Peak # 18	20.01093	4.433581	150.447	235.6875	0.330393	0.100
Peak # 19	20.41269	4.347219	117.9435	203.7759	0.2590128	0.250
Peak # 20	20.7621	4.274841	143.6874	229.3326	0.3155484	0.146
Peak # 21	22.59736	3.931636	57.59861	153.2617	0.1264909	0.179
Peak # 22	23.0917	3.848574	47.79654	145.3939	0.1049648	0.222

Peak # 23	23.80311	3.735136	47.23293	145.9101	0.1037271	0.250
Peak # 24	24.35631	3.65154	118.0796	215.7209	0.2593118	0.170
Peak # 25	25.63398	3.472358	54.12675	146.5311	0.1188664	0.100
Peak # 26	26.4743	3.364018	165.1317	261.6809	0.3626417	0.106
Peak # 27	27.51233	3.239408	144.2079	250.5756	0.3166913	0.122
Peak # 28	29.09444	3.066751	56.66905	168.875	0.1244495	0.150
Peak # 29	30.76101	2.904293	47.74388	156.956	0.1048492	0.218
Peak # 30	31.99164	2.795325	54.65399	155.6174	0.1200243	0.100
Peak # 31	36.23993	2.476788	45.47268	131.7606	0.09986144	0.111

In some embodiments of the present invention, the hydrochloride crystal form C1 of the compound of Formula I-1 has the onsets of the endothermic peaks at 39.76°C ± 2°C and 153.80°C ± 2°C in its differential scanning calorimetry (DSC) curve, and decomposition begins above 214.75°C ± 2°C.

In another preferred embodiment, the hydrochloride crystal form C1 has a differential scanning calorimetry pattern substantially as shown in Figure 30.

In some embodiments of the present invention, the DSC pattern of the hydrochloride crystal form C1 of the compound of Formula I-1 is shown in Figure 30.

In some embodiments of the present invention, the hydrochloride crystal form C1 of the compound of Formula I-1 has three weight loss steps at 26.03°C ± 2°C, 100.00°C ± 2°C, and 150.00°C ± 2°C in its thermogravimetric analysis (TGA) curve.

In another preferred embodiment, the hydrochloride crystal form C1 has a thermogravimetric analysis pattern substantially as shown in Figure 31.

In some embodiments of the present invention, the TGA pattern of the hydrochloride crystal form C1 of the compound of Formula I-1 is shown in Figure 31.

The present invention also provides a method for preparing the hydrochloride crystal form C1 of the compound of Formula I-1, comprising adding the compound of Formula I-1 and hydrochloric acid to ethyl acetate, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to hydrochloric acid is selected from 0.8 to 1.2, the hydrochloride crystal form C1 of the compound of Formula I-1 is an ethyl acetate solvate and hydrate crystal form, with an ethyl acetate content of 0.62 equivalents and a water content of 3.0 equivalents.

In another preferred embodiment, the hydrochloride crystal form C1 is an ethyl acetate solvate and hydrate crystal form, wherein the ethyl acetate content is 0.1 to 1 equivalent and the water content is 1 to 5 equivalents.

The present invention also provides the hydrochloride crystal form C2 of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 7.56±0.2°, 7.79±0.2°, 12.32 ± 0.2°, 13.21 ± 0.2°, 13.63 ± 0.2°, 15.10 ± 0.2°, 15.56 ± 0.2°, 18.58 ± 0.2°, 19.36 ± 0.2°, 19.66±0.2°, 19.82±0.2°, 20.91±0.2°, 24.35±0.2°, 26.56±0.2°, 30.74±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hydrochloride crystal form C2 of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 7.56±0.2°, 7.79±0.2°, 9.65±0.2°, 11.48±0.2°, 12.32 ± 0.2°, 13.21 ± 0.2°, 13.63 ± 0.2°, 15.10 ± 0.2°, 15.56 ± 0.2°, 16.86±0.2°, 17.16±0.2°, 17.41±0.2°, 17.77±0.2°, 18.58±0.2°, 19.36±0.2°, 19.66±0.2°, 19.82±0.2°, 20.32±0.2°, 20.91±0.2°, 22.71±0.2°, 23.21±0.2°, 23.80±0.2°, 24.35±0.2°, 25.71±0.2°, 26.56±0.2°, 27.53±0.2°, 27.80±0.2°, 28.20±0.2°, 29.15±0.2°, 30.74±0.2°, 32.06±0.2°, 36.30±0.2°, 38.22±0.2°.

In another preferred embodiment, the hydrochloride crystal form C2 has an X-ray powder diffraction pattern substantially as shown in Figure 32.

In some embodiments of the present invention, the X-ray diffraction (XRPD) pattern of the hydrochloride crystal form C2 of the compound of Formula I-1 is shown in Figure 32.

Table 18 XRPD analysis data for the hydrochloride crystal form C2 of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	7.561379	11.68225	594.0467	654.5096	0.4930706	0.153
Peak # 2	7.785987	11.34575	665.0544	725.5987	0.5520085	0.143
Peak # 3	9.653943	9.154226	64.07269	124.0171	0.05318161	0.100
Peak # 4	11.47599	7.704572	59.76658	119.5923	0.04960746	0.100
Peak # 5	12.32226	7.177275	486.3391	550.8688	0.4036712	0.100
Peak # 6	13.20849	6.697635	382.8189	452.7995	0.3177474	0.100
Peak # 7	13.63449	6.489313	383.4615	454.04	0.3182808	0.102
Peak # 8	15.10227	5.861764	417.983	490.954	0.3469343	0.110
Peak # 9	15.55625	5.691705	359.4082	431.791	0.298316	0.100
Peak # 10	16.8609	5.254121	157.987	227.7439	0.1311324	0.100
Peak # 11	17.16267	5.162411	180.6607	252.0321	0.149952	0.249
Peak # 12	17.41028	5.089545	224.9247	297.1292	0.186692	0.132
Peak # 13	17.77288	4.986517	60.75385	133.3784	0.0504269	0.100
Peak # 14	18.58392	4.770684	327.1711	410.2261	0.2715586	0.102
Peak # 15	19.35654	4.581967	330.6791	422.6897	0.2744703	0.152
Peak # 16	19.66373	4.511075	642.4008	736.7739	0.5332054	0.141
Peak # 17	19.82029	4.475794	1204.79	1300.107	1	0.141
Peak # 18	20.31755	4.36736	218.6828	315.8102	0.1815111	0.229
Peak # 19	20.91171	4.244595	405.4756	502.4253	0.3365528	0.110
Peak # 20	22.71078	3.912256	178.8163	287.4753	0.1484211	0.150
Peak # 21	23.21358	3.828644	150.452	262.2883	0.1248782	0.283
Peak # 22	23.79538	3.736332	153.2322	266.4649	0.1271858	0.169
Peak # 23	24.35296	3.652033	290.4572	402.7315	0.2410853	0.185
Peak # 24	25.71424	3.461702	106.9341	225.8246	0.08875742	0.149
Peak # 25	26.56012	3.353343	433.4701	562.3314	0.3597888	0.100
Peak # 26	27.52862	3.237527	341.6432	479.7618	0.2835706	0.127
Peak # 27	27.8036	3.206129	133.144	272.6549	0.1105122	0.236
Peak # 28	28.20096	3.161851	78.81534	219.3735	0.0654183	0.108
Peak #29	29.15277	3.060749	104.427	242.8467	0.08667652	0.174
Peak # 30	30.74315	2.90594	210.473	344.75	0.1746968	0.189

Peak # 31	32.06215	2.789339	87.68976	212.1315	0.07278425	0.163
Peak # 32	36.29795	2.472962	112.9378	222.361	0.0937406	0.138
Peak # 33	38.21926	2.352947	80.73588	192.5904	0.06701239	0.238

In some embodiments of the present invention, the hydrochloride crystal form C2 of the compound of Formula I-1 has the onsets of the endothermic peaks at 33.27°C ± 2°C and 155.72°C ± 2°C in its differential scanning calorimetry (DSC) curve, and decomposition of the sample begins above 212.45°C ± 2°C.

In another preferred embodiment, the hydrochloride crystal form C2 has a differential scanning calorimetry pattern substantially as shown in Figure 33.

In some embodiments of the present invention, the DSC pattern of the hydrochloride crystal form C2 of the compound of Formula I-1 is shown in Figure 33.

In some embodiments of the present invention, the hydrochloride crystal form C2 of the compound of Formula I-1 has three weight loss steps at 28.19°C ± 2°C, 115.00°C ± 2°C, and 150.00°C ± 2°C in its thermogravimetric analysis (TGA) curve.

In another preferred embodiment, the hydrochloride crystal form C2 has a thermogravimetric analysis pattern substantially as shown in Figure 34.

In some embodiments of the present invention, the TGA pattern of the hydrochloride crystal form C2 of the compound of Formula I-1 is shown in Figure 34.

The present invention also provides a method for preparing the hydrochloride crystal form C2 of the compound of Formula I-1, comprising adding the compound of Formula I-1 and hydrochloric acid to 2-methyl-tetrahydrofuran, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to hydrochloric acid is selected from 0.8 to 1.2, and the hydrochloride crystal form C2 of the compound of Formula I-1 is a 2-methyl tetrahydrofuran solvate and hydrate crystal form, with a 2-methyl tetrahydrofuran content of 0.21 equivalents and a water content of 2.8 equivalents.

In another preferred embodiment, the hydrochloride crystal form C2 is a 2-methyl-tetrahydrofuran solvate and hydrate crystal form, wherein the 2-methyl-tetrahydrofuran content is 0.05 to 0.5 equivalents and the water content is 1 to 5 equivalents.

The present invention also provides the hydrochloride crystal form D of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 6.60±0.2°, 7.79±0.2°, 9.84±0.2°, 13.31 ± 0.2°, 15.23 ± 0.2°, 15.93 ± 0.2°, 20.09 ± 0.2°, 20.41 ± 0.2°, 21.23 ± 0.2°, 21.80 ± 0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hydrochloride crystal form D of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 6.60±0.2°, 7.26±0.2°, 7.79±0.2°, 8.48±0.2°, 9.84±0.2°, 11.18±0.2°, 13.31±0.2°, 13.89±0.2°, 14.64±0.2°, 14.98±0.2°, 15.23±0.2°, 15.93±0.2°, 16.27±0.2°, 17.04±0.2°, 18.21±0.2°, 19.33±0.2°, 20.09±0.2°, 20.41±0.2°, 21.23±0.2°, 21.80±0.2°, 23.49±0.2°, 24.79±0.2°, 28.43±0.2°.

In another preferred embodiment, the hydrochloride crystal form D has an X-ray powder diffraction pattern substantially as shown in Figure 35.

In some embodiments of the present invention, the XRPD pattern of the hydrochloride crystal form D of the compound of Formula I-1 is shown in Figure 35.

Table 19 XRPD analysis data for the hydrochloride crystal form D of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	6.601512	13.37856	164.5807	360.2378	0.1722114	0.100
Peak # 2	7.256653	12.17213	58.27498	262.8102	0.06097686	0.111
Peak # 3	7.786158	11.3455	216.3087	427.6613	0.2263378	0.100

Peak # 4	8.479876	10.41884	94.11929	310.7975	0.09848309	0.100
Peak # 5	9.837548	8.983783	292.5006	516.1531	0.3060622	0.100
Peak # 6	11.17929	7.90838	73.00758	297.2161	0.07639254	0.277
Peak # 7	13.30976	6.6469	222.7104	477.5637	0.2330362	0.166
Peak # 8	13.88618	6.372257	72.43765	337.7217	0.07579618	0.133
Peak # 9	14.63502	6.047843	144.9248	428.148	0.1516442	0.108
Peak # 10	14.98003	5.90932	217.5238	511.2758	0.2276092	0.380
Peak # 11	15.22908	5.813237	300.9823	601.7073	0.3149371	0.185
Peak # 12	15.92681	5.560104	334.7283	652.176	0.3502478	0.198
Peak # 13	16.26554	5.445069	139.724	463.7961	0.1462023	0.356
Peak # 14	17.03894	5.199618	77.78125	421.2977	0.08138753	0.183
Peak #15	18.21142	4.867415	117.7768	497.4332	0.1232375	0.100
Peak # 16	19.32967	4.588276	229.9395	646.4288	0.2406005	0.100
Peak # 17	20.08674	4.41702	708.8257	1144.215	0.74169	0.100
Peak # 18	20.40698	4.348422	955.69	1397.604	1	0.156
Peak # 19	21.2275	4.182158	313.6636	768.3183	0.3282064	0.236
Peak # 20	21.80498	4.072686	320.5857	780.7736	0.3354495	0.287
Peak # 21	23.48703	3.784683	59.54105	519.681	0.06230164	0.125
Peak # 22	24.78517	3.589319	87.48044	546.9264	0.09153642	0.283
Peak # 23	28.43383	3.136483	65.95297	507.909	0.06901085	0.100

In some embodiments of the present invention, the hydrochloride crystal form D of the compound of Formula I-1 has the onsets of the endothermic peaks at 55.20°C ± 2°C and 164.37°C ± 2°C in its differential scanning calorimetry (DSC) curve, and decomposition of the sample begins above 211.35°C ± 2°C.

In another preferred embodiment, the hydrochloride crystal form D has a differential scanning calorimetry pattern substantially as shown in Figure 36.

In some embodiments of the present invention, the DSC pattern of the hydrochloride crystal form D of the compound of Formula I-1 is shown in Figure 36.

In some embodiments of the present invention, the hydrochloride crystal form D of the compound of Formula I-1 has two weight loss steps at 36.24°C ± 2°C and 110.00°C ± 2°C in its thermogravimetric analysis (TGA) curve.

In another preferred embodiment, the hydrochloride crystal form D has a thermogravimetric analysis pattern substantially as shown in Figure 37.

In some embodiments of the present invention, the TGA pattern of the hydrochloride crystal form D of the compound of Formula I-1 is shown in Figure 37.

The present invention also provides a method for preparing the hydrochloride crystal form D of the compound of Formula I-1, comprising adding the compound of Formula I-1 and hydrochloric acid to butanone, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to hydrochloric acid is selected from 0.8 to 1.2, and the hydrochloride crystal form D of the compound of Formula I-1 is an anhydrous crystal form.

The present invention also provides the hydrochloride crystal form E1 of the compound

of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 6.15±0.2°, 7.66 ± 0.2 °, 7.90 ± 0.2 °, 13.06 ± 0.2 °, 14.06 ± 0.2 °, 16.25 ± 0.2 °, 18.37 ± 0.2 °, 19.01 ± 0.2°, 19.75 ± 0.2 °, 20.19 ± 0.2 ° , 21.81 ± 0.2 ° , 23.56 ± 0.2 °, 24.95 ± 0.2 ° , 25.18 ± 0.2 °, 25.63 ± 0.2°, 26.71±0.2°, 27.10±0.2°, 27.91±0.2°, 29.81±0.2°, 32.93±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hydrochloride crystal form E1 of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 6.15±0.2°, 7.66 ± 0.2°, 7.90 ± 0.2°, 8.41 ± 0.2°, 9.49 ± 0.2°, 9.91 ± 0.2°, 10.88 ± 0.2°, 11.42 ± 0.2°, 13.06±0.2°, 13.66±0.2°, 14.06±0.2°, 14.69±0.2°, 15.32±0.2°, 15.52±0.2°, 15.88±0.2°, 16.25±0.2°, 16.81±0.2°, 17.35±0.2°, 18.37±0.2°, 19.01±0.2°, 19.75±0.2°, 20.19±0.2°, 21.15±0.2°, 21.51±0.2°, 21.81±0.2°, 22.50±0.2°, 22.87±0.2°, 23.56±0.2°, 24.95±0.2°, 25.18±0.2°, 25.63±0.2°, 26.71±0.2°, 27.10±0.2°, 27.91±0.2°, 28.47±0.2°, 29.30±0.2°, 29.81±0.2°, 30.12±0.2°, 32.93±0.2°, 34.96±0.2°.

In another preferred embodiment, the hydrochloride crystal form E1 has an X-ray powder diffraction pattern substantially as shown in Figure 38.

In some embodiments of the present invention, the X-ray diffraction (XRPD) pattern of the hydrochloride crystal form E1 of the compound of Formula I-1 is shown in Figure 38.

Table 20 XRPD analysis data for the hydrochloride crystal form E1 of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	6.145037	14.37131	302.5578	499.1663	0.2048961	0.100
Peak # 2	7.657481	11.53586	704.3558	925.7552	0.476999	0.166
Peak # 3	7.895144	11.18912	1359.082	1582.423	0.9203882	0.122
Peak #4	8.406717	10.50935	126.4409	351.9904	0.08562741	0.100
Peak # 5	9.487387	9.314556	269.7384	513.6247	0.1826704	0.100
Peak # 6	9.912072	8.916405	216.5638	468.4002	0.1466598	0.100
Peak # 7	10.87609	8.128153	501.5989	764.5867	0.3396893	0.100
Peak # 8	11.42041	7.741942	388.9748	654.0305	0.2634188	0.103
Peak # 9	13.0554	6.775825	780.8158	1077.419	0.5287787	0.100
Peak # 10	13.66123	6.476674	386.5541	712.326	0.2617795	0.100
Peak # 11	14.05527	6.295974	1337.484	1680.198	0.9057618	0.166
Peak # 12	14.69153	6.024707	287.5207	654.2143	0.1947128	0.174
Peak # 13	15.32495	5.777086	541.0035	927.4278	0.3663747	0.141
Peak # 14	15.51518	5.706679	615.061	1006.604	0.4165273	0.127
Peak # 15	15.88049	5.576216	593.2246	993.5515	0.4017395	0.100
Peak # 16	16.24859	5.45071	1265.391	1673.182	0.8569396	0.100
Peak # 17	16.80916	5.270176	302.3594	718.8266	0.2047618	0.124
Peak # 18	17.3498	5.10715	190.8611	612.6349	0.1292536	0.104
Peak # 19	18.37336	4.824878	1145.505	1605.355	0.7757506	0.100
Peak # 20	19.00938	4.664856	933.6566	1421.984	0.6322845	0.121

Peak # 21	19.75294	4.490902	1276.167	1792.503	0.8642372	0.143
Peak # 22	20.1886	4.394964	1476.64	2006.738	1	0.108
Peak # 23	21.1496	4.197384	506.0891	1059.635	0.3427301	0.132
Peak # 24	21.51016	4.127835	703.582	1263.474	0.4764749	0.100
Peak # 25	21.80766	4.07219	1196.181	1760.296	0.8100696	0.205
Peak # 26	22.49543	3.949219	424.1585	994.5509	0.2872457	0.245
Peak # 27	22.87291	3.884891	627.939	1199.706	0.4252485	0.100
Peak # 28	23.56058	3.773034	1049.806	1620.304	0.7109421	0.109
Peak # 29	24.94623	3.566509	489.7659	1058.782	0.3316759	0.205
Peak # 30	25.18339	3.533457	337.6172	908.0272	0.2286388	0.210
Peak # 31	25.63268	3.472533	183.0638	754.5255	0.1239732	0.135
Peak # 32	26.70567	3.335397	778.4288	1371.446	0.5271622	0.163
Peak # 33	27.10295	3.2874	496.8693	1098.879	0.3364864	0.226
Peak # 34	27.90941	3.194215	564.1411	1179.394	0.3820437	0.137
Peak # 35	28.46869	3.132721	384.4941	1004.999	0.2603845	0.167
Peak # 36	29.30478	3.045216	189.4714	811.8213	0.1283125	0.284
Peak # 37	29.81338	2.994414	368.8845	988.831	0.2498134	0.244
Peak # 38	30.11576	2.965034	245.5084	862.7616	0.1662615	0.309
Peak # 39	32.93307	2.717536	268.7507	882.8731	0.1820015	0.168
Peak # 40	34.95511	2.564826	179.9061	751.8131	0.1218347	0.133

In some embodiments of the present invention, the hydrochloride crystal form E1 of the compound of Formula I-1 has the onsets of the endothermic peaks at 13.36°C ± 2°C and 174.06°C ± 2°C in its differential scanning calorimetry (DSC) curve, and decomposition of the sample begins at 211.29°C ± 2°C.

In another preferred embodiment, the hydrochloride crystal form E1 has a differential scanning calorimetry pattern substantially as shown in Figure 39.

In some embodiments of the present invention, the DSC pattern of the hydrochloride crystal form E1 of the compound of Formula I-1 is shown in Figure 39.

In some embodiments of the present invention, the hydrochloride crystal form E1 of the compound of Formula I-1 has three weight loss steps at 25.81°C ± 2°C, 120.00°C ± 2°C, and 160.00°C ± 2°C in its thermogravimetric analysis (TGA) curve.

In another preferred embodiment, the hydrochloride crystal form E1 has a thermogravimetric analysis pattern substantially as shown in Figure 40.

In some embodiments of the present invention, the TGA pattern of the hydrochloride crystal form E1 of the compound of Formula I-1 is shown in Figure 40.

The present invention also provides a method for preparing the hydrochloride crystal form E1 of the compound of Formula I-1, comprising adding the compound of Formula I-1 and hydrochloric acid to ethanol, and then performing recrystallization or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to hydrochloric acid is selected from 0.8 to 1.2, and the hydrochloride crystal form E1 of the compound of Formula I-1 is a hydrate crystal form with a water content of 1.7 equivalents.

In another preferred embodiment, the hydrochloride crystal form E1 of the compound of

formula (I) is a hydrate crystal form, wherein the water content is 0.5 to 4 equivalents.

The present invention also provides the hydrochloride crystal form E2 of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 7.88±0.2°, 10.90±0.2°, 13.10±0.2°, 14.14±0.2°, 16.30±0.2°, 19.01±0.2°, 19.75±0.2°, 21.54±0.2°, 21.84±0.2°, 23.63±0.2°, 24.96±0.2°, 26.78±0.2°, 29.91±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hydrochloride crystal form E2 of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 7.88±0.2°, 9.51±0.2°, 10.90±0.2°, 11.49 ± 0.2°, 13.10 ± 0.2°, 13.64 ± 0.2 ° , 14.14 ± 0.2°, 14.76 ± 0.2°, 15.39 ± 0.2°, 15.75 ± 0.2°, 16.30±0.2°, 16.93±0.2°, 19.01±0.2°, 19.75±0.2°, 20.69±0.2°, 21.54±0.2°, 21.84±0.2°, 22.19±0.2°, 22.57±0.2°, 23.01±0.2°, 23.63±0.2°, 24.96±0.2°, 25.90±0.2°, 26.32±0.2°, 26.78±0.2°, 27.19±0.2°, 27.48±0.2°, 27.94±0.2°, 28.68±0.2°, 29.07±0.2°, 29.50±0.2°, 29.91±0.2°, 31.74±0.2°, 32.96±0.2°, 33.66±0.2°.

In another preferred embodiment, the hydrochloride crystal form E2 has an X-ray powder diffraction pattern substantially as shown in Figure 41.

In some embodiments of the present invention, the X-ray diffraction (XRPD) pattern of the hydrochloride crystal form E2 of the compound of Formula I-1 is shown in Figure 41.

Table 21 XRPD analysis data for the hydrochloride crystal form E2 of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	7.884071	11.20481	540.4462	605.2851	0.7774932	0.100
Peak # 2	9.512653	9.289872	103.279	168.8765	0.1485786	0.100
Peak # 3	10.89717	8.112479	210.551	276.9264	0.3029015	0.100
Peak # 4	11.48909	7.695814	43.11554	110.4364	0.0620266	0.100
Peak # 5	13.10177	6.75195	192.5077	264.6825	0.2769442	0.100
Peak # 6	13.63865	6.487342	77.58062	155.1348	0.1116085	0.100
Peak # 7	14.13521	6.260545	695.1138	775.9518	1	0.100
Peak # 8	14.76314	5.995642	28.98997	111.9226	0.04170537	0.133
Peak # 9	15.39103	5.752432	33.00134	117.8404	0.04747616	0.121
Peak # 10	15.74691	5.623217	62.01804	146.7878	0.08921998	0.100
Peak # 11	16.30386	5.432357	432.7301	515.7111	0.6225314	0.100
Peak # 12	16.92825	5.233366	61.63427	140.1845	0.08866789	0.100
Peak # 13	19.01114	4.664429	210.1703	287.2018	0.3023539	0.115
Peak # 14	19.75051	4.49145	445.9855	532.7929	0.6416007	0.109
Peak # 15	20.69488	4.288574	111.2609	205.316	0.1600614	0.100
Peak # 16	21.54478	4.12128	168.5169	267.2058	0.2424307	0.360
Peak # 17	21.84486	4.06534	251.1638	351.1669	0.3613276	0.271
Peak # 18	22.19098	4.002708	154.7814	255.5625	0.2226706	0.100
Peak # 19	22.57326	3.935779	98.63	199.3557	0.1418904	0.148
Peak # 20	23.01374	3.861435	105.6459	205.1103	0.1519836	0.100

Peak # 21	23.62687	3.762597	325.2303	420.8155	0.4678806	0.106
Peak # 22	24.95749	3.564925	196.3293	294.1708	0.282442	0.100
Peak # 23	25.89573	3.437852	40.57758	148.8828	0.05837544	0.163
Peak # 24	26.32397	3.382887	50.33425	163.4267	0.07241153	0.100
Peak # 25	26.7799	3.326319	265.6382	383.6885	0.3821507	0.118
Peak # 26	27.19104	3.276951	182.0309	303.3774	0.261872	0.349
Peak # 27	27.47843	3.243327	83.98383	206.9736	0.1208203	0.100
Peak # 28	27.9352	3.191324	112.1196	236.6009	0.1612967	0.196
Peak # 29	28.68201	3.109905	100.0596	224.0822	0.1439471	0.191
Peak # 30	29.06967	3.069308	59.76442	182.13	0.0859779	0.187
Peak # 31	29.50209	3.025297	98.35264	217.703	0.1414914	0.100
Peak # 32	29.90704	2.98525	144.627	260.0349	0.2080623	0.120
Peak # 33	31.74403	2.816562	90.48898	199.877	0.1301787	0.130
Peak # 34	32.95559	2.71573	84.64176	195.0735	0.1217668	0.157
Peak # 35	33.65558	2.66083	72.07199	181.9605	0.1036837	0.165

In some embodiments of the present invention, the hydrochloride crystal form E2 of the compound of Formula I-1 has the onsets of the endothermic peaks at 14.99°C ± 2°C and 174.19°C ± 2°C in its differential scanning calorimetry (DSC) curve, and decomposition of the sample begins at 213.17°C ± 2°C.

In another preferred embodiment, the hydrochloride crystal form E2 has a differential scanning calorimetry pattern substantially as shown in Figure 42.

In some embodiments of the present invention, the DSC pattern of the hydrochloride crystal form E2 of the compound of Formula I-1 is shown in Figure 42.

In some embodiments of the present invention, the hydrochloride crystal form E2 of the compound of Formula I-1 has three weight loss steps at 33.18°C ± 2°C, 90.00°C ± 2°C, and 140.00°C ± 2°C in its thermogravimetric analysis (TGA) curve.

In another preferred embodiment, the hydrochloride crystal form E2 has a thermogravimetric analysis pattern substantially as shown in Figure 43.

In some embodiments of the present invention, the TGA pattern of the hydrochloride crystal form E2 of the compound of Formula I-1 is shown in Figure 43.

The present invention also provides a method for preparing the hydrochloride crystal form E2 of the compound of Formula I-1, comprising drying the hydrochloride crystal form F of the compound of Formula I-1 under vacuum at 25°C, 50°C, or 100°C, wherein the ratio of the compound of Formula I-1 to hydrochloric acid is selected from 0.8 to 1.2, and the hydrochloride crystal form E2 of the compound of Formula I-1 is a hydrate crystal form with a water content of 1.8 equivalents.

In another preferred embodiment, the hydrochloride crystal form E2 of the compound of formula (I) is prepared by subjecting the hydrochloride crystal form F of the compound of formula (I) to vacuum at 10°C to 70°C.

In another preferred embodiment, the hydrochloride crystal form E2 of the compound of formula (I) is prepared by drying the hydrochloride crystal form F of the compound of formula (I) at 80°C to 120°C.

In another preferred embodiment, the hydrochloride crystal form E2 of the compound of formula (I) is a hydrate crystal form, wherein the water content is 0.5 to 4 equivalents.

The present invention also provides the hydrochloride crystal form F of the compound

of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 7.65 ± 0.2°, 11.47 ± 0.2 °, 13.93 ± 0.2°, 14.80 ± 0.2°, 15.25 ± 0.2 °, 19.84 ± 0.2 °, 20.09 ± 0.2°, 21.51 ± 0.2 °, 23.22 ± 0.2 °, 25.06 ± 0.2 °, 26.68 ± 0.2 ° , 28.87 ± 0.2 °, 32.45 ± 0.2°, 33.59 ± 0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hydrochloride crystal form F of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 6.85±0.2°, 7.65±0.2°, 10.21±0.2°, 10.70±0.2°, 11.47±0.2°, 13.93±0.2°, 14.80±0.2°, 15.25±0.2°, 16.60±0.2°, 16.88±0.2°, 17.84±0.2°, 19.00±0.2°, 19.16±0.2°, 19.84±0.2°, 20.09±0.2°, 20.34±0.2°, 21.51±0.2°, 22.35±0.2°, 23.22±0.2°, 23.86±0.2°, 25.06±0.2°, 25.31±0.2°, 25.63±0.2°, 26.68±0.2°, 28.10±0.2°, 28.87±0.2°, 30.53±0.2°, 32.45±0.2°, 33.59±0.2°.

In another preferred embodiment, the hydrochloride crystal form F has an X-ray powder diffraction pattern substantially as shown in Figure 44.

In some embodiments of the present invention, the X-ray powder diffraction (XRPD) pattern of the hydrochloride crystal form F of the compound of Formula I-1 is shown in Figure 44.

Table 22 XRPD analysis data for the hydrochloride crystal form F of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	6.848274	12.89704	50.41388	108.1367	0.09768955	0.100
Peak # 2	7.651177	11.54535	516.0621	576.032	1	0.100
Peak # 3	10.20579	8.660445	49.75304	111.4053	0.096409	0.100
Peak # 4	10.70466	8.257937	69.10229	130.8267	0.133903	0.100
Peak #5	11.47234	7.707018	361.2969	420.3412	0.7001035	0.100
Peak # 6	13.93093	6.351884	397.6063	461.8362	0.7704621	0.100
Peak # 7	14.80051	5.98059	260.9636	327.9683	0.5056826	0.100
Peak # 8	15.25096	5.804945	153.9308	220.6624	0.2982796	0.108
Peak # 9	16.60372	5.334918	34.92417	97.03252	0.06767435	0.155
Peak # 10	16.88418	5.246928	60.09497	120.1826	0.1164491	0.183
Peak # 11	17.83583	4.969059	73.02078	128.1677	0.1414961	0.100
Peak # 12	19.00091	4.666917	115.9687	180.328	0.2247185	0.128
Peak # 13	19.16145	4.628178	78.67841	145.1145	0.1524592	0.128
Peak # 14	19.83859	4.471706	220.5375	294.1044	0.4273469	0.172
Peak # 15	20.08921	4.416483	227.1443	302.6826	0.440149	0.184
Peak # 16	20.34485	4.361562	44.52192	121.6991	0.0862724	0.197
Peak # 17	21.51468	4.126979	342.1507	422.0398	0.6630028	0.116
Peak # 18	22.35365	3.973946	135.1561	215.3622	0.2618989	0.110
Peak # 19	23.22226	3.827231	214.9216	298.199	0.4164645	0.154
Peak # 20	23.85788	3.726686	87.52694	170.3065	0.1696054	0.210
Peak # 21	25.06488	3.549895	214.0289	298.1458	0.4147348	0.168
Peak # 22	25.30611	3.516599	90.23993	175.521	0.1748625	0.178

Peak # 23	25.63199	3.472623	125.4472	211.7709	0.2430855	0.106
Peak # 24	26.68101	3.338423	102.6051	191.2798	0.1988232	0.141
Peak # 25	28.09525	3.173506	86.42886	182.8679	0.1674776	0.175
Peak # 26	28.86665	3.090432	110.8668	209.6979	0.2148323	0.144
Peak # 27	30.53301	2.925459	35.61448	133.7473	0.069012	0.100
Peak # 28	32.44866	2.756991	82.21487	181.7001	0.159312	0.123
Peak # 29	33.58943	2.665919	45.26086	135.2353	0.08770428	0.196

In some embodiments of the present invention, the hydrochloride crystal form F of the compound of Formula I-1 has the onsets of the endothermic peaks at 36.03°C ± 2°C and 172.45°C ± 2°C in its differential scanning calorimetry (DSC) curve, and decomposition of the sample begins at 212.66°C ± 2°C.

In another preferred embodiment, the hydrochloride crystal form F has a differential scanning calorimetry pattern substantially as shown in Figure 45.

In some embodiments of the present invention, the DSC pattern of the hydrochloride crystal form F of the compound of Formula I-1 is shown in Figure 45.

In some embodiments of the present invention, the hydrochloride crystal form F of the compound of Formula I-1 has three weight loss steps at 33.35°C ± 2°C, 100.00°C ± 2°C, and 150.00°C ± 2°C in its thermogravimetric analysis (TGA) curve.

In another preferred embodiment, the hydrochloride crystal form F has a thermogravimetric analysis pattern substantially as shown in Figure 46.

In some embodiments of the present invention, the TGA pattern of the hydrochloride crystal form F of the compound of Formula I-1 is shown in Figure 46.

The present invention also provides a method for preparing the hydrochloride crystal form F of the compound of Formula I-1, comprising adding the compound of Formula I-1 and hydrochloric acid to ethanol, acetone, ethyl acetate, acetonitrile, tetrahydrofuran, or a mixed solvent of methyl isobutyl ketone/trifluoroethanol, and then performing recrystallization at 50°C or slurrying to obtain it, the ratio of the compound of Formula I-1 to hydrochloric acid is selected from 0.8 to 1.2, the hydrochloride crystal form F of the compound of Formula I-1 is a hydrate crystal form with a water content of 2.0 equivalents.

In another preferred embodiment, the hydrochloride crystal form F of the compound of formula (I) is a hydrate crystal form, wherein the water content is 1 to 4 equivalents.

The present invention also provides the hydrochloride crystal form G of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 5.83±0.2°, 9.97±0.2°, 13.26±0.2°, 14.17±0.2°, 15.52±0.2°, 16.77±0.2°, 18.37±0.2°, 20.27±0.2°, 20.48±0.2°, 21.35±0.2°, 21.82±0.2°, 22.65±0.2°, 23.04±0.2°, 24.43±0.2°, 26.24±0.2°, 26.54±0.2°, 28.94±0.2°, 30.18±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hydrochloride crystal form G of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 5.83±0.2°, 7.18±0.2°, 9.97±0.2°, 11.63±0.2°, 12.00±0.2°, 12.35±0.2°, 13.26±0.2°, 13.58±0.2°, 14.17±0.2°, 14.60±0.2°, 15.52±0.2°, 16.77±0.2°, 17.64±0.2°, 18.37±0.2°, 18.81±0.2°, 19.14±0.2°, 19.80±0.2°, 20.27±0.2°, 20.48±0.2°, 21.35±0.2°, 21.82±0.2°, 22.65±0.2°, 23.04±0.2°, 23.35±0.2°, 24.43±0.2°, 25.47±0.2°, 26.24±0.2°, 26.54±0.2°, 26.84±0.2°, 27.92±0.2°, 28.94±0.2°, 29.31±0.2°, 30.18±0.2°.

In another preferred embodiment, the hydrochloride crystal form G has an X-ray powder diffraction pattern substantially as shown in Figure 47.

In some embodiments of the present invention, the X-ray powder diffraction (XRPD) pattern of the hydrochloride crystal form G of the compound of Formula I-1 is shown in Figure 47.

Table 23 XRPD analysis data for the hydrochloride crystal form G of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	5.828182	15.15189	579.1664	753.4305	0.6023378	0.100
Peak # 2	7.17844	12.30457	172.8027	365.0822	0.1797163	0.100
Peak # 3	9.974504	8.860736	346.1045	556.5733	0.3599515	0.100
Peak # 4	11.62806	7.604156	506.9125	722.6564	0.5271932	0.100
Peak # 5	11.99626	7.371572	122.0042	338.9887	0.1268854	0.100
Peak # 6	12.34862	7.162008	128.8925	346.0245	0.1340493	0.171
Peak # 7	13.25774	6.672863	324.0526	556.4399	0.3370174	0.153
Peak # 8	13.58265	6.513966	171.4265	412.3184	0.178285	0.100
Peak # 9	14.16958	6.245436	598.4322	852.499	0.6223745	0.111
Peak # 10	14.59519	6.064257	283.763	545.6206	0.2951159	0.100
Peak # 11	15.51762	5.705785	961.5308	1251.04	1	0.100
Peak # 12	16.7697	5.282487	931.9397	1272.279	0.969225	0.205
Peak # 13	17.63585	5.024953	178.8619	547.5662	0.1860179	0.140
Peak # 14	18.37159	4.825339	771.5197	1159.492	0.8023869	0.116
Peak # 15	18.80623	4.714787	372.962	770.2344	0.3878836	0.100
Peak # 16	19.1386	4.633651	288.6279	691.9684	0.3001754	0.100
Peak # 17	19.80226	4.479828	214.2406	626.9946	0.222812	0.100
Peak # 18	20.26602	4.378349	301.9755	719.1638	0.314057	0.247
Peak # 19	20.48124	4.332824	436.0151	854.6628	0.4534594	0.221
Peak # 20	21.35452	4.157567	768.4391	1191.466	0.7991831	0.193
Peak # 21	21.8184	4.07021	387.7249	811.9121	0.4032371	0.121
Peak # 22	22.64517	3.923443	357.5557	779.4445	0.371861	0.137
Peak # 23	23.04393	3.856443	885.9234	1304.702	0.9213678	0.100
Peak # 24	23.34855	3.806815	376.3249	791.8521	0.391381	0.259
Peak # 25	24.42592	3.641291	722.9464	1152.347	0.7518703	0.191
Peak # 26	25.47185	3.494093	192.4108	637.1698	0.2001088	0.250
Peak # 27	26.2382	3.393751	388.4084	838.7321	0.4039479	0.112
Peak # 28	26.53974	3.355873	427.7524	878.9491	0.444866	0.256
Peak #29	26.83974	3.319039	219.5827	670.9071	0.2283678	0.233
Peak # 30	27.92213	3.192788	126.4753	572.1395	0.1315354	0.191
Peak # 31	28.94164	3.082595	395.4236	826.9805	0.4112438	0.119
Peak # 32	29.31307	3.044374	215.0207	639.3233	0.2236233	0.100

Peak # 33	30.18123	2.958751	262.0633	665.0064	0.272548	0.174

In some embodiments of the present invention, the hydrochloride crystal form G of the compound of Formula I-1 has the onsets of the endothermic peaks at 59.42°C ± 2°C, 151.02°C ± 2°C, and 166.01°C ± 2°C in its differential scanning calorimetry (DSC) curve.

In another preferred embodiment, the hydrochloride crystal form G has a differential scanning calorimetry pattern substantially as shown in Figure 48.

In some embodiments of the present invention, the DSC pattern of the hydrochloride crystal form G of the compound of Formula I-1 is shown in Figure 48.

In some embodiments of the present invention, the hydrochloride crystal form G of the compound of Formula I-1 has three weight loss steps at 26.28°C ± 2°C, 120.00°C ± 2°C, and 150.00°C ± 2°C in its thermogravimetric analysis (TGA) curve.

In another preferred embodiment, the hydrochloride crystal form G has a thermogravimetric analysis pattern substantially as shown in Figure 49.

In some embodiments of the present invention, the TGA pattern of the hydrochloride crystal form G of the compound of Formula I-1 is shown in Figure 49.

The present invention also provides a method for preparing the hydrochloride crystal form G of the compound of Formula I-1, comprising adding the compound of Formula I-1 and hydrochloric acid to water, and then performing suspension recrystallization at 25°C, 50°C, or under heating-cooling cycles or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to hydrochloric acid is selected from 0.8 to 1.2, the hydrochloride crystal form G of the compound of Formula I-1 is a hydrate crystal form with a water content of 3.0 equivalents.

In another preferred embodiment, the hydrochloride crystal form G of the compound of formula (I) is a hydrate crystal form, wherein the water content is 1.0 to 6 equivalents.

The present invention also provides the hydrochloride crystal form H of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 5.83±0.2°, 7.16±0.2°, 10.02±0.2°, 11.64±0.2°, 13.23 ± 0.2 °, 14.58 ± 0.2°, 16.67 ± 0.2°, 18.40 ± 0.2°, 18.62 ± 0.2°, 20.23 ± 0.2°, 20.54 ± 0.2°, 21.40±0.2°, 22.62±0.2°, 22.78±0.2°, 23.36±0.2°, 24.73±0.2°, 26.23±0.2°, 26.57±0.2°, 26.91±0.2°, 29.30±0.2°, 30.21±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hydrochloride crystal form H of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 5.83±0.2°, 7.16±0.2°, 10.02±0.2°, 11.64±0.2°, 12.35 ± 0.2°, 13.23 ± 0.2°, 13.59 ± 0.2°, 14.58 ± 0.2°, 15.51 ± 0.2°, 15.97 ± 0.2°, 16.67±0.2°, 17.63±0.2°, 18.40±0.2°, 18.62±0.2°, 19.11±0.2°, 20.23±0.2°, 20.54±0.2°, 21.40±0.2°, 22.07±0.2°, 22.62±0.2°, 22.78±0.2°, 23.36±0.2°, 24.73±0.2°, 24.98±0.2°, 26.23±0.2°, 26.57±0.2°, 26.91±0.2°, 27.88±0.2°, 29.01±0.2°, 29.30±0.2°, 29.61±0.2°, 30.21±0.2°, 31.21±0.2°, 32.12±0.2°, 34.66±0.2°.

In another preferred embodiment, the hydrochloride crystal form H has an X-ray powder diffraction pattern substantially as shown in Figure 50.

In some embodiments of the present invention, the X-ray powder diffraction (XRPD) pattern of the hydrochloride crystal form H of the compound of Formula I-1 is shown in Figure 50.

Table 24 XRPD analysis data for the hydrochloride crystal form H of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	5.830629	15.14553	1285.098	1470.157	1	0.100
Peak # 2	7.162398	12.3321	377.9528	573.1634	0.2941044	0.100

Peak # 3	10.01798	8.822379	706.8278	901.1703	0.5500187	0.100
Peak # 4	11.6369	7.598398	793.7754	997.5475	0.6176772	0.100
Peak #5	12.34503	7.164086	105.4623	314.7852	0.0820656	0.100
Peak # 6	13.23145	6.686064	823.9066	1041.888	0.6411238	0.100
Peak # 7	13.59459	6.508269	401.2484	621.5343	0.3122319	0.100
Peak # 8	14.57996	6.070556	742.7775	974.6781	0.5779932	0.100
Peak # 9	15.50704	5.709655	380.8936	631.5181	0.2963928	0.100
Peak # 10	15.97407	5.543761	171.5876	429.1406	0.133521	0.155
Peak # 11	16.6685	5.31433	1043.568	1307.615	0.8120532	0.105
Peak # 12	17.62552	5.027874	219.7633	491.7105	0.171009	0.216
Peak # 13	18.40211	4.817406	1027.482	1307.842	0.7995363	0.141
Peak # 14	18.61999	4.761522	548.1824	829.8808	0.4265687	0.141
Peak # 15	19.11054	4.640391	363.7106	646.7841	0.2830218	0.183
Peak # 16	20.23249	4.385529	650.7493	943.71	0.5063812	0.111
Peak # 17	20.54409	4.31971	816.0809	1113.529	0.6350342	0.201
Peak # 18	21.40318	4.148226	761.1138	1066.179	0.5922615	0.170
Peak # 19	22.07037	4.024309	60.53448	366.7205	0.04710497	0.100
Peak # 20	22.62083	3.927608	474.4857	778.4302	0.3692215	0.202
Peak # 21	22.77518	3.90134	428.924	731.7242	0.3337676	0.202
Peak # 22	23.35825	3.805256	580.0465	876.5105	0.4513638	0.100
Peak # 23	24.73165	3.596966	435.214	762.8337	0.3386622	0.164
Peak # 24	24.97894	3.561912	239.3857	574.4449	0.1862782	0.170
Peak # 25	26.23346	3.394353	689.8587	1053.781	0.5368143	0.200
Peak # 26	26.56802	3.352364	373.9151	743.0274	0.2909624	0.141
Peak # 27	26.91138	3.310365	474.4957	847.8385	0.3692293	0.233
Peak # 28	27.87534	3.198041	319.8667	699.1384	0.2489046	0.100
Peak #29	29.00736	3.075759	319.4596	694.5037	0.2485878	0.100
Peak # 30	29.30335	3.045362	580.9927	952.9413	0.4521	0.139
Peak # 31	29.61104	3.014414	311.5282	679.3771	0.242416	0.100
Peak # 32	30.20776	2.956213	486.7111	844.0698	0.3787347	0.169
Peak # 33	31.21426	2.863146	132.2233	464.1539	0.1028897	0.149
Peak # 34	32.11699	2.784701	156.8051	469.2422	0.122018	0.137
Peak # 35	34.65822	2.586115	156.4141	451.3805	0.1217138	0.157

In some embodiments of the present invention, the hydrochloride crystal form H of the compound of Formula I-1 has the onsets of the endothermic peaks at 51.49°C ± 2°C and 153.61°C ± 2°C in its differential scanning calorimetry (DSC) curve, and decomposition of

the sample begins at 211.73°C ± 2°C.

In another preferred embodiment, the hydrochloride crystal form H has a differential scanning calorimetry pattern substantially as shown in Figure 51.

In some embodiments of the present invention, the DSC pattern of the hydrochloride crystal form H of the compound of Formula I-1 is shown in Figure 51.

In some embodiments of the present invention, the hydrochloride crystal form H of the compound of Formula I-1 has three weight loss steps at 26.12°C ± 2°C, 110.00°C ± 2°C, and 150.00°C ± 2°C in its thermogravimetric analysis (TGA) curve.

In another preferred embodiment, the hydrochloride crystal form H has a thermogravimetric analysis pattern substantially as shown in Figure 52.

In some embodiments of the present invention, the TGA pattern of the hydrochloride crystal form H of the compound of Formula I-1 is shown in Figure 52.

The present invention also provides a method for preparing the hydrochloride crystal form H of the compound of Formula I-1, comprising adding the compound of Formula I-1 and hydrochloric acid to a methanol/water mixed solvent, and then performing suspension recrystallization at 25°C or 50°C or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to hydrochloric acid is selected from 0.8 to 1.2, the hydrochloride crystal form H of the compound of Formula I-1 is a hydrate crystal form, with a water content of 3.9 equivalents.

In another preferred embodiment, the hydrochloride crystal form H of the compound of formula (I) is a hydrate crystal form, wherein the water content is 2 to 8 equivalents.

The present invention also provides the hydrochloride crystal form I of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 6.68±0.2°, 12.31±0.2°, 12.54 ± 0.2°, 13.34 ± 0.2°, 14.05 ± 0.2°, 14.96 ± 0.2°, 17.92 ± 0.2 °, 19.03 ± 0.2°, 19.74 ± 0.2°, 19.99 ± 0.2°, 20.96 ± 0.2°, 21.42 ± 0.2°, 21.62 ± 0.2°, 26.81±0.2°, 27.21±0.2°, 27.60±0.2°, 27.78±0.2°, 30.07±0.2°, 31.00±0.2°, 34.83±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hydrochloride crystal form I of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 6.68±0.2°, 9.50±0.2°, 12.31±0.2°, 12.54 ± 0.2°, 13.34 ± 0.2°, 14.05 ± 0.2°, 14.96 ± 0.2°, 15.38 ± 0.2°, 17.18 ± 0.2°, 17.92±0.2°, 19.03±0.2°, 19.74±0.2°, 19.99±0.2°, 20.96±0.2°, 21.42±0.2°, 21.62±0.2°, 21.99±0.2°, 22.98±0.2°, 23.52±0.2°, 23.80±0.2°, 24.38±0.2°, 25.92±0.2°, 26.81±0.2°, 27.21±0.2°, 27.60±0.2°, 27.78±0.2°, 28.26±0.2°, 28.74±0.2°, 30.07±0.2°, 31.00±0.2°, 32.69±0.2°, 34.02±0.2°, 34.83±0.2°.

In another preferred embodiment, the hydrochloride crystal form I has an X-ray powder diffraction pattern substantially as shown in Figure 53.

In some embodiments of the present invention, the X-ray diffraction (XRPD) pattern of the hydrochloride crystal form I of the compound of Formula I-1 is shown in Figure 53.

Table 25 XRPD analysis data for the hydrochloride crystal form I of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	6.683047	13.21552	6066.766	6257.472	1	0.100
Peak # 2	9.502496	9.29978	589.4446	779.7198	0.09715961	0.100
Peak # 3	12.30501	7.187298	1473.677	1683.435	0.2429098	0.123
Peak # 4	12.54249	7.05174	1045.291	1257.185	0.1722979	0.127
Peak # 5	13.34207	6.630879	3563.501	3783.915	0.5873806	0.100
Peak # 6	14.04679	6.299753	1592.864	1818.627	0.2625557	0.100
Peak # 7	14.95737	5.918223	1689.783	1912.131	0.2785311	0.100

Peak # 8	15.37841	5.757124	366.1042	582.8315	0.06034585	0.100
Peak # 9	17.17957	5.157372	679.5376	900.721	0.1120099	0.100
Peak # 10	17.91742	4.946615	2463.704	2704.65	0.4060984	0.100
Peak # 11	19.02736	4.66049	1726.037	1982.815	0.2845069	0.100
Peak # 12	19.74237	4.493283	1203.647	1471.858	0.1984002	0.192
Peak # 13	19.98544	4.43918	1433.109	1702.924	0.2362228	0.173
Peak # 14	20.96464	4.233996	1457.9	1735.907	0.2403092	0.100
Peak # 15	21.42234	4.144559	5250.236	5529.593	0.8654093	0.100
Peak # 16	21.61991	4.107128	1554.836	1833.5	0.2562874	0.100
Peak # 17	21.98783	4.039227	591.0263	866.3695	0.09742032	0.100
Peak # 18	22.98335	3.866472	515.3694	786.2349	0.0849496	0.100
Peak # 19	23.52402	3.778814	255.2394	529.0739	0.04207174	0.166
Peak # 20	23.80309	3.735139	274.9154	548.0394	0.04531498	0.232
Peak # 21	24.38212	3.647733	666.5188	933.2823	0.1098639	0.116
Peak # 22	25.92394	3.434175	635.7052	928.6979	0.1047848	0.117
Peak # 23	26.81065	3.322574	1095.841	1412.559	0.1806302	0.100
Peak # 24	27.2072	3.275041	877.7557	1200.082	0.1446826	0.117
Peak # 25	27.60325	3.228944	689.9982	1014.847	0.1137341	0.134
Peak # 26	27.77863	3.208954	1194.642	1519.628	0.1969159	0.134
Peak # 27	28.25596	3.155821	372.9469	695.2362	0.06147375	0.100
Peak # 28	28.7368	3.1041	304.8406	620.1004	0.05024763	0.100
Peak #29	30.06931	2.969508	807.1132	1116.959	0.1330384	0.171
Peak # 30	30.99668	2.882746	682.3029	984.0446	0.1124657	0.100
Peak # 31	32.68733	2.737403	496.4317	815.9324	0.08182806	0.100
Peak # 32	34.01857	2.633264	468.1613	783.8876	0.07716818	0.178
Peak # 33	34.83157	2.57364	645.0126	947.0595	0.106319	0.108

In some embodiments of the present invention, the hydrochloride crystal form I of the compound of Formula I-1 has the onsets of the endothermic peaks at 18.15°C ± 2°C and 194.49°C ± 2°C in its differential scanning calorimetry (DSC) curve, and decomposition of the sample begins at 215.51°C ± 2°C

In another preferred embodiment, the hydrochloride crystal form I has a differential scanning calorimetry pattern substantially as shown in Figure 54.

In some embodiments of the present invention, the DSC pattern of the hydrochloride crystal form I of the compound of Formula I-1 is shown in Figure 54.

In some embodiments of the present invention, the hydrochloride crystal form I of the compound of Formula I-1 has three weight loss steps at 28.31°C ± 2°C, 70.00°C ± 2°C, and 173.00°C ± 2°C in its thermogravimetric analysis (TGA) curve.

In another preferred embodiment, the hydrochloride crystal form I has a thermogravimetric analysis pattern substantially as shown in Figure 55.

In some embodiments of the present invention, the TGA pattern of the hydrochloride crystal form I of the compound of Formula I-1 is shown in Figure 55.

The present invention also provides a method for preparing the hydrochloride crystal form I of the compound of Formula I-1, comprising adding the compound of Formula I-1 and hydrochloric acid to methanol or a methanol/tert-butyl methyl ether mixed solvent, and then performing suspension recrystallization in a tert-butyl methyl ether or slurrying to obtain it, the ratio of the compound of Formula I-1 to hydrochloric acid is selected from 0.8 to 1.2, and the hydrochloride crystal form I of the compound of Formula I-1 is an anhydrous crystal form.

In another preferred embodiment, the hydrochloride crystal form I of the compound of formula (I) is an anhydrous crystal form.

The present invention also provides the hydrochloride crystal form J1 of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 6.80 ± 0.2°, 11.69 ± 0.2°, 14.87 ± 0.2°, 15.98 ± 0.2°, 18.05±0.2°, 19.49±0.2°, 20.41±0.2°, 21.55±0.2°, 21.70±0.2°, 22.06±0.2°, 23.69±0.2°, 24.92±0.2°, 25.13±0.2°, 29.07±0.2°, 30.16±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hydrochloride crystal form J1 of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 6.80±0.2°, 7.82±0.2°, 7.95±0.2°, 10.08±0.2°, 11.69 ± 0.2°, 12.30 ± 0.2°, 12.60 ± 0.2°, 13.60 ± 0.2°, 14.87 ± 0.2°, 15.98 ± 0.2°, 16.25 ± 0.2°, 18.05±0.2°, 18.60±0.2°, 18.79±0.2°, 19.49±0.2°, 20.41±0.2°, 20.82±0.2°, 21.55±0.2°, 21.70±0.2°, 22.06±0.2°, 22.88±0.2°, 23.69±0.2°, 24.92±0.2°, 25.13±0.2°, 26.19±0.2°, 26.57±0.2°, 29.07±0.2°, 30.16±0.2°, 31.85±0.2°, 32.80±0.2°.

In another preferred embodiment, the hydrochloride crystal form J1 has an X-ray powder diffraction pattern substantially as shown in Figure 56.

In some embodiments of the present invention, the X-ray diffraction (XRPD) pattern of the hydrochloride crystal form J1 of the compound of Formula I-1 is shown in Figure 56.

Table 26 XRPD analysis data for the hydrochloride crystal form J1 of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	6.795494	12.99709	1045.542	1237.377	0.3823281	0.100
Peak # 2	7.822898	11.2923	230.3243	429.0735	0.0842237	0.101
Peak # 3	7.947547	11.11546	173.3303	372.1519	0.06338246	0.101
Peak # 4	10.08289	8.765732	113.045	325.6056	0.04133766	0.100
Peak # 5	11.69263	7.562305	581.4788	792.2735	0.212632	0.100
Peak # 6	12.29569	7.192721	271.5138	485.7134	0.09928567	0.160
Peak # 7	12.5974	7.021128	160.1172	374.2798	0.05855079	0.186
Peak # 8	13.6026	6.504458	195.112	411.141	0.07134749	0.100
Peak # 9	14.87382	5.951278	2734.673	2980.22	1	0.100
Peak # 10	15.97916	5.542004	742.0891	1013.763	0.271363	0.100
Peak # 11	16.25086	5.449955	156.1842	432.9994	0.05711259	0.129
Peak # 12	18.05202	4.910034	797.7896	1127.659	0.2917313	0.100
Peak # 13	18.59785	4.767141	489.3123	835.8884	0.178929	0.213
Peak # 14	18.7898	4.718873	408.4137	759.966	0.1493465	0.213

Peak # 15	19.4894	4.55103	554.901	920.6138	0.2029131	0.100
Peak # 16	20.41075	4.347628	1084.362	1459.224	0.3965236	0.100
Peak # 17	20.81767	4.263556	308.0087	683.4725	0.1126309	0.100
Peak # 18	21.55439	4.119464	785.2869	1156.483	0.2871594	0.270
Peak # 19	21.69789	4.092543	917.0377	1286.597	0.3353373	0.270
Peak # 20	22.05619	4.026863	513.4854	877.8127	0.1877685	0.100
Peak # 21	22.87765	3.884097	242.5795	597.0117	0.08870515	0.100
Peak # 22	23.6933	3.752199	965.4345	1321.158	0.3530348	0.100
Peak # 23	24.92196	3.569928	433.7296	789.9819	0.1586039	0.223
Peak # 24	25.13496	3.540156	587.4705	941.8578	0.214823	0.149
Peak # 25	26.18639	3.400348	228.3669	583.2324	0.08350793	0.100
Peak # 26	26.56552	3.352674	207.2965	567.4351	0.07580306	0.127
Peak # 27	29.07455	3.068804	275.8094	631.2031	0.1008565	0.100
Peak # 28	30.16433	2.96037	409.7868	740.9128	0.1498486	0.100
Peak #29	31.851	2.807346	160.3939	484.1836	0.05865197	0.206
Peak # 30	32.79772	2.728441	190.6454	520.0348	0.06971417	0.182

In some embodiments of the present invention, the hydrochloride crystal form J1 of the compound of Formula I-1 has the onsets of the endothermic peaks at 70.82°C ± 2°C and 165.48°C ± 2°C in its differential scanning calorimetry (DSC) curve, and decomposition of the sample begins at 212.96°C ± 2°C.

In another preferred embodiment, the hydrochloride crystal form J1 has a differential scanning calorimetry pattern substantially as shown in Figure 57.

In some embodiments of the present invention, the DSC pattern of the hydrochloride crystal form J1 of the compound of Formula I-1 is shown in Figure 57.

In some embodiments of the present invention, the hydrochloride crystal form J1 of the compound of Formula I-1 has two weight loss steps at 33.94°C ± 2°C and 110.00°C ± 2°C in its thermogravimetric analysis (TGA) curve.

In another preferred embodiment, the hydrochloride crystal form J1 has a thermogravimetric analysis pattern substantially as shown in Figure 58.

In some embodiments of the present invention, the TGA pattern of the hydrochloride crystal form J1 of the compound of Formula I-1 is shown in Figure 58.

The present invention also provides a method for preparing the hydrochloride crystal form J1 of the compound of Formula I-1, comprising adding the compound of Formula I-1 and hydrochloric acid to 2-methyl-tetrahydrofuran, and then performing suspension recrystallization at 50°C or under heating-cooling cycles or slurrying to obtain it, the ratio of the compound of Formula I-1 to hydrochloric acid is selected from 0.8 to 1.2, the hydrochloride crystal form J1 of the compound of Formula I-1 is a solvate of 2-methyl tetrahydrofuran and water, with a 2-methyl tetrahydrofuran content of 0.75 equivalents and a water content of 0.98 equivalents.

In another preferred embodiment, the hydrochloride crystal form J1 of the compound of formula (I) is a solvate of 2-methyl-tetrahydrofuran and water, wherein the content of 2-methyl-tetrahydrofuran is 0.1 to 2 equivalents and the content of water is 0.1 to 2 equivalents.

The present invention also provides the hydrochloride crystal form J2 of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks

at the following 2θ angles: 6.78±0.2°, 11.59±0.2°, 12.24 ± 0.2°, 13.56 ± 0.2°, 14.69 ± 0.2°, 17.45 ± 0.2°, 18.12 ± 0.2°, 18.89 ± 0.2°, 19.51 ± 0.2°, 21.28±0.2°, 21.46±0.2°, 22.23±0.2°, 24.09±0.2°, 24.86±0.2°, 24.99±0.2°, 29.00±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hydrochloride crystal form J2 of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 6.78±0.2°, 7.96±0.2°, 8.31±0.2°, 11.59±0.2°, 12.24 ± 0.2°, 13.56 ± 0.2°, 14.69 ± 0.2 °, 16.44 ± 0.2°, 16.63 ± 0.2°, 17.45 ± 0.2°, 18.12 ± 0.2°, 18.89±0.2°, 19.51±0.2°, 20.12±0.2°, 20.35±0.2°, 20.49±0.2°, 21.28±0.2°, 21.46±0.2°, 22.23±0.2°, 22.75±0.2°, 23.27±0.2°, 24.09±0.2°, 24.86±0.2°, 24.99±0.2°, 25.37±0.2°, 25.65±0.2°, 26.54±0.2°, 27.62±0.2°, 28.61±0.2°, 29.00±0.2°, 30.43±0.2°, 32.10±0.2°, 33.01±0.2°, 36.96±0.2°.

In another preferred embodiment, the hydrochloride crystal form J2 has an X-ray powder diffraction pattern substantially as shown in Figure 59.

In some embodiments of the present invention, the X-ray diffraction (XRPD) pattern of the hydrochloride crystal form J2 of the compound of Formula I-1 is shown in Figure 59.

Table 27 XRPD analysis data for the hydrochloride crystal form J2 of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	6.780673	13.02546	486.214	549.5581	0.2816536	0.100
Peak # 2	7.958976	11.09953	123.6075	188.0724	0.07160323	0.161
Peak # 3	8.310797	10.63043	73.68546	139.4296	0.04268445	0.107
Peak # 4	11.59174	7.627896	375.3433	450.2339	0.2174286	0.100
Peak # 5	12.23828	7.226334	153.1708	226.7464	0.08872864	0.100
Peak # 6	13.55637	6.526536	180.8496	254.4021	0.1047624	0.100
Peak # 7	14.68543	6.027195	1726.283	1805.761	1	0.100
Peak # 8	16.4355	5.389143	215.2298	299.1415	0.1246781	0.184
Peak # 9	16.62825	5.327103	129.1316	213.7627	0.07480326	0.184
Peak # 10	17.44625	5.079131	220.9248	310.6566	0.1279771	0.103
Peak # 11	18.1169	4.892595	133.8183	226.216	0.07751816	0.100
Peak # 12	18.88617	4.695011	516.7839	612.7637	0.2993622	0.100
Peak # 13	19.5106	4.546134	397.7841	496.3569	0.2304281	0.100
Peak # 14	20.11981	4.409835	184.1742	286.9377	0.1066883	0.320
Peak # 15	20.34798	4.360898	241.6843	346.9122	0.1400027	0.238
Peak # 16	20.48667	4.331687	265.6085	372.0766	0.1538615	0.238
Peak # 17	21.28307	4.171363	432.1003	541.9163	0.2503067	0.121
Peak # 18	21.45671	4.137996	276.4566	386.148	0.1601456	0.121
Peak # 19	22.22805	3.996116	497.313	614.4642	0.2880831	0.100
Peak # 20	22.75281	3.905124	142.7566	265.5026	0.08269595	0.156
Peak # 21	23.27106	3.819316	113.8295	241.2689	0.06593904	0.171
Peak # 22	24.09327	3.690806	385.4814	518.8451	0.2233013	0.130
Peak # 23	24.85536	3.579343	212.2231	344.9595	0.1229364	0.175

Peak # 24	24.98804	3.560637	267.8217	399.8474	0.1551436	0.175
Peak # 25	25.3711	3.507738	162.8907	291.8631	0.09435921	0.226
Peak # 26	25.64969	3.470267	130.3427	256.16	0.07550482	0.219
Peak # 27	26.53912	3.355949	103.8878	220.8986	0.06018002	0.100
Peak # 28	27.62185	3.226811	76.33185	194	0.04421745	0.256
Peak #29	28.60708	3.11788	106.999	228.0308	0.06198227	0.100
Peak # 30	29.00274	3.07624	319.7704	443.9528	0.1852363	0.100
Peak # 31	30.42807	2.935309	124.64	247.0201	0.07220139	0.100
Peak # 32	32.10201	2.785966	131.7526	254.2239	0.07632156	0.113
Peak # 33	33.0099	2.711386	81.86591	203.6693	0.04742322	0.136
Peak # 34	36.95634	2.430403	74.8323	193.9958	0.04334879	0.176

In some embodiments of the present invention, the hydrochloride crystal form J2 of the compound of Formula I-1 has the onsets of the endothermic peaks at 77.60°C ± 2°C and 163.47°C ± 2°C in its differential scanning calorimetry (DSC) curve, and decomposition of the sample begins at 211.78°C ± 2°C.

In another preferred embodiment, the hydrochloride crystal form J2 has a differential scanning calorimetry pattern substantially as shown in Figure 60.

In some embodiments of the present invention, the DSC pattern of the hydrochloride crystal form J2 of the compound of Formula I-1 is shown in Figure 60.

In some embodiments of the present invention, the hydrochloride crystal form J2 of the compound of Formula I-1 has two weight loss steps at 28.73°C ± 2°C and 120.00°C ± 2°C in its thermogravimetric analysis (TGA) curve.

In another preferred embodiment, the hydrochloride crystal form J2 has a thermogravimetric analysis pattern substantially as shown in Figure 61.

In some embodiments of the present invention, the TGA pattern of the hydrochloride crystal form J2 of the compound of Formula I-1 is shown in Figure 61.

The present invention also provides a method for preparing the hydrochloride crystal form J2 of the compound of Formula I-1, comprising heating the hydrochloride crystal form J1 of the compound of Formula I-1 to 110°C to obtain it, wherein the ratio of the compound of Formula I-1 to hydrochloric acid is selected from 0.8 to 1.2, the hydrochloride crystal form J2 of the compound of Formula I-1 is a solvate of 2-methyl-tetrahydrofuran and water, with a 2-methyl-tetrahydrofuran content of 0.39 equivalents and a water content of 0.94 equivalents.

In another preferred embodiment, the hydrochloride crystal form J2 of the compound of formula (I) is prepared by heating the hydrochloride crystal form J1 of the compound of formula (I) to 90°C to 130°C.

In another preferred embodiment, the hydrochloride crystal form J2 of the compound of formula (I) is a solvate of 2-methyl-tetrahydrofuran and water, wherein the content of 2-methyl-tetrahydrofuran is 0.2 to 0.8 equivalents and the content of water is 0.5 to 2 equivalents.

The present invention also provides the hydrochloride crystal form K of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 6.79 ± 0.2°, 11.61 ± 0.2°, 14.93 ± 0.2°, 16.08 ± 0.2°, 18.05 ± 0.2°, 18.63 ± 0.2°, 20.49 ± 0.2°, 20.64 ± 0.2°, 21.52 ± 0.2°, 21.72 ± 0.2°, 21.93±0.2°, 23.68±0.2°, 25.19±0.2°, 26.25±0.2°, 26.57±0.2°, 29.91±0.2°, 32.56±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hydrochloride crystal form K of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 6.79±0.2°, 7.83±0.2°, 8.04±0.2°, 10.00±0.2°, 10.74 ± 0.2°, 11.61 ± 0.2°, 12.25 ± 0.2 °, 12.64 ± 0.2°, 13.57 ± 0.2°, 14.93 ± 0.2°, 16.08 ± 0.2°, 18.05±0.2°,

18.63±0.2°, 19.43±0.2°, 20.15±0.2°, 20.49±0.2°, 20.64±0.2°, 21.52±0.2°, 21.72±0.2°, 21.93±0.2°, 23.27±0.2°, 23.68±0.2°, 24.73±0.2°, 25.19±0.2°, 26.25±0.2°, 26.57±0.2°, 27.42±0.2°, 28.02±0.2°, 28.67±0.2°, 29.13±0.2°, 29.91±0.2°, 32.56±0.2°.

In another preferred embodiment, the hydrochloride crystal form K has an X-ray powder diffraction pattern substantially as shown in Figure 62.

In some embodiments of the present invention, the X-ray powder diffraction (XRPD) pattern of the hydrochloride crystal form K of the compound of Formula I-1 is shown in Figure 62.

Table 28 XRPD analysis data for the hydrochloride crystal form K of compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	6.794806	12.9984	691.3811	875.0555	0.192033	0.100
Peak # 2	7.83426	11.27594	288.9213	486.3343	0.08024868	0.120
Peak # 3	8.038795	10.9895	203.2409	403.895	0.05645072	0.120
Peak # 4	9.997069	8.840785	117.7202	330.8371	0.03269712	0.100
Peak # 5	10.74072	8.230294	107.3294	320.8759	0.02981103	0.100
Peak # 6	11.60559	7.618825	687.957	909.0914	0.191082	0.100
Peak # 7	12.25333	7.217494	245.9523	473.5915	0.06831394	0.100
Peak # 8	12.63822	6.998539	204.09	432.644	0.05668657	0.100
Peak # 9	13.57036	6.519837	198.4962	429.6321	0.05513286	0.100
Peak # 10	14.92862	5.929554	3600.324	3866.778	1	0.100
Peak # 11	16.0831	5.506421	1376.485	1669.815	0.3823225	0.100
Peak # 12	18.04593	4.911676	1009.741	1363.736	0.2804584	0.100
Peak # 13	18.63182	4.758526	671.5975	1046.877	0.1865381	0.100
Peak # 14	19.42977	4.564864	496.6809	892.7581	0.1379545	0.100
Peak # 15	20.14869	4.403579	441.9977	848.7093	0.1227661	0.100
Peak # 16	20.48797	4.331416	1028.155	1437.222	0.2855728	0.128
Peak # 17	20.64182	4.299478	583.2937	992.8682	0.1620114	0.128
Peak # 18	21.52175	4.125638	978.1533	1383.857	0.2716848	0.100
Peak # 19	21.72215	4.088027	1036.466	1439.683	0.2878813	0.308
Peak # 20	21.92503	4.050655	739.6849	1139.781	0.2054495	0.308
Peak # 21	23.27148	3.819247	248.8957	653.3616	0.06913146	0.102
Peak # 22	23.67982	3.754304	1547.461	1952.999	0.4298115	0.100
Peak # 23	24.72815	3.597466	280.2606	677.2075	0.07784315	0.158
Peak # 24	25.18878	3.532713	791.9027	1179.913	0.2199532	0.104
Peak # 25	26.25322	3.391844	441.882	818.9271	0.122734	0.100
Peak # 26	26.57399	3.351624	425.2781	809.8372	0.1181222	0.210
Peak # 27	27.41809	3.250327	260.4725	657.5086	0.07234696	0.100

Peak # 28	28.02496	3.181306	278.7974	678.9731	0.07743675	0.112
Peak #29	28.66725	3.111473	222.631	620.5598	0.06183639	0.100
Peak # 30	29.12559	3.063542	364.7587	757.3303	0.1013127	0.100
Peak # 31	29.90952	2.985008	394.9463	771.1329	0.1096974	0.179
Peak # 32	32.55656	2.748099	310.4091	669.1288	0.08621699	0.227

In some embodiments of the present invention, the hydrochloride crystal form K of the compound of Formula I-1 has the onsets of the endothermic peaks at 80.73°C ± 2°C and 171.74°C ± 2°C in its differential scanning calorimetry (DSC) curve, and decomposition of the sample begins at 211.42°C ± 2°C.

In another preferred embodiment, the hydrochloride crystal form K has a differential scanning calorimetry pattern substantially as shown in Figure 63.

In some embodiments of the present invention, the DSC pattern of the hydrochloride crystal form K of the compound of Formula I-1 is shown in Figure 63.

In some embodiments of the present invention, the hydrochloride crystal form K of the compound of Formula I-1 has three weight loss steps at 33.39°C ± 2°C, 125.00°C ± 2°C, and 155.00°C ± 2°C in its thermogravimetric analysis (TGA) curve.

In another preferred embodiment, the hydrochloride crystal form K has a thermogravimetric analysis pattern substantially as shown in Figure 64.

In some embodiments of the present invention, the TGA pattern of the hydrochloride crystal form K of the compound of Formula I-1 is shown in Figure 64.

The present invention also provides a method for preparing the hydrochloride crystal form K of the compound of Formula I-1, comprising adding the compound of Formula I-1 and hydrochloric acid to methyl tert-butyl ether, and then performing suspension recrystallization at 50°C or under heating-cooling cycles or slurrying to obtain it, the ratio of the compound of Formula I-1 to hydrochloric acid is selected from 0.8 to 1.2, and the hydrochloride crystal form K of the compound of Formula I-1 is a solvate of methyl tert-butyl ether and water, with a methyl tert-butyl ether content of 0.5 equivalents and a water content of 0.93 equivalents.

In another preferred embodiment, the hydrochloride crystal form K of the compound of formula (I) is a solvate of methyl tert-butyl ether and water, wherein the content of methyl tert-butyl ether is 0.1 to 1 equivalent and the content of water is 0.5 to 2 equivalents.

The present invention also provides the hydrochloride crystal form L of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 8.15±0.2°, 12.72±0.2°, 13.59±0.2°, 15.07±0.2°, 15.56 ± 0.2°, 16.60 ± 0.2°, 16.89 ± 0.2°, 17.56 ± 0.2°, 19.74 ± 0.2°, 20.52 ± 0.2°, 21.69±0.2°, 22.60±0.2°, 25.57±0.2°, 27.48±0.2°, 29.54±0.2°, 29.80±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hydrochloride crystal form L of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 7.70±0.2°, 8.15±0.2°, 8.82±0.2°, 9.85±0.2°, 11.25±0.2°, 12.72±0.2°, 13.59±0.2°, 14.68±0.2°, 15.07±0.2°, 15.56±0.2°, 16.60±0.2°, 16.89±0.2°, 17.56±0.2°, 18.53±0.2°, 18.98±0.2°, 19.74±0.2°, 20.29±0.2°, 20.52±0.2°, 21.30±0.2°, 21.69±0.2°, 22.60±0.2°, 22.79±0.2°, 24.38±0.2°, 25.57±0.2°, 26.21±0.2°, 26.50±0.2°, 26.97±0.2°, 27.48±0.2°, 28.17±0.2°, 28.60±0.2°, 29.54±0.2°, 29.80±0.2°, 31.17±0.2°, 33.28±0.2°.

In another preferred embodiment, the hydrochloride crystal form L has an X-ray powder diffraction pattern substantially as shown in Figure 65.

In some embodiments of the present invention, the hydrochloride crystal form L of the compound of Formula I-1 is shown in Figure 65.

Table 29 XRPD analysis data for the hydrochloride crystal form L of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	7.699858	11.47246	131.7752	336.0659	0.02713539	0.100
Peak # 2	8.145549	10.84571	388.0066	598.1743	0.07989903	0.100
Peak # 3	8.823183	10.0142	89.33794	302.069	0.01839663	0.100
Peak # 4	9.853885	8.968925	197.7117	412.7841	0.04071316	0.100
Peak # 5	11.24898	7.859537	369.8264	581.4573	0.07615533	0.100
Peak # 6	12.71896	6.954291	1487.639	1717.048	0.3063374	0.100
Peak # 7	13.58705	6.511866	1030.956	1271.22	0.2122963	0.100
Peak # 8	14.6791	6.029779	391.6135	655.8375	0.08064177	0.100
Peak # 9	15.07415	5.872634	902.8954	1182.24	0.1859259	0.100
Peak # 10	15.55735	5.691307	1063.293	1357.591	0.2189553	0.100
Peak # 11	16.60393	5.334851	1276.309	1618.283	0.2628199	0.175
Peak # 12	16.89181	5.244576	4856.211	5212.304	1	0.100
Peak # 13	17.55518	5.047862	946.9635	1330.313	0.1950005	0.100
Peak # 14	18.52686	4.785248	321.5662	731.5641	0.0662175	0.147
Peak # 15	18.98341	4.671179	102.7261	519.8016	0.02115355	0.100
Peak # 16	19.74166	4.493443	1663.331	2084.444	0.3425161	0.100
Peak # 17	20.29493	4.372176	825.2653	1243.265	0.1699401	0.169
Peak # 18	20.5165	4.325457	1295.536	1710.853	0.2667791	0.134
Peak # 19	21.29701	4.168664	519.0574	937.0649	0.1068853	0.100
Peak # 20	21.68984	4.094043	2100.771	2521.513	0.4325947	0.100
Peak # 21	22.59681	3.93173	1945.966	2363.155	0.400717	0.100
Peak # 22	22.79003	3.898831	552.5369	967.1934	0.1137794	0.100
Peak # 23	24.38056	3.647962	656.4279	1057.281	0.1351728	0.100
Peak # 24	25.56504	3.481566	1270.748	1697.177	0.2616749	0.100
Peak # 25	26.20858	3.397519	857.4071	1291.179	0.1765589	0.189
Peak # 26	26.4961	3.3613	814.4917	1249.304	0.1677216	0.174
Peak # 27	26.9705	3.303243	232.8028	666.3146	0.04793919	0.100
Peak # 28	27.47811	3.243364	1526.117	1954.071	0.3142608	0.100
Peak # 29	28.17182	3.165055	141.1872	554.5795	0.02907353	0.109
Peak # 30	28.59997	3.118639	289.7929	690.1832	0.0596747	0.188
Peak # 31	29.54222	3.02128	500.3598	880.1282	0.103035	0.203
Peak # 32	29.80236	2.995497	633.8278	1010.739	0.130519	0.198
Peak # 33	31.17271	2.866868	252.4929	605.6007	0.0519938	0.160
Peak # 34	33.27863	2.690104	190.787	534.211	0.03928722	0.185

In some embodiments of the present invention, the hydrochloride crystal form L of the

compound of Formula I-1 has the onsets of the endothermic peaks at 180.17°C ± 2°C in its differential scanning calorimetry (DSC) curve, and decomposition of the sample begins at 212.43°C ± 2°C.

In another preferred embodiment, the hydrochloride crystal form L has a differential scanning calorimetry pattern substantially as shown in Figure 66.

In some embodiments of the present invention, the DSC pattern of the hydrochloride crystal form L of the compound of Formula I-1 is shown in Figure 66.

In some embodiments of the present invention, the hydrochloride crystal form L of the compound of Formula I-1 has two weight loss steps at 33.53°C ± 2°C and 140.00°C ± 2°C in its thermogravimetric analysis (TGA) curve.

In another preferred embodiment, the hydrochloride crystal form L has a thermogravimetric analysis pattern substantially as shown in Figure 67.

In some embodiments of the present invention, the TGA pattern of the hydrochloride crystal form L of the compound of Formula I-1 is shown in Figure 67.

The present invention also provides a method for preparing the hydrochloride crystal form L of the compound of Formula I-1, comprising adding the compound of Formula I-1 and hydrochloric acid to toluene, and then performing suspension recrystallization at 25°C, 50°C, or under heating-cooling cycles or slurrying to obtain it, wherein the ratio of the compound of Formula I-1 to hydrochloric acid is selected from 0.8 to 1.2, and the hydrochloride crystal form L of the compound of Formula I-1 is a solvate of toluene, with a toluene content of 0.46 equivalents.

In another preferred embodiment, the hydrochloride crystal form L of the compound of formula (I) is a toluene solvate, wherein the toluene content is 0.2 to 1 equivalent.

The present invention also provides the hydrochloride crystal form M of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 6.84 ± 0.2°, 7.21 ± 0.2°, 14.17 ± 0.2°, 14.90 ± 0.2°, 18.94 ± 0.2°, 19.46 ± 0.2°, 19.71 ± 0.2°, 19.96 ± 0.2°, 20.82 ± 0.2°, 22.60±0.2°, 24.17±0.2°, 25.17±0.2°, 25.45±0.2°, 27.17±0.2°, 28.09±0.2°, 28.88±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hydrochloride crystal form M of the compound of formula I-1 has characteristic diffraction peaks at the following 2θ angles: 6.84±0.2°, 7.21±0.2°, 8.92±0.2°, 10.07±0.2°, 10.69±0.2°, 10.89±0.2°, 11.24±0.2°, 13.23±0.2°, 14.17±0.2°, 14.90±0.2°, 15.59±0.2°, 16.74±0.2°, 17.67±0.2°, 18.29±0.2°, 18.94±0.2°, 19.46±0.2°, 19.71±0.2°, 19.96±0.2°, 20.82±0.2° , 21.49±0.2°, 21.83±0.2°, 22.60±0.2°, 23.14±0.2°, 23.54±0.2°, 24.17±0.2°, 25.17±0.2°, 25.45±0.2°, 26.10±0.2°, 27.17±0.2°, 27.61±0.2°, 28.09±0.2°, 28.88±0.2°, 29.42±0.2°, 30.12±0.2°, 32.48±0.2°, 35.22±0.2°.

In another preferred embodiment, the hydrochloride crystal form M has an X-ray powder diffraction pattern substantially as shown in Figure 68.

In some embodiments of the present invention, the X-ray powder diffraction (XRPD) pattern of the hydrochloride crystal form M of the compound of Formula I-1 is shown in Figure 68.

Table 30 XRPD analysis data for the hydrochloride crystal form M of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	6.84472	12.90373	549.0949	615.6407	0.2778722	0.165
Peak # 2	7.211685	12.24792	391.2005	460.1923	0.1979689	0.100
Peak # 3	8.922095	9.903405	211.9704	281.5079	0.1072687	0.100
Peak # 4	10.07171	8.775435	181.1558	251.1664	0.0916748	0.100
Peak # 5	10.69185	8.267802	310.0935	381.4751	0.1569243	0.101

Peak # 6	10.88628	8.120569	260.1903	332.5287	0.1316706	0.101
Peak # 7	11.24487	7.862399	152.6891	225.697	0.07726907	0.133
Peak # 8	13.22875	6.687422	265.7502	344.6351	0.1344842	0.100
Peak # 9	14.16762	6.246297	July 1976	2066.746	1	0.100
Peak # 10	14.90028	5.940766	745.1891	838.3379	0.3771066	0.100
Peak # 11	15.58676	5.680631	351.6713	441.7771	0.177965	0.100
Peak # 12	16.74027	5.291707	195.157	284.6572	0.09876018	0.100
Peak # 13	17.66522	5.016665	220.666	313.7185	0.1116691	0.126
Peak # 14	18.29257	4.846004	266.1616	359.0701	0.1346924	0.100
Peak # 15	18.94302	4.681048	442.7134	543.266	0.2240373	0.100
Peak # 16	19.46487	4.556712	520.9281	631.4868	0.2636183	0.100
Peak # 17	19.70504	4.501712	909.2918	1023.447	0.4601516	0.217
Peak # 18	19.95502	4.445879	693.7634	810.9916	0.3510824	0.295
Peak # 19	20.81669	4.263753	1294.718	1417.268	0.6551984	0.100
Peak # 20	21.48724	4.132186	414.7583	540.3758	0.2098905	0.179
Peak # 21	21.82966	4.068136	385.2101	512.3789	0.1949375	0.100
Peak # 22	22.59636	3.931808	1560.034	1689.713	0.789463	0.100
Peak # 23	23.14369	3.840045	310.0418	438.7188	0.1568982	0.160
Peak # 24	23.5415	3.776049	285.9931	411.8756	0.1447282	0.100
Peak # 25	24.17295	3.678821	614.5384	737.225	0.3109902	0.100
Peak # 26	25.16647	3.535795	517.7031	646.9673	0.2619862	0.174
Peak # 27	25.4543	3.496462	643.7325	778.7833	0.325764	0.188
Peak # 28	26.09795	3.411669	351.5211	496.2128	0.177889	0.100
Peak #29	27.16983	3.279461	944.2617	1104.001	0.4778483	0.101
Peak # 30	27.61049	3.228113	145.7133	309.4552	0.07373893	0.135
Peak # 31	28.09237	3.173826	448.1052	613.7818	0.2267659	0.100
Peak # 32	28.87765	3.089279	616.2469	779.606	0.3118548	0.100
Peak # 33	29.41578	3.033977	180.7685	338.6228	0.09147878	0.107
Peak # 34	30.12402	2.964239	214.1834	359.9441	0.1083886	0.105
Peak # 35	32.4794	2.754451	212.3529	339.9138	0.1074622	0.100
Peak # 36	35.21609	2.546415	164.973	299.9358	0.0834854	0.157

In some embodiments of the present invention, the hydrochloride crystal form M of the compound of Formula I-1 has the onsets of the endothermic peaks at 31.74°C ± 2°C and 150.05°C ± 2°C in its differential scanning calorimetry (DSC) curve, and decomposition of the sample begins at 215.09°C ± 2°C.

In another preferred embodiment, the hydrochloride crystal form M has a differential scanning calorimetry pattern substantially as shown in Figure 69.

In some embodiments of the present invention, the DSC pattern of the hydrochloride

crystal form M of the compound of Formula I-1 is shown in Figure 69.

In some embodiments of the present invention, the hydrochloride crystal form M of the compound of Formula I-1 has two weight loss steps at 32.98°C ± 2°C and 115.00°C ± 2°C in its thermogravimetric analysis (TGA) curve.

In another preferred embodiment, the hydrochloride crystal form M has a thermogravimetric analysis pattern substantially as shown in Figure 70.

In some embodiments of the present invention, the TGA pattern of the hydrochloride crystal form M of the compound of Formula I-1 is shown in Figure 70.

The present invention also provides a method for preparing the hydrochloride crystal form M of the compound of Formula I-1, comprising adding the compound of Formula I-1 and hydrochloric acid to isopropanol/dimethyl sulfoxide, isopropyl acetate/dimethyl sulfoxide, or a mixed solvent of water/dimethyl sulfoxide, and then performing suspension recrystallization at 25°C, 50°C, or under heating-cooling cycles or slurrying to obtain it, the ratio of the compound of Formula I-1 to hydrochloric acid is selected from 0.8 to 1.2, the hydrochloride crystal form M of the compound of Formula I-1 is a solvate of dimethyl sulfoxide and water, with a dimethyl sulfoxide content of 3.4 equivalents and a water content of 13.7 equivalents.

In another preferred embodiment, the hydrochloride crystal form M of the compound of formula (I) is a solvate of dimethyl sulfoxide and water, wherein the content of dimethyl sulfoxide is 1 to 7 equivalents and the content of water is 5 to 25 equivalents.

The present invention also provides the hydrochloride crystal form N of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 6.61 ± 0.2°, 7.80 ± 0.2°, 13.17 ± 0.2°, 15.24 ± 0.2°, 16.02 ± 0.2°, 16.19 ± 0.2°, 20.10 ± 0.2°, 21.57 ± 0.2°, 21.95 ± 0.2°, 28.42 ± 0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hydrochloride crystal form N of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 6.61±0.2°, 7.80±0.2°, 9.75±0.2°, 11.19±0.2°, 12.53 ± 0.2°, 13.17 ± 0.2°, 14.61 ± 0.2°, 15.24 ± 0.2°, 16.02 ± 0.2°, 16.19 ± 0.2°, 18.51±0.2°, 19.36±0.2°, 20.10±0.2°, 21.57±0.2°, 21.95±0.2°, 23.47±0.2°, 25.60±0.2°, 27.32±0.2°, 28.42±0.2°, 29.12±0.2°.

In another preferred embodiment, the hydrochloride crystal form N has an X-ray powder diffraction pattern substantially as shown in Figure 71.

In some embodiments of the present invention, the XRPD pattern of the hydrochloride crystal form N of the compound of Formula I-1 is shown in Figure 71.

Table 31 XRPD analysis data for the hydrochloride crystal form N of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	6.609798	13.36181	794.7955	980.8873	0.3862052	0.100
Peak # 2	7.795767	11.33153	487.4999	690.8655	0.2368848	0.100
Peak # 3	9.745835	9.068117	34.00436	256.8145	0.01652332	0.133
Peak # 4	11.18676	7.903115	155.3221	382.2601	0.07547374	0.141
Peak # 5	12.52697	7.060439	86.51295	323.2003	0.04203818	0.159
Peak # 6	13.16559	6.719363	421.9255	664.773	0.2050211	0.190
Peak # 7	14.60967	6.058279	86.97061	345.4379	0.04226056	0.133
Peak # 8	15.23705	5.810213	304.1442	589.247	0.147789	0.271
Peak # 9	16.0249	5.52629	820.8987	1132.93	0.3988892	0.225

Peak # 10	16.18629	5.471551	893.4421	1210.095	0.4341393	0.225
Peak # 11	18.5144	4.788438	351.1131	770.6374	0.1706121	0.174
Peak # 12	19.35669	4.581933	455.0124	908.4713	0.2210986	0.105
Peak # 13	20.09929	4.414289	2057.962	2534.464	1	0.100
Peak # 14	21.57023	4.116475	320.2355	823.3632	0.1556081	0.100
Peak # 15	21.95477	4.045236	557.7156	1063.636	0.2710039	0.291
Peak # 16	23.47203	3.787067	201.8493	701.9348	0.09808215	0.109
Peak #17	25.59957	3.476949	170.8813	642.3811	0.08303423	0.126
Peak # 18	27.31775	3.262038	172.0372	641.0505	0.08359591	0.164
Peak # 19	28.42086	3.137885	858.4133	1341.339	0.4171182	0.100
Peak # 20	29.12304	3.063805	213.3153	697.6971	0.1036537	0.238

In some embodiments of the present invention, the hydrochloride crystal form N of the compound of Formula I-1 has the onsets of the endothermic peaks at 47.38°C ± 2°C and 167.91°C ± 2°C in its differential scanning calorimetry (DSC) curve, and decomposition of the sample begins at 212.57°C ± 2°C.

In another preferred embodiment, the hydrochloride crystal form N has a differential scanning calorimetry pattern substantially as shown in Figure 72.

In some embodiments of the present invention, the DSC pattern of the hydrochloride crystal form N of the compound of Formula I-1 is shown in Figure 72.

In some embodiments of the present invention, the hydrochloride crystal form N of the compound of Formula I-1 has three weight loss steps at 33.22°C ± 2°C, 75.00°C ± 2°C, and 150.00°C ± 2°C in its thermogravimetric analysis (TGA) curve.

In another preferred embodiment, the hydrochloride crystal form N has a thermogravimetric analysis pattern substantially as shown in Figure 73.

In some embodiments of the present invention, the TGA pattern of the hydrochloride crystal form N of the compound of Formula I-1 is shown in Figure 73.

The present invention also provides a method for preparing the hydrochloride crystal form N of the compound of Formula I-1, comprising adding the compound of Formula I-1 and hydrochloric acid to methanol, and then performing suspension recrystallization at 25°C or slurrying to obtain it, the ratio of the compound of Formula I-1 to hydrochloric acid is selected from 0.8 to 1.2, and the hydrochloride crystal form N of the compound of Formula I-1 is a hydrate crystal form, with a water content of 3.0 equivalents.

In another preferred embodiment, the hydrochloride crystal form N of the compound of formula (I) is a hydrate crystal form, wherein the water content is 1 to 6 equivalents.

The present invention also provides the hydrochloride crystal form O of the compound of Formula I-1, and its X-ray powder diffraction pattern has characteristic diffraction peaks at the following 2θ angles: 6.14±0.2°, 9.90±0.2°, 13.54 ± 0.2°, 14.40 ± 0.2°, 15.33 ± 0.2°, 15.51 ± 0.2°, 15.87 ± 0.2°, 16.79 ± 0.2°, 18.36±0.2°, 20.17±0.2°, 21.14±0.2°, 22.51±0.2°, 22.84±0.2°, 24.59±0.2°, 25.28±0.2°, 26.82±0.2°, 27.07±0.2°, 27.93±0.2°.

In some embodiments of the present invention, the X-ray powder diffraction pattern of the hydrochloride crystal form O of the compound of Formula I-1 has characteristic diffraction peaks at the following 2θ angles: 6.14±0.2°, 8.39±0.2°, 9.90±0.2°, 11.28±0.2°, 13.19 ± 0.2°, 13.54 ± 0.2°, 14.40 ± 0.2°, 15.33 ± 0.2°, 15.51 ± 0.2°, 15.87 ± 0.2°, 16.79 ± 0.2°, 17.32±0.2°, 18.36±0.2°, 19.03±0.2°, 19.38±0.2°, 19.84±0.2°, 20.17±0.2°, 20.39±0.2°, 21.14±0.2°, 21.82±0.2°, 22.51±0.2°, 22.84±0.2°, 23.77±0.2°, 24.59±0.2°, 25.28±0.2°, 26.21±0.2°, 26.82±0.2°, 27.07±0.2°, 27.93±0.2°, 28.45±0.2°, 29.24±0.2°, 29.70±0.2°, 30.12±0.2°,

30.91±0.2°, 31.32±0.2°, 32.02±0.2°, 32.81±0.2°, 33.99±0.2°, 35.51±0.2°, 37.27±0.2°.

In another preferred embodiment, the hydrochloride crystal form O has an X-ray powder diffraction pattern substantially as shown in Figure 74.

In some embodiments of the present invention, the XRPD pattern of the hydrochloride crystal form O of the compound of Formula I-1 is shown in Figure 74.

Table 32 XRPD analysis data for the hydrochloride crystal form O of the compound of Formula I-1

Name	Angle	d Value	Net Intensity	Gross Intensity	Rel. Intensity	FWHM
Peak #1	6.140894	14.38099	1107.957	1293.828	0.3147685	0.100
Peak # 2	8.388501	10.53213	408.1169	632.1091	0.1159452	0.100
Peak # 3	9.903625	8.923991	940.8444	1184.968	0.2672921	0.100
Peak # 4	11.27951	7.838338	283.761	536.4181	0.08061594	0.100
Peak # 5	13.19286	6.705534	181.3849	438.5068	0.0515311	0.100
Peak # 6	13.54282	6.533034	1454.357	1725.367	0.4131799	0.100
Peak # 7	14.39867	6.146578	1165.407	1462.794	0.3310898	0.100
Peak # 8	15.33	5.775193	1091.177	1411.573	0.3100013	0.209
Peak # 9	15.50935	5.708809	1968.812	2294.23	0.5593358	0.209
Peak # 10	15.87208	5.579152	1217.473	1551.602	0.3458818	0.100
Peak # 11	16.79091	5.275862	1137.58	1502.341	0.3231842	0.100
Peak # 12	17.31762	5.116568	762.1778	1150.802	0.2165332	0.100
Peak # 13	18.35663	4.829239	3,033.994	3474.369	0.8619518	0.100
Peak # 14	19.03416	4.658839	835.817	1306.477	0.237454	0.169
Peak # 15	19.38	4.576475	502.326	985.8411	0.1427098	0.108
Peak # 16	19.84427	4.470439	1056.817	1554.823	0.3002395	0.100
Peak # 17	20.17144	4.398664	3519.912	4026.221	1	0.100
Peak # 18	20.38873	4.352273	1279.111	1790.063	0.363393	0.100
Peak # 19	21.14244	4.198789	1425.925	1947.604	0.4051024	0.105
Peak # 20	21.8204	4.069841	566.3649	1090.542	0.1609031	0.125
Peak # 21	22.50812	3.947022	756.1846	1275.989	0.2148305	0.191
Peak # 22	22.83675	3.89096	979.7973	1495.056	0.2783585	0.178
Peak # 23	23.77264	3.739855	546.3175	1050.328	0.1552077	0.105
Peak # 24	24.58534	3.618039	980.3226	1470.129	0.2785077	0.122
Peak # 25	25.27836	3.520397	896.8149	1367.909	0.2547834	0.136
Peak # 26	26.21456	3.396758	248.3358	716.5672	0.0705517	0.100
Peak # 27	26.82125	3.321285	737.2324	1215.387	0.2094463	0.100
Peak # 28	27.06781	3.291589	750.5667	1231.206	0.2132345	0.191
Peak # 29	27.92502	3.192464	1087.508	1569.829	0.3089589	0.100

Peak # 30	28.45316	3.134396	279.407	757.3731	0.07937898	0.101
Peak # 31	29.24147	3.051666	309.071	791.8425	0.08780645	0.161
Peak # 32	29.70277	3.005313	501.2726	988.7209	0.1424106	0.121
Peak # 33	30.11823	2.964796	490.5232	979.5004	0.1393567	0.105
Peak # 34	30.91374	2.890291	465.6483	950.4669	0.1322898	0.100
Peak # 35	31.32369	2.853393	169.9911	649.0291	0.04829413	0.129
Peak # 36	32.01775	2.793105	265.0306	734.7343	0.07529467	0.163
Peak # 37	32.81191	2.727294	268.0586	727.3953	0.07615492	0.130
Peak # 38	33.98699	2.635639	302.6802	746.7783	0.08599085	0.131
Peak # 39	35.51149	2.525907	319.0914	750.0336	0.09065324	0.193
Peak # 40	37.27088	2.410611	289.6581	733.1247	0.08229129	0.248

In some embodiments of the present invention, the hydrochloride crystal form O of the compound of Formula I-1 has the onsets of the endothermic peaks starting at 12.36°C ± 2°C and 174.87°C ± 2°C in its differential scanning calorimetry (DSC) curve, with decomposition of the sample begins at 212.00°C ± 2°C.

In another preferred embodiment, the hydrochloride crystal form O has a differential scanning calorimetry pattern substantially as shown in Figure 75.

In some embodiments of the present invention, the DSC pattern of the hydrochloride crystal form O of the compound of Formula I-1 is shown in Figure 75.

In some embodiments of the present invention, the hydrochloride crystal form O of the compound of Formula I-1 has three weight loss steps at 27.70°C ± 2°C, 115.00°C ± 2°C, and 160.00°C ± 2°C in its thermogravimetric analysis (TGA) curve.

In another preferred embodiment, the hydrochloride crystal form O has a thermogravimetric analysis pattern substantially as shown in Figure 76.

In some embodiments of the present invention, the TGA pattern of the hydrochloride crystal form O of the compound of Formula I-1 is shown in Figure 76.

The present invention also provides a method for preparing the hydrochloride crystal form O of the compound of Formula I-1, comprising adding the compound of Formula I-1 and hydrochloric acid to dichloromethane, and then performing suspension recrystallization at 25°C or slurrying to obtain it, the ratio of the compound of Formula I-1 to hydrochloric acid is selected from 0.8 to 1.2, and the hydrochloride crystal form O of the compound of Formula I-1 is a hydrate crystal form, with a water content of 0.9 equivalents.

In another preferred embodiment, the hydrochloride crystal form O of the compound of formula (I) is a hydrate crystal form, wherein the water content is 0.4 to 2 equivalents.

In another aspect, the present invention provides a method for preparing a crystal form of a pharmaceutically acceptable salt of the compound of formula (I), characterized by comprising the following steps:

a. dissolving or dispersing the compound of formula (I) and an acid in a molar ratio of 1: (0.8–3) in 1–20 times of solvent A;

b. performing suspension, recrystallization, or slurrying treatment;

wherein the acid is not selected from hydrochloric acid (preferably, the acid is selected from the group consisting of: maleic acid, fumaric acid, glycolic acid, L-malic acid, succinic acid, sulfuric acid, L-tartaric acid, hippuric acid, glutaric acid, p-toluenesulfonic acid, or methanesulfonic acid);

wherein the solvent A is selected from the group consisting of: acetonitrile, dichloromethane, tetrahydrofuran, or a combination thereof;

or the acid is hydrochloric acid or hydrogen chloride in dioxane; and the solvent A is selected from the group consisting of: ethyl acetate, 2-methyl-tetrahydrofuran, butanone, ethanol, acetone, ethyl acetate, acetonitrile, tetrahydrofuran, methyl isobutyl ketone, trifluoroethanol, water, methanol, tert-butyl methyl ether, toluene, isopropanol, dimethyl sulfoxide, isopropyl acetate, dichloromethane, or a combination thereof.

In another preferred embodiment, the solvent A is selected from the group consisting of: methyl isobutyl ketone/trifluoroethanol, methanol/water, methanol/tert-butyl methyl ether, isopropanol/dimethyl sulfoxide, isopropyl acetate/dimethyl sulfoxide, water/dimethyl sulfoxide.

In another preferred embodiment, the suspension comprises the following steps:

a. suspending the compound of formula (I), acid, and solvent at 45–65°C for 1–3 h;

b. allowing the mixture to cool naturally to 20–30°C and continuing performing the suspension for at least 48 h;

c. centrifuging the resulting suspension through a 0.4–0.5 μm filter membrane at a speed of 12,000–16,000 rpm;

d. vacuum-drying the resulting solid at 45–65°C.

In another aspect, the present invention provides a method for preparing a crystal form of a pharmaceutically acceptable salt of the compound of formula (I), characterized in that the method is a crystal form transformation by converting one crystal form of a pharmaceutically acceptable salt of the compound of formula (I) into another crystal form thereof;

wherein the method of the crystal form transformation comprises the following steps:

a. dissolving or dispersing a crystal form of a pharmaceutically acceptable salt of the compound of formula (I) in 1 to 20 times of solvent A;

b. performing suspension treatment;

c. centrifuging the resulting suspension through a 0.4 to 0.5 μm filter membrane at a speed of 12,000 to 16,000 rpm;

wherein the solvent A is selected from the group consisting of: ethanol, acetone, ethyl acetate, acetonitrile, tetrahydrofuran, methyl isobutyl ketone, trifluoroethanol, methanol, 2-methyl-tetrahydrofuran, methyl tert-butyl ether, toluene, isopropanol, dimethyl sulfoxide, isopropyl acetate, dimethyl sulfoxide, methanol, dichloromethane, water, or combinations thereof.

In another preferred embodiment, the solvent A is selected from the group consisting of: methyl isobutyl ketone/trifluoroethanol, methanol/water, isopropanol/dimethyl sulfoxide, isopropyl acetate/dimethyl sulfoxide, dimethyl sulfoxide/water.

In another preferred embodiment, the suspension treatment comprises the step of stirring at a rate of 300–400 rpm at 20–30°C.

In another preferred embodiment, the suspension treatment comprises the step of stirring at a rate of 300–400 rpm at 40–60°C.

In another preferred embodiment, the suspension treatment comprises the step of performing 8 to 12 heating-cooling cycles at a rate of 0.05 to 0.2°C/min between 5 and 50°C while stirring at a rate of 300 to 400 rpm, with the final temperature of the suspension being 10 to 15°C.

In another preferred embodiment, the suspension treatment comprises the step of filtering through a 0.4–0.5 μm filter membrane to obtain a clear solution, followed by performing suspension treatment after adding methyl tert-butyl ether at a ratio of 1: (8–12).

In another aspect, the present invention also provides a pharmaceutical composition comprising the compound of formula (I), the crystal form A, or a crystal form of the compound of formula (I);

and

one or more pharmaceutically acceptable carriers, excipients, adjuvants, ingredients, and/or diluents.

In another preferred embodiment, the pharmaceutical composition further comprises other therapeutic agents.

In another preferred embodiment, the other therapeutic agents are selected from the group consisting of: chemotherapeutic agents, kinase inhibitors, targeted epigenetic modulators, antibody drugs, immune checkpoint inhibitors, or combinations thereof. In another preferred embodiment, the chemotherapeutic agent is selected from the group consisting of: cisplatin, doxorubicin, paclitaxel, etoposide, irinotecan, cyclophosphamide, gemcitabine, ifosfamide, tamoxifen, toremifene, fulvestrant, anastrozole, exemestane, goserelin, leprorelin, melphalan, chlorambucil, busulfan, floxuridine, cytarabine, oxaliplatin, leucovorin, pentostatin, and diethylstilbestrol.

In another preferred embodiment, the kinase inhibitor is selected from the group consisting of: Akt, TGF-βR, Pim, PKA, PKG, PKC, CaM kinase, CDK2, CDK4, CDK4/6, MEK, ERK, MAPK, mTOR, EGFR, HER2, HER3, HER4, PDGFαR, PDGFβR, CSFIR, KIT, c-Met, TRKA, TRKB, TRKC, FLT3, VEGFR, BTK, FAK, SYK, FRK, JAK, HPK1, AXL, ALK, and B-Raf inhibitors. In another preferred embodiment, the targeted epigenetic modulator is selected from the group consisting of: bromodomain inhibitors, histone lysine methyltransferases, histone arginine methyltransferases, histone demethylases, histone deacetylases, histone acetylases, and DNA methyltransferases. In another preferred embodiment, the antibody drug is selected from the group consisting of: anti-HER2 antibodies, anti-VEGFR antibodies, anti-EGFR antibodies, anti-c-MET antibodies, and anti-CD20 antibodies.

In another preferred embodiment, the immune checkpoint inhibitor is selected from the group consisting of: CD27, CD28, CD40, CD122, CD96, CD73, CD47, OX40, GITR, A2AR, B7-H3, B7-H4, BTLA, CTLA-4, LAG3, TIM3, VISTA, PD-1, PD-L1, and PD-L2.

In another aspect, the present invention also provides a use of the compound of the formula (I), the crystal form A, the crystal form of the compound of formula (I), and the pharmaceutical composition in preparing a medicament for the prevention and/or treatment of diseases associated with increased activity or expression of FGFR2.

In another preferred embodiment, the increased activity or expression of FGFR2 is selected from the group consisting of: FGFR2 amplification, FGFR2 gene mutation, FGFR2 gene fusion/rearrangement, FGFR2 gene translocation, and FGFR2 gene activation.

In another preferred embodiment, the diseases associated with increased activity or expression of FGFR2 are selected from the group consisting of: cholangiocarcinoma, liver cancer, breast cancer, prostate cancer, lung cancer, thyroid cancer, gastric cancer, ovarian cancer, esophageal cancer, pancreatic cancer, cervical cancer, colorectal cancer, salivary gland cancer, endometrial cancer, and urothelial cancer, and the like.

In another preferred embodiment, the cholangiocarcinoma is intrahepatic cholangiocarcinoma.

In another preferred embodiment, the liver cancer is hepatocellular carcinoma.

In another preferred embodiment, the lung cancer is lung squamous cell carcinoma or non-small cell lung cancer.

Description of the Drawings

Figure 1 shows the XRPD pattern of crystal form A of the compound of Formula I-1.

Figure 2 shows the DSC pattern of crystal form A of the compound of Formula I-1.

Figure 3 shows the TGA pattern of crystal form A of the compound of Formula I-1.

Figure 4 shows the XRPD pattern of maleate crystal form A of the compound of Formula I-1.

Figure 5 shows the XRPD pattern of monomaleate crystal form B of the compound of Formula I-1.

Figure 6 shows the DSC pattern of monomaleate crystal form B of the compound of

Formula I-1.

Figure 7 shows the TGA spectrum of monomaleate crystal form B of the compound of Formula I-1.

Figure 8 shows the XRPD pattern of fumarate crystal form A of the compound of Formula I-1.

Figure 9 shows the XRPD pattern of hemifumarate crystal form B of the compound of Formula I-1.

Figure 10 shows the DSC pattern of hemifumarate crystal form B of the compound of Formula I-1.

Figure 11 shows the TGA pattern of hemifumarate crystal form B of the compound of Formula I-1.

Figure 12 shows the XRPD pattern of monoglycolate crystal form A of the compound of Formula I-1.

Figure 13 shows the DSC pattern of monoglycolate crystal form A of the compound of Formula I-1.

Figure 14 shows the TGA pattern of monoglycolate, crystal form A of the compound of Formula I-1.

Figure 15 shows the XRPD pattern of glycolate crystal form B of the compound of Formula I-1, .

Figure 16 shows the XRPD pattern of the mono-L-malate crystal form A of the compound of Formula I-1.

Figure 17 shows the DSC pattern of mono-L-malate crystal form A of the compound of Formula I-1.

Figure 18 shows the TGA spectrum of mono-L-malate crystal form A of the compound of Formula I-1.

Figure 19 shows the XRPD pattern of monosuccinate crystal form A of the compound of Formula I-1.

Figure 20 shows the DSC pattern of monosuccinate crystal form A of the compound of Formula I-1.

Figure 21 shows the TGA pattern of monosuccinate crystal form A of the compound of Formula I-1.

Figure 22 shows the XRPD pattern of sulfate crystal form A of the compound of Formula I-1.

Figure 23 shows the XRPD pattern of L-tartrate crystal form A of the compound of Formula I-1.

Figure 24 shows the XRPD pattern of hippurate crystal form A of the compound of Formula I-1.

Figure 25 shows the XRPD pattern of glutarate crystal form A of the compound of Formula I-1.

Figure 26 shows the XRPD pattern of p-toluenesulfonate crystal form A of the compound of Formula I-1.

Figure 27 shows the XRPD pattern of p-toluenesulfonate crystal form B of the compound of Formula I-1.

Figure 28 shows the XRPD pattern of methanesulfonate crystal form A of the compound of Formula I-1.

Figure 29 shows the XRPD pattern of hydrochloride crystal form C1 of the compound of Formula I-1.

Figure 30 shows the DSC pattern of hydrochloride crystal form C1 of the compound of Formula I-1.

Figure 31 shows the TGA pattern of hydrochloride crystal form C1 of the compound of Formula I-1.

Figure 32 shows the XRPD pattern of hydrochloride crystal form C2 of the compound of Formula I-1.

Figure 33 shows the DSC pattern of hydrochloride crystal form C2 of the compound of Formula I-1.

Figure 34 shows the TGA pattern of hydrochloride crystal form C2 of the compound of Formula I-1.

Figure 35 shows the XRPD pattern of hydrochloride crystal form D of the compound of Formula I-1.

Figure 36 shows the DSC pattern of hydrochloride crystal form D of the compound of Formula I-1.

Figure 37 shows the TGA pattern of hydrochloride crystal form D of the compound of Formula I-1.

Figure 38 shows the XRPD pattern of hydrochloride crystal form E1 of the compound of Formula I-1.

Figure 39 shows the DSC pattern of hydrochloride crystal form E1 of the compound of Formula I-1.

Figure 40 shows the TGA pattern of hydrochloride crystal form E1 of the compound of Formula I-1.

Figure 41 shows the XRPD pattern of hydrochloride crystal form E2 of the compound of Formula I-1.

Figure 42 shows the DSC pattern of hydrochloride crystal form E2 of the compound of Formula I-1.

Figure 43 shows the TGA pattern of hydrochloride crystal form E2 of the compound of Formula I-1.

Figure 44 shows the XRPD pattern of hydrochloride crystal form F of the compound of Formula I-1.

Figure 45 shows the DSC pattern of hydrochloride crystal form F of the compound of Formula I-1.

Figure 46 shows the TGA pattern of hydrochloride crystal form F of the compound of Formula I-1.

Figure 47 shows the XRPD pattern of hydrochloride, crystal form G of the compound of Formula I-1.

Figure 48 shows the DSC pattern of hydrochloride crystal form G of the compound of Formula I-1.

Figure 49 shows the TGA pattern of hydrochloride crystal form G of the compound of Formula I-1.

Figure 50 shows the XRPD pattern of hydrochloride crystal form H of the compound of Formula I-1.

Figure 51 shows the DSC pattern of hydrochloride crystal form H of the compound of Formula I-1.

Figure 52 shows the TGA pattern of hydrochloride crystal form H of the compound of Formula I-1.

Figure 53 shows the XRPD pattern of hydrochloride crystal form I of the compound of Formula I-1.

Figure 54 shows the DSC pattern of hydrochloride crystal form I of the compound of Formula I-1.

Figure 55 shows the TGA pattern of hydrochloride crystal form I of the compound of Formula I-1.

Figure 56 shows the XRPD pattern of hydrochloride crystal form J1 of the compound of Formula I-1.

Figure 57 shows the DSC pattern of hydrochloride crystal form J1 of the compound of

Formula I-1.

Figure 58 shows the TGA pattern of hydrochloride crystal form J1 of the compound of Formula I-1.

Figure 59 shows the XRPD pattern of hydrochloride crystal form J2 of the compound of Formula I-1.

Figure 60 shows the DSC pattern of hydrochloride crystal form J2 of the compound of Formula I-1.

Figure 61 shows the TGA pattern of hydrochloride crystal form J2 of the compound of Formula I-1.

Figure 62 shows the XRPD pattern of hydrochloride crystal form K of the compound of Formula I-1.

Figure 63 shows the DSC pattern of hydrochloride crystal form K of the compound of Formula I-1.

Figure 64 shows the TGA pattern of hydrochloride crystal form K of the compound of Formula I-1.

Figure 65 shows the XRPD pattern of hydrochloride crystal form L of the compound of Formula I-1.

Figure 66 shows the DSC pattern of hydrochloride crystal form L of the compound of Formula I-1.

Figure 67 shows the TGA pattern of hydrochloride crystal form L of the compound of Formula I-1.

Figure 68 shows the XRPD pattern of hydrochloride crystal form M of the compound of Formula I-1.

Figure 69 shows the DSC pattern of hydrochloride crystal form M of the compound of Formula I-1.

Figure 70 shows the TGA pattern of hydrochloride crystal form M of the compound of Formula I-1.

Figure 71 shows the XRPD pattern of hydrochloride crystal form N of the compound of Formula I-1.

Figure 72 shows the DSC pattern of hydrochloride crystal form N of the compound of Formula I-1.

Figure 73 shows the TGA pattern of hydrochloride crystal form N of the compound of Formula I-1.

Figure 74 shows the XRPD pattern of hydrochloride crystal form O of the compound of Formula I-1.

Figure 75 shows the DSC pattern of hydrochloride crystal form O of the compound of Formula I-1.

Figure 76 shows the TGA pattern of hydrochloride crystal form O of the compound of Formula I-1.

Detailed Description of the Invention

To address the issues in the prior art, the inventors conducted in-depth research on the various forms of the compound of formula I and developed multiple crystal forms and acid salt forms of the compound of formula I, particularly the hydrochloride, which significantly improved the physicochemical properties of the compound of formula I, such as solubility, hygroscopicity, and chemical stability. The crystalline acid salt compound raw materials comply with industrial production standards and meet the requirements for pharmaceutical formulation development. With important clinical application potential, these compounds are expected to accelerate the development of a new generation of FGFR2 inhibitors. Based on this, the present invention was completed.

Definitions

Unless otherwise specified, the following terms and phrases used herein are intended to have the meanings set forth below. A particular phrase or term should not be considered ambiguous or unclear in the absence of a specific definition, but should be understood in its ordinary sense. When trade names appear herein, they are intended to refer to the corresponding products or their active ingredients.

As used herein, the term "n or more 2θ values selected from the group consisting of" refers to any positive integer greater than or equal to n (e.g., n, n+1, …), where the upper limit Nup is the total number of 2θ peaks in that set. For example, "1 or more" includes not only 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, …positive integers up to the upper limit Nup, but also includes ranges such as "2 or more", "3 or more", "4 or more", "5 or more", "6 or more", "7 or more", "8 or more", "9 or more" and "10 or more". For example, "3 or more" includes not only 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21,…up to the upper limit Nup, but also includes ranges such as "4 or more", "5 or more", "6 or more", "7 or more", "8 or more", "9 or more" and "10 or more".

As used herein, "dissolving or dispersing the compound of formula (I) in 1 to 5 times of solvent" means dissolving or dispersing 1 gram of the compound of formula (I) in 1 to 5 milliliters of solvent, wherein the solvent includes, but is not limited to, acetonitrile, alcoholic solvents, ester solvents, ether solvents, or mixtures of alcoholic solvents and water.

The intermediate compounds of the present invention may be prepared by various synthetic methods known to those skilled in the art, including the specific embodiments listed below, embodiments formed by combining them with other chemical synthesis methods, and equivalent substitutions known to those skilled in the art; preferred embodiments include, but are not limited to, the examples of the present invention.

The chemical reactions of the specific embodiments of the present invention are carried out in suitable solvents, which must be appropriate for the chemical transformations of the present invention and the reagents and materials required therein. To obtain the compounds of the present invention, it may sometimes be necessary for those skilled in the art to modify or select synthetic steps or reaction procedures based on existing embodiments.

The present invention will be described in detail below through examples, these examples do not intended to exert any limitation on the scope of the invention.

All solvents used in the present invention are commercially available and can be used without further purification.

The following abbreviations are used in the present invention:

Abbreviation	Full Name
EtOH	Ethanol
MeOH	Methanol
IPA	Isopropyl alcohol
MTBE	Methyl tert-butyl ether
MIBK	Methyl isobutyl ketone
EA	Ethyl acetate
IPAc	Isopropyl acetate
ACN	Acetonitrile
THF	Tetrahydrofuran
2-MeTHF	2-Methyl-1,4-dihydrofuran

DCM	Dichloromethane
DMSO	Dimethyl sulfoxide
FaSSGF	Fasted-state simulated gastric fluid
FaSSIF-v1	Fasted-state simulated intestinal fluid - Version 1
FeSSIF-v1	Fed-State simulated intestinal fluid - Version 1
XRPD	X-ray powder diffraction
DSC	Differential Scanning Calorimetry
TGA	Thermogravimetric Analysis
DVS	Dynamic Vapor Sorption
PLM	Polarizing Microscope
^{1}H-NMR	Hydrogen Nuclear Magnetic Resonance Spectroscopy
KF	Karl Fischer (titrator)
HPLC	High-Performance Liquid Chromatography
IC	Ion Chromatography
LOQ	Limit of quantification

The test items and methods used in this invention are as follows:

X-ray Powder Diffractometer (XRPD)	
Instrument	Bruker D8 Advance
Method 1	
X-ray Path	Reflection Mode
Detector	LYNXEYE_XE_T (1D mode)
Opening Angle	2.9°(max)
Radioactive Source	Cu/K-Alpha1 (λ=1.5406 Å)
X-ray source power	40 kV, 40 mA
Primary beam slit	Dual motorized slits: 20.0 mm; Primary Soller slit: 2.5°
Secondary beam slit	Secondary Soller slit: 2.5°
Scanning mode	Continuous scan
Scan type	Dual-beam mode
Step size	0.02°
Time per step	0.4 s/step
Scan range	2°to 40°
Sample rotation speed	15 rpm
Sample plate	Monocrystalline silicon wafer, flat wafer
Method 2	
X-ray path	Reflection mode

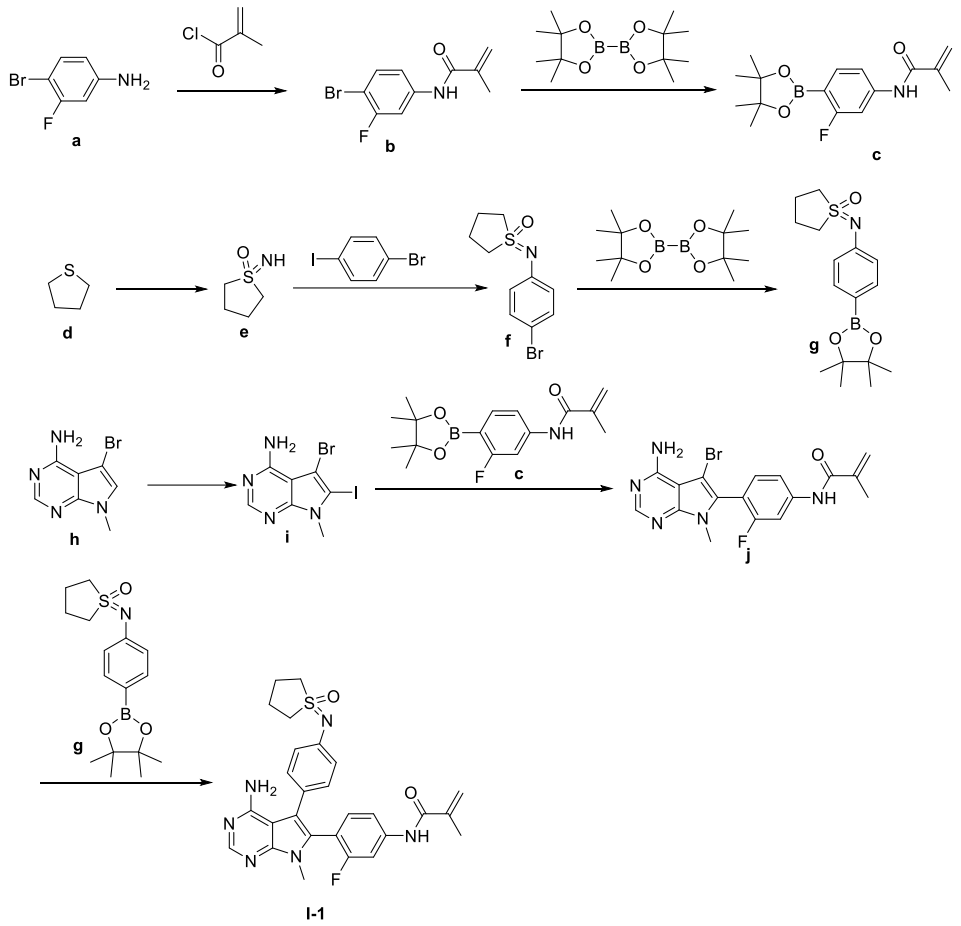
Detector	LYNXEYE_XE_T (1D mode)
Opening Angle	2.9°(max)
Radioactive Source	Cu/K-Alpha1 (λ=1.5406 Å)
X-ray source power	40 kV, 40 mA
Primary beam slit	Dual main motorized slits: 10.0 mm; Primary Soller slit: 2.5°
Secondary beam slit	Secondary Soller slit: 2.5°
Scanning mode	Continuous scan
Scan type	Dual-beam mode
Step size	0.02°
Time per step	0.12 s/step
Scan Range	3°to 40°
Sample rotation speed	15 rpm
Sample plate	Monocrystalline silicon wafer, flat plate

Differential Scanning Calorimeter (DSC)	
Instrument	TA Instruments Discovery 2500
Sample tray	Tzero tray and Tzero hermetic lid with apertures of approximately 0.7 mm in diameter
Temperature Range	~30 to 250°C
Heating rate	10°C/min
Nitrogen flow rate	50 mL/min
Sample mass	~0.5–5 mg
Thermogravimetric Analyzer (TGA)	
Instrument	TA Instruments Discovery 5500
Sample tray	Aluminum dish, open-top
Starting Temperature	Ambient temperature (below 35°C)
Final temperature	300°C
Heating rate	10°C/min
Nitrogen flow rate	Equilibrium: 10 mL/min; Sample chamber: 25 mL/min
Sample volume	~1–10 mg
High-Performance Liquid Chromatography (HPLC)	
Instrument	Agilent 1260 Infinity II Binary Pump
Method 1	For purity and solubility determination
HPLC Method	Wavelength: 220 nm Column: Waters Sunfire C18 150 × 460 5μm Detector: DAD

	Column temperature: 40°C Flow rate: 1.2 mL/min Mobile phase A: 0.1% trifluoroacetic acid Mobile phase B: Acetonitrile Diluent: Acetonitrile Injection volume: 5 μL Gradient: Time (min) / Mobile Phase A (%) / Mobile Phase B (%) 0.00 / 95 / 5 9.00 / 5 / 95 13.00 / 5 / 95 13.10 / 95 / 5 17.00 / 95 / 5
Method 2	For HPLC-IC hyphenated analysis
HPLC Method	Wavelength: 220 nm Column: Waters Sunfire C18 150 × 460 μm, 5 μm Detector: DAD Column temperature: 40°C Flow rate: 1.2 mL/min Mobile phase A: 0.1% trifluoroacetic acid Mobile phase B: Acetonitrile Diluent: Acetonitrile/water (1:1, v/v) Injection volume: 8 μL Gradient: Time (min) / Mobile Phase A (%) / Mobile Phase B (%) 0.00 / 95 / 5 9.00 / 5 / 95 13.00 / 5 / 95 13.10 / 95 / 5 17.00 / 95 / 5

To better understand the content of the present invention, further explanation is provided below with reference to specific examples; however, the specific examples are not intended to limit the scope of the present invention.

Example 1: Preparation of Compound (I-1)



Step 1:

Compound **a** (5.0 g, 26.3 mmol) and triethylamine (8.0 g, 11 ml) were dissolved in DCM (50 ml). At 0 °C, 2-methacryloyl chloride (3.03 g, 2.8 ml) was added dropwise to the reaction solution and stirred for 1 h. The reaction solution was diluted with water (100 mL) and extracted three times with DCM (100 mL). The organic phase was washed with saturated saline solution, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (EA/PE = 1/4) to obtain compound **b** (4.9 g, 72%), as a pale yellowish-white solid.

MS (ESI) m/z 258, 260 $[M + H]^+$.

Step 2:

Compound **b** (2.0 g, 7.75 mmol), bis(pinacolato)diboron (3.94 g, 15.5 mmol), $Pd(dppf)Cl_2$(567 mg, 0.77 mmol), AcOK (2.28 g, 23.25 mmol), and 1,4-dioxane (20 mL) were placed in a sealed tube, which was purged with argon three times. The mixture was reacted at 90°C for 5 h. The reaction was quenched with water and extracted with DCM. The organic phase was washed with saturated saline, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (EA/PE = 1/8 to 1/4) to obtain compound **c** (1.52 g, 64%), as a yellow solid.

MS (ESI) m/z 306 $[M + H]^+$.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70–7.65 (m, 2H), 7.53 (dd, J = 11.5, 1.9 Hz, 1H), 7.20 (dd, J = 8.2, 1.9 Hz, 1H), 5.78 (s, 1H), 5.48 (d, J = 1.7 Hz, 1H), 2.04 (s, 3H), 1.34 (s, 12H).

Step 3:

Compound **d** (2.00 g, 19.6 mmol) and ammonium carbamate (2.29 g, 29.4 mmol) were added sequentially to a flask, followed by the addition of MeOH (40 mL) and iodobenzene diacetate (13.24 g, 41.1 mmol). The reaction solution was stirred uncovered at room temperature for 30 min, then

concentrated under reduced pressure to remove the solvent to obtain the crude product. The crude product was purified by column chromatography (MeOH/DCM = 1/80) to obtain compound **e** (1.62 g), as a white solid.

MS (ESI) m/z 120 $[M + H]^+$.

Step 4:

Compound **e** (282 mg, 2.35 mmol), cesium carbonate (892 mg, 2.74 mmol), 1-bromo-4-iodobenzene (552 mg, 1.96 mmol), $Pd_2(dba)_3$(40 mg, 0.05 mmol), and Xantphos (77 mg, 0.13 mmol) were added to 1,4-dioxane (10 mL), and the reaction solution was heated to 105°C and reacted for 13 h. The reaction solution was filtered through diatomaceous earth; the filtrate was washed with ethyl acetate (50 mL) and saturated saline solution (50 mL), and the organic phase was dried over anhydrous sodium sulfate and concentrated under reduced pressure to obtain the crude product. The crude product was purified by column chromatography (PE/EtOAc = 4/1 to 1/1) to obtain compound **f** (410 mg), as a yellow oily liquid.

MS (ESI) m/z 274 $[M + H]^+$.

Step 5:

To a 100 mL round-bottom flask were added sequentially compound **f** (1.02 g, 3.10 mmol), bis(pinacolato)diboron (0.973 g, 3.83 mmol), Pd(dppf)Cl_2(0.461 mg, 0.63 mmol), potassium acetate (0.943 g, 9.61 mmol), and 1,4-dioxane (20 mL). The mixture was heated to 100°C and reacted for 4 h. After monitoring the reaction to completion, the mixture was cooled to room temperature, filtered through diatomaceous earth, and extracted with ethyl acetate (50 mL × 3), and the organic phases was combined, washed with saturated saline solution (50 mL), and concentrated under reduced pressure to obtain the crude product. The crude product was purified by column chromatography (PE/EtOAc = 1/1) to obtain compound **g** (0.80 g), as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.3 Hz, 2H), 6.98 (d, J = 8.3 Hz, 2H), 3.37–3.30 (m, 1H), 3.15–3.08 (m, 1H), 2.20 (dd, J = 29.3, 6.9 Hz, 2H), 1.26 (s, 6H).

Step 6:

Compound **h** (10.6 g, 0.0466 mol) was dissolved in dichloromethane (100 mL) and trifluoroacetic acid (26.7 g, 0.2334 mol), and stirred at 10°C. N-iodobutyric imide (10.5 g, 0.0466 mol) was added portionwise, and the mixture was reacted for 4 h. Upon completion of the reaction, 150 mL of saturated sodium bicarbonate solution was slowly added dropwise at 10°C, resulting in the precipitation of solids, which was filtrated and dried to obtain compound **i** (13.4 g), as a purple solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 5.61 (s, 2H), 3.80 (s, 3H).

Step 7:

Compound **i** (2 g, 6.5 mmol), compound **c** (2.3 g, 6.5 mmol), tetrakis(triphenylphosphine)palladium (0.65 g, 0.56 mmol), and potassium phosphate (3.6 g, 0.017 mmol) were added to a reaction flask, which was purged with nitrogen three times. Then DMF (35 mL) and water (5 mL) were added, and stirred at 50°C for 16 h. Upon completion of the reaction, water (150 mL) and dichloromethane (200 mL) were added for extraction and liquid-liquid separation. The organic phase was washed with saturated saline solution and concentrated to obtain the crude product. The crude product was purified by column chromatography to obtain compound **j** (1.1 g), as a pale yellow solid.

ESI-MS m/z 404.2 $[M+H]^+$

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.82 (dd, J = 11.7, 2.1 Hz, 1H), 7.69 (s, 1H), 7.44–7.33 (m, 2H), 5.87 (s, 1H), 5.66 (s, 2H), 5.58 (q, J = 1.5 Hz, 1H), 3.66 (d, J = 1.1 Hz, 3H), 2.12 (dd, J = 1.6, 0.9 Hz, 3H).

Step 8:

To a 25 mL round-bottom flask were added sequentially compound **g** (45 mg, 0.14 mmol), compound **j** (50 mg, 0.12 mmol), $Pd(dppf)Cl_2$(20 mg, 0.03 mmol), potassium phosphate (80 mg, 0.38 mmol), 1,4-dioxane (5 mL), and water (1 mL). The reaction was heated to 80°C and reacted for 0.5 h. After monitoring the reaction to completion, the reaction was cooled to room temperature, filtered through diatomaceous earth, and extracted with ethyl acetate (20 mL × 3), and the organic layers were combined, washed with saturated saline solution (20 mL), and concentrated under reduced pressure to obtain the crude product. The crude product was purified by column chromatography (DCM/MeOH = 6/1) to obtain the compound of Formula I-1 (22 mg), as a white solid.

MS (ESI) m/z 519.4 $[M + H]^+$

^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.65–7.61 (m, 1H), 7.48 (s, 1H), 7.05 (d, J = 7.7 Hz, 2H), 7.00 (t, J = 4.1 Hz, 2H), 6.91 (d, J = 8.5 Hz, 2H), 5.73 (s, 1H), 5.45 (d, J = 1.3 Hz, 1H), 4.98 (s, 2H), 3.59 (d, J = 0.9 Hz, 3H), 3.36 (dd, J = 12.6, 6.0 Hz, 2H), 3.13 (dd, J = 12.8, 6.6 Hz, 2H), 2.29–2.19 (m, 3H), 1.99 (d, J = 10.1 Hz, 3H).

Example 2: Preparation of crystal form A of the compound of Formula I-1

The compound of formula I-1 (61 g) was added to 100 mL of ethyl acetate, stirred at room temperature overnight, filtered, and dried to obtain a sample of crystal form A of the compound of formula I-1 (58.2 g), as a white solid.

Example 3: Preparation of the maleate crystal form A of the compound of Formula I-1

3.1: Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of maleic acid were weighed into a 2-mL glass vial, and 0.15 mL of acetonitrile was added to perform a screening experiment using the suspension method. The resulting sample was suspened at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspened at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane, and the resulting solid was vacuum-dried at 50°C for 2 h to yield a sample of the maleate crystal form A of the compound of Formula I-1.

3.2: Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of counterion were weighed into a 2-mL glass vial, and 0.15 mL of dichloromethane was added to perform a screening experiment using the suspension method. The resulting sample was suspended at 50°C for 2 hours, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 hours. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane, and the resulting solid was vacuum-dried at 50°C for 2 hours to yield a sample of the maleate crystal form A of the compound of Formula I-1.

Example 4: Preparation of the monomaleate crystal form B of the compound of Formula I-1

Approximately 20 mg of compound of Formula I-1 and 1.0 equivalent of maleic acid were weighed into a 2-mL glass vial, 0.15 mL of tetrahydrofuran was added to perform a screening experiment using the suspension method. The resulting sample was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane, and the resulting solid was vacuum-dried at 50°C for 2 h to obtain a sample of the monomaleate form B of the compound of Formula I-1.

Example 5: Preparation of the fumarate crystal form A of the Compound of Formula I-1

5.1: Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of fumaric acid were weighed into a 2 mL glass vial, and 0.15 mL of acetonitrile was added to perform a screening experiment using the suspension method. The resulting sample was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane, and the resulting solid was vacuum-dried at 50°C for 2 h to yield a sample of the fumarate crystal form A of the compound of Formula I-1.

5.2: Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of fumaric acid were weighed into a 2-mL glass vial, and 0.15 mL of dichloromethanewas added to perform a screening experiment using the suspension method. The resulting sample was suspended at 50°C for 2 hours, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 hours. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane, and the resulting solid was vacuum-dried at 50°C for 2 hours to obtain a sample of the fumarate crystal form A of the compound of Formula I-1.

Example 6: Preparation of the hemifumarate crystal form B of the compound of Formula I-1

Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of fumaric acid were weighed into a 2-mL glass vial, and 0.15 mL of tetrahydrofuran was added to perform a screening experiment using the suspension method. The resulting sample was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane, and the resulting solid was vacuum-dried at 50°C for 2 h to yield a sample of the hemifumarate crystal form B of the compound of Formula I-1.

Example 7: Preparation of the monoglycolate crystal form A of the compound of Formula I-1

Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of glycolic acid were weighed into a 2 mL glass vial, and 0.15 mL of acetonitrile was added to perform a screening experiment using the suspension method. The resulting sample was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane, and the resulting solid was vacuum-dried at 50°C for 2 h to yield a sample of the monoglycolate crystal form A of the compound of Formula I-1.

Example 8: Preparation of the glycolate crystal form B of the Compound of Formula I-1

8.1: Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of glycolic acid were weighed into a 2 mL glass vial, and 0.15 mL of tetrahydrofuran was added to perform a screening experiment using the suspension method. The resulting mixture was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane, and the resulting solid was vacuum-dried at 50°C for 2 h to yield a sample of the glycolate crystal form B of the compound of Formula I-1.

8.2: Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of glycolic acid were weighed into a 2-mL glass vial, and 0.15 mL of dichloromethane was added to perform a screening experiment using the suspension method. The resulting sample was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane, and the resulting solid was vacuum-dried at 50°C for 2 h to obtain a sample of the glycolate form B of the compound of Formula I-1.

Example 9: Preparation of the mono L-malate crystal form A of the compound of Formula I-1

9.1: Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of L-malic acid were weighed into a 2-mL glass vial, and 0.15 mL of tetrahydrofuran was added to perform a screening experiment using the suspension method. The resulting mixture was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane. The resulting solid was vacuum-dried at 50°C for 2 h to yield a sample of the mono L-malate crystal form A of the compound of Formula I-1.

9.2: Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of glycolic acid were weighed into a 2-mL glass vial, and 0.15 mL of dichloromethane was added to perform a screening experiment using the suspension method. The resulting sample was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane. The resulting solid was vacuum-dried at 50°C for 2 h to yield a sample of the mono L-malate crystal form A of the compound of Formula I-1.

9.3: Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of glycolic acid were weighed into a 2-mL glass vial, and 0.15 mL of acetonitrile was added to perform a screening experiment using the suspension method. The resulting sample was suspended at 50°C for 2 hours, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 hours. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane. The resulting solid was vacuum-dried at 50°C for 2 hours to yield a sample of the mono L-malate crystal form A of compound of Formula I-1.

Example 10: Preparation of the monosuccinate crystal form A of the compound of Formula I-1

10.1: Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of succinic acid were weighed into a 2 mL glass vial, and 0.15 mL of acetonitrile was added to perform a screening experiment using the suspension method. The resulting mixture was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane. The resulting solid was vacuum-dried at 50°C for 2 h to obtain a sample of the monosuccinate crystal form A of compound of Formula I-1.

10.2: Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of succinic acid were weighed into a 2-mL glass vial, and 0.15 mL of dichloromethane was added to perform a screening experiment using the suspension method. The resulting sample was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane. The resulting solid was vacuum-dried at 50°C for 2 h to obtain a sample of the monosuccinate crystal form A of the compound of Formula I-1.

Example 11: Preparation of the sulfate crystal form A of the compound of Formula I-1

Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of sulfuric acid were weighed into a 2 mL glass vial, and 0.15 mL of acetonitrile was added to perform a screening experiment using the suspension method. The resulting sample was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane. The resulting solid was vacuum-dried at 50°C for 2 h to yield a sample of the sulfate crystal form A of the compound of Formula I-1.

Example 12: Preparation of the L-tartrate crystal form A of the compound of Formula I-1

Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of L-tartaric acid were weighed into a 2-mL glass vial, and 0.15 mL of acetonitrile was added to perform a screening experiment using the suspension method. The resulting sample was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane. The resulting solid was vacuum-dried at 50°C for 2 h to obtain a sample of the L-tartarate crystal form A of the compound of Formula I-1.

Example 13: Preparation of the hippurate crystal form A of the compound of Formula I-1

Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of hippuric acid were weighed into a 2 mL glass vial, and 0.15 mL of tetrahydrofuran was added to perform a screening experiment using the suspension method. The resulting sample was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane. The resulting solid was vacuum-dried at 50°C for 2 h to yield a sample of the hippurate crystal form A of the compound of Formula I-1.

Example 14: Preparation of the glutarate crystal form A of the compound of Formula I-1

14.1: Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of glutaric acid were weighed into a 2-mL glass vial, and 0.15 mL of acetonitrile was added to perform a screening experiment using the suspension method. The resulting mixture was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane. The resulting solid was vacuum-dried at 50°C for 2 h to yield a sample of the glutarate crystal form A of the compound of Formula I-1.

14.2: Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of glutaric acid were weighed into a 2-mL glass vial, and 0.15 mL of dichloromethane was added to perform a screening experiment using the suspension method. The resulting sample was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane. The resulting solid was vacuum-dried at 50°C for 2 h to yield a sample of the glutarate crystal form A of the compound of Formula I-1.

Example 15: Preparation of the p-toluenesulfonate crystal form A of the compound of Formula I-1

Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of p-toluenesulfonic acid were weighed into a 2 mL glass vial, and 0.15 mL of acetonitrile was added to perform a screening experiment using the suspension method. The resulting mixture was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane. The resulting solid was vacuum-dried at 50°C for 2 h to obtain a sample of the p-toluenesulfonate crystal form A of the compound of Formula I-1.

Example 16: Preparation of the p-toluenesulfonate crystal form B of the compound of Formula I-1

Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of p-toluenesulfonic acid were weighed into a 2 mL glass vial, and 0.15 mL of tetrahydrofuran was added to perform a screening experiment using the suspension method. The resulting sample was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane. The resulting solid was vacuum-dried at 50°C for 2 h to obtain a sample of the p-toluenesulfonate crystal form B of the compound of Formula I-1.

Example 17: Preparation of the methanesulfonate crystal form A of the compound of Formula I-1

Approximately 20 mg of the compound of Formula I-1 and 1.0 equivalent of methanesulfonic acid were weighed into a 2 mL glass vial, and 0.15 mL of tetrahydrofuran was added to perform a screening experiment using the suspension method. The resulting mixture was suspended at 50°C for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane. The resulting solid was vacuum-dried at 50°C for 2 h to obtain a sample of the methanesulfonate crystal form A of the compound of Formula I-1.

Example 18: Preparation of the hydrochloride crystal form C1 of the compound of Formula I-1

Compound of Formula I-1 (16.5 g) was added to ethyl acetate (165 mL), cooled to approximately 0°C, and 1.0 equivalent of a 4 M solution of hydrochloric acid in dioxane was added dropwise. After the addition was complete, the mixture was allowed to warm to room temperature and stirred overnight, then filtered and dried to obatin a sample of the hydrochloride crystal form C1 of the compound of Formula I-1 (18.3 g), as a white solid.

Example 19: Preparation of the hydrochloride crystal form C2 of the compound of Formula I-1

Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, 0.2–0.5 mL of 2-methyl-tetrahydrofuran was added, and the mixture was suspended under magnetic stirring at 25°C at a speed of 300–400 rpm. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the sample of the hydrochloride crystal form C2 of the compound of Formula I-1.

Example 20: Preparation of the hydrochloride crystal form D of the compound of Formula I-1

Approximately 40 mg of the compound of Formula I-1 and 1.05 equivalents of hydrochloric acid (dilute hydrochloric acid diluted 10-fold with acetone) were weighed into a 2 mL glass vial, and the screening solvent was added to perform the screening experiment using the suspension method. The resulting sample was suspended at 50°C (35°C, dichloromethane) for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane. The resulting solid was vacuum-dried at 50°C for 2 h to yield a sample of the hydrochloride crystal form D of the compound of Formula I-1.

Example 21: Preparation of the hydrochloride crystal form E1 of the compound of Formula I-1

3.0 g of the compound of Formula I-1 was weighed to a 40 mL glass bottle. 4.6 mL of ethanol and approximately 1.2 equivalents of HCl (a 12 N HCl aqueous solution was diluted with ethanol to 1.2 N) were added, and stirred for 10 minutes at 50°C. Approximately 5 mg of

the seed crystal of hydrochloride crystal form E2 of the compound of Formula I-1 was added to the system, and stirred at 50°C for 2 h, then the solution was cooled naturally to 25°C and stirred at 25°C for 3 days. ~0.1 equivalents of HCl (12N HCl aqueous solution was diluted with ethanol to 1.2N) was added to the system and stirred at 25°C for another 1 day. The solid fraction was collected by vacuum filtration, and the resulting solid was dried under vacuum at 25°C for approximately 17 hours. The obtained solid was then dried further under vacuum at 50°C for 2 hours to yield a sample of the hydrochloride crystal form E1 of the compound of Formula I-1 (2.8 g), as a nearly white solid.

Example 22: Preparation of the hydrochloride crystal form E2 of the compound of Formula I-1

Approximately 40 mg of the compound of Formula I-1 and 1.05 equivalents of hydrochloric acid (dilute hydrochloric acid diluted 10-fold with ethanol) were weighed into a 2 mL glass vial, and the screening solvent was added to perform the screening experiment using the suspension method. The resulting sample was suspended at 50°C (35°C, dichloromethane) for 2 h, then allowed to cool naturally to 25°C, and suspended at 25°C for at least 48 h. The resulting suspension was centrifuged at 14,000 rpm through a 0.45 μm nylon filter membrane. The resulting solid was a sample of hydrochloride crystal form F of the compound of Formula I-1, and it was vacuum-dried at 50°C for 2 h to obtain a sample of the hydrochloride crystal form E2 of the compound of Formula I-1.

Example 23: Preparation of the hydrochloride crystal form F of the compound of Formula I-1

23.1: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.2–0.5 mL of ethanol was added, and the mixture was suspended under magnetic stirring at 25°C at a speed of 300–400 rpm. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was a sample of the hydrochloride crystal form F of the compound of Formula I-1.

23.2: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.2–0.5 mL of acetone was added, and the mixture was suspended under magnetic stirring at 25°C at a speed of 300–400 rpm. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was a sample of the hydrochloride crystal form F of the compound of Formula I-1.

23.3: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of formula I-1 were weighed, and 0.2–0.5 mL of acetonitrile was added, and the mixture was suspended under magnetic stirring at 25°C at a speed of 300–400 rpm. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was a sample of the hydrochloride crystal form F of the compound of Formula I-1.

23.4: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of formula I-1 were weighed, and 0.2–0.5 mL of tetrahydrofuran was added, and the mixture was suspended under magnetic stirring at 25°C at a speed of 300–400 rpm. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was a sample of the hydrochloride crystal form F of the compound of Formula I-1.

23.5: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.2–0.5 mL of methyl isobutyl ketone/trifluoroethanol (9:1, v/v) was added, and the mixture was suspended under magnetic stirring at 25°C at a speed of 300–400 rpm. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form F of compound of Formula I-1.

23.6: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of ethanol was added, and the mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 50°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form F of compound of Formula I-1.

23.7: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of acetone was added, and the mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 50°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form F of the compound of Formula I-1.

23.8: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of ethyl acetate was added, and the mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 50°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form F of the compound of Formula I-1.

23.9: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of acetonitrile was added, and the mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 50°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form F of the compound of Formula I-1.

23.10: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of tetrahydrofuran was added, and the mixture was suspended under magnetic stirring at 50°C at a speed of 300–400 rpm. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form F of the compound of Formula I-1.

23.11: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of methyl isobutyl ketone/trifluoroethanol (9/1, v/v) was added, and the mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 50°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form F of the compound of Formula I-1.

23.12: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of ethanol was added. The mixture was subjected to 10 heating-cooling cycles between 5°C and 50°C at a rate of 0.1°C/min, while suspended under magnetic stirring at a speed of 300–400 rpm, and the temperature at sampling was 10°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form F of the compound of Formula I-1.

23.13: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of acetone was added. The mixture was subjected to 10 heating-cooling cycles between 5°C and 50°C at a rate of 0.1°C/min, while suspended under magnetic stirring at a speed of 300–400 rpm, and the temperature at sampling was 10°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form F of the compound of Formula I-1.

23.14: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of ethyl acetate was added. The mixture was subjected to 10 heating-cooling cycles between 5°C and 50°C at a rate of 0.1°C/min, while suspended under magnetic stirring at a speed of 300–400 rpm, and the temperature at sampling was 10°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form F of the compound of Formula I-1.

23.15: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of acetonitrile was added. The mixture was subjected to 10 heating-cooling cycles between 5°C and 50°C at a rate of 0.1°C/min, while suspended under magnetic stirring at a speed of 300–400 rpm, and the temperature at sampling was 10°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form F of the compound of Formula I-1.

23.16: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of tetrahydrofuran was added. The mixture was subjected to 10 heating-cooling cycles between 5°C and 50°C at a rate of 0.1°C/min, while suspended under magnetic stirring at a speed of 300–400 rpm, and the temperature at sampling was 10°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form F of the compound of Formula I-1.

23.17: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of methyl isobutyl ketone/trifluoroethanol (9:1, v/v) was added. The mixture was subjected to 10 heating-cooling cycles between 5°C and 50°C at a rate of 0.1°C/min, while suspended under magnetic stirring at a speed of 300–400 rpm, and the temperature at sampling was 10°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form F of the compound of Formula I-1.

Example 24: Preparation of the hydrochloride crystal form G of the compound of Formula I-1

24.1: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.2–0.5 mL of water was added, and the mixture was suspended under magnetic stirring at 25°C at a speed of 300–400 rpm. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form G of the compound of Formula I-1.

24.2: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of methanol was added, and the mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 50°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form G of the compound of Formula I-1.

24.3: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of methyl isobutyl ketone/trifluoroethanol (9:1, v/v) was added. The mixture was subjected to 10 heating-cooling cycles between 5°C and 50°C at a rate of 0.1°C/min, while suspended under magnetic stirring at a speed of 300–400 rpm, and the temperature at sampling was 10°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form G of the compound of Formula I-1.

Example 25: Preparation of the hydrochloride crystal form H of the compound of Formula I-1

25.1: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.2–0.5 mL of methanol/water (1:1, v/v) was added, and the mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 25°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm

nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form H of the compound of Formula I-1.

25.2: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of methanol/water (1:1, v/v) was added, and the mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 50°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form H of the compound of Formula I-1.

Example 26: Preparation of the hydrochloride crystal form I of the compound of Formula I-1

26.1: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of methanol was added, and the mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 50°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form I of the compound of Formula I-1.

26.2: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and the minimum volume of methanol was added to dissolve it thoroughly at 25°C. The resulting dilute suspension was filtered through a 0.45 μm nylon filter cartridge to obtain a clear solution. 0.8 mL of each clear solution was taken, and 8 mL of methyl tert-butyl ether was added slowly to each. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form I of the compound of Formula I-1.

Example 27: Preparation of the hydrochloride crystal form J1 of the compound of Formula I-1

27.1: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of 2-methyl-tetrahydrofuran was added, and the mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 50°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form J1 of the compound of Formula I-1.

27.2: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of 2-methyl tetrahydrofuran was added. The mixture was subjected to 10 heating-cooling cycles between 5°C and 50°C at a rate of 0.1°C/min, while suspended under magnetic stirring at a speed of 300–400 rpm, and the temperature at sampling was 10°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form J1 of the compound of Formula I-1.

Example 28: Preparation of the hydrochloride crystal form J2 of the compound of Formula I-1

The sample of the hydrochloride crystal form J1 of the compound of Formula I-1 was heated to 110°C to obtain a solid sample of the hydrochloride crystal form J2 of the compound of Formula I-1.

Example 29: Preparation of the hydrochloride crystal form K of the compound of Formula I-1

29.1: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of methyl tert-butyl ether was added, and the mixture was suspended under magnetic stirring at 50°C at a speed of 300–400 rpm. The

resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form K of the compound of Formula I-1.

29.2: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of methyl tert-butyl ether was added. The mixture was subjected to 10 heating-cooling cycles between 5°C and 50°C at a rate of 0.1°C/min, while suspended under magnetic stirring at a speed of 300–400 rpm, and the temperature at sampling was 10°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form K of the compound of Formula I-1.

29.3: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of toluene was added. The mixture was subjected to 10 heating-cooling cycles between 5°C and 50°C at a rate of 0.1°C/min, while suspended under magnetic stirring at a speed of 300–400 rpm, and the temperature at sampling was 10°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form K of the compound of Formula I-1.

Example 30: Preparation of the hydrochloride crystal form L of the compound of Formula I-1

30.1: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of toluene was added. The mixture was suspended under magnetic stirring at 25°C at a speed of 300–400 rpm. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form L of the compound of Formula I-1.

30.2: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of toluene was added. The mixture was suspended under magnetic stirring at 50°C at a speed of 300–400 rpm. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form L of the compound of Formula I-1.

Example 31: Preparation of the hydrochloride crystal form M of the compound of Formula I-1

31.1: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of isopropanol/dimethyl sulfoxide (9:1, v/v) was added. The mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 25°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form M of the compound of Formula I-1.

31.2: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of isopropyl acetate/dimethyl sulfoxide (9:1, v/v) was added. The mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 25°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form M of the compound of Formula I-1.

31.3: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of dimethyl sulfoxide/water (1/1, v/v) was added. The mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 25°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm

nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form M of the compound of Formula I-1.

31.4: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of isopropanol/dimethyl sulfoxide (9:1, v/v) was added. The mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 50°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form M of the compound of Formula I-1.

31.5: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of isopropyl acetate/dimethyl sulfoxide (9:1, v/v) was added. The mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 50°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form M of the compound of Formula I-1.

31.6: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of dimethyl sulfoxide/water (1/1, v/v) was added. The mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 50°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form M of the compound of Formula I-1.

31.7: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of isopropanol/dimethyl sulfoxide (9:1, v/v) was added. The mixture was subjected to 10 heating-cooling cycles between 5°C and 50°C at a rate of 0.1°C/min, while suspended under magnetic stirring at a speed of 300–400 rpm, and the temperature at sampling was 10°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form M of the compound of Formula I-1.

31.8: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of isopropyl acetate/dimethyl sulfoxide (9:1, v/v) was added. The mixture was subjected to 10 heating-cooling cycles between 5°C and 50°C at a rate of 0.1°C/min, while suspended under magnetic stirring at a speed of 300–400 rpm, and the temperature at sampling was 10°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form M of the compound of Formula I-1.

31.9: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of dimethyl sulfoxide/water (1:1, v/v) was added. The mixture was subjected to 10 heating-cooling cycles between 5°C and 50°C at a rate of 0.1°C/min, while suspended under magnetic stirring at a speed of 300–400 rpm, and the temperature at sampling was 10°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form M of the compound of Formula I-1.

Example 32: Preparation of the hydrochloride crystal form N of the compound of Formula I-1

32.1: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.2–0.5 mL of methanol was added. The mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 25°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form N of the compound of Formula I-1.

32.2: Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.1–0.5 mL of methanol was added. The mixture was subjected

to 10 heating-cooling cycles between 5°C and 50°C at a rate of 0.1°C/min, while suspended under magnetic stirring at a speed of 300–400 rpm, and the temperature at sampling was 10°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form N of the compound of Formula I-1.

Example 33: Preparation of the hydrochloride crystal form O of the compound of Formula I-1

Approximately 40 mg of the hydrochloride crystal form E1 of the compound of Formula I-1 was weighed, and 0.2–0.5 mL of dichloromethane was added. The mixture was suspended under magnetic stirring at a speed of 300–400 rpm at 25°C. The resulting suspension was subjected to centrifugal filtration at 14,000 rpm using a 0.45 μm nylon-membrane centrifuge tube. The resulting solid was the hydrochloride crystal form O of the compound of Formula I-1.

Experimental Example 1: Solid Stability and Solubility of the Hydrochloride Crystal Form I of the Compound of Formula I-1

1.1 Solid Stability of the Hydrochloride Crystal Form I of the Compound of Formula I-1

An open container containing the hydrochloride crystal form I of the compound of formula I-1 was placed at 25°C/60% RH for one week. A sealed container containing the hydrochloride crystal form I of the compound of formula I-1 was placed at 60°C for one week. Stability samples under these conditions were subjected to XRPD, HPLC, and stoichiometric ratio testing, and visual observation was performed for color changes of the samples.

Table 33 Solid Stability of Hydrochloride Crystal Form I of the Compound of Formula I-1

Experiment No.	Initial Purity	99.6%	
	Initial stoichiometric ratio (IC-HPLC)	Compound of formula (I): HCl = 1:0.97	
		Purity	Color
1	Solid, 25°C/60% RH, open container, 1 week		
	Solid (HPLC)	99.5%	No color change
	Stoichiometric ratio (IC-HPLC)	Compound of formula (I): HCl = 1:0.99	
	Solid (XRPD)	Hydrochloride crystal form I (no change)	
2	Solid, 60°C, sealed container, 1 week		
	Solid (HPLC)	99.6%	No color change
	Stoichiometric ratio (IC-HPLC)	Compound of formula (I): HCl = 1:0.98	
	Solid (XRPD)	Hydrochloride crystal form I (no change)	

1.2 Solubility of the Free-base Crystal Form A of the Compound of Formula I-1

10 mg of the free-base crystal form A of the compound of formula I-1 or 10.8 mg (equivalent to 10 mg of the free-base anhydrous form) of the hydrochloride crystal form I of the compound of formula I-1 was weighed and placed in an 8 mL glass vial. 5 mL of dissolution medium was added. The resulting suspension/clear solution was stirred at 37°C and 400 rpm for 2 h, 8 h, and 24 h, then the resulting suspension/clear solution was centrifuged at 37°C and 14,000 rpm for 5 min. The solubility of the supernatant was determined by HPLC,

and the pH of the supernatant was measured by a pH meter, and the residual solid was detected by XRPD.

Table 34 Solubility testing of the free-base crystal form A of compound of formula I-1

Method	Solubility at 37°C, target concentration of 2 mg/mL (calculated as free-base form), equilibrated for 24 h, LOQ: 0.0003 mg/mL			
Experiment No.	Dissolution Medium	Solubility (mg/mL)		Residual solid XRPD
		2 h	24 h (pH)	
1	Water	0.0012	0.0013 (7.72)	Free-base form A
2	FaSSGF, pH 1.6	0.38	0.42 (1.55)	Free-base form A
3	FaSSIF-v1, pH 6.5	0.0004	0.0011 (6.50)	Free-base form A
4	FeSSIF-v1, pH 5.0	0.0045	0.0066 (4.97)	Free-base form A

Table 35 Solubility testing of the hydrochloride crystal form I of the compound of Formula I-1

Method	Solubility at 37°C, target concentration of 2 mg/mL (calculated as free-base form), equilibrated for 24 h, LOQ: 0.0002 mg/mL				
Experiment No.	Dissolution Medium	Solubility (mg/mL)			Residual solid XRPD
		2 h	8h	24 h (pH)	
1	Water	0.12	0.10	0.10 (2.55)	Free-base form A
2	FaSSGF, pH 1.6	≥2.0	≥2.0	1.7 (1.56)	-
3	FaSSIF-v1, pH 6.5	0.001	0.001	0.002 (6.18)	Free-base form A
4	FeSSIF-v1, pH 5.0	0.015	0.015	0.015 (4.90)	Free-base form A

Conclusion: The hydrochloride crystal form I of the compound of Formula I-1 exhibited no change in total impurities or crystal form, showing favorable physical stability. Moreover, compared with the free-base crystal form of the compound of formula I-1, hydrochloride crystal form I of the compound of Formula I-1 displayed significantly improved solubility in all four media tested.

Experiment Example 2: FGFR2 receptor activity inhibition assay for the hydrochloride crystal form I

2.3 Assessment of the activity of hydrochloride crystal form I of the compound of Formula I-1 on FGFR2 background cells

This experiment investigates the compound's ability to inhibit cell proliferation by assessing its effect on in vitro cell viability in seven tumor cell lines (KATO III, NCI-H716, SNU-16, AN3CA, MFE-296, SUM52PE, MFM223).

The cell lines were cultured in an incubator at 37°C and 5% CO_2 under standard conditions, passaged periodically, and cells in the logarithmic growth phase were used for plating. The test compounds were prepared as 10 mM solutions using DMSO.

Preparation of the compound storage plate (tube): A 4-fold serial dilution with DMSO was set up from the highest to the lowest concentration to generate a total of 9 concentrations,

and the internal reference compound was likewise subjected to 4-fold serial dilution to generate another 9 concentrations. Next, the compound working solutions were prepared as follows: 98 μL of cell culture medium was added to each well of a flat-bottomed 96-well transparent plate, and 2 μL of compound was pipetted from the compound storage plate to the cell culture medium in the 96-well plate. 2 μL of DMSO was added to the solvent control well. After the compound or DMSO was added, it was mixed thoroughly by pipetting.

Cell seeding and drug administration: 1) Cells were stained with trypan blue and live cells were counted, cell viability must be ≥90%; 2) The cell concentration was adjusted to an appropriate level; 3) 95 μL of cell suspension was added to each well of the compound assay plate (6,000–10,000 cells/well), and cell-free medium (containing 0.1% DMSO) was added to the Min control wells; 4) Compound administration in the compound assay plate: 5 μL of a 20× compound stock solution was added to the cell culture plate as shown in Table 1. 5 μL of a DMSO-cell culture medium mixture was added to the Max control well. The final DMSO concentration was 0.1%; 5) The culture plate was incubated in a 37°C, 5% CO_2 incubator for 72–96 hours.

The assay was performed according to the instructions for the Promega CellTiter-Glo Luminescent Cell Viability Assay Kit (Promega-G7573): 1) CellTiter-Glo buffer was thawed and equilibrated to room temperature; 2) CellTiter-Glo substrate was equilibrated to room temperature; 3) CellTiter-Glo buffer was added to one bottle of CellTiter-Glo substrate to dissolve the substrate, thereby the CellTiter-Glo working solution was prepared; 4) Slow vortex was performed to ensure complete dissolution; 5) The cell culture plate was taken and placed for 10 minutes to be equilibrated to room temperature; 6) 50 μL of CellTiter-Glo working solution (equivalent to half the volume of the cell culture medium in each well) was added to each well; 7) The plate was shaken on a shaking incubator for 2 minutes to induce cell lysis; 8) The plate was placed at room temperature for 10 minutes to stabilize the luminescence signal; 9) The luminescence signal was measured using a SpectraMax Paradigm reader.

The cell proliferation inhibition rate data is calculated using the following formula:

Inhibition Rate (Inh%) = 100 - (RLU_{Drug} - RLU_{Min}) / (RLU_{Max} - RLU_{Min}) × 100%.

The inhibition rates corresponding to different compound concentrations was calculated in Excel, then GraphPad Prism software was used to plot inhibition rate curves and the relevant parameters were calculated, including the maximum and minimum inhibition rates, IC_{50} value.

Table 36 Results of the inhibitory effects of test compounds on the proliferation of FGFR2 background cell lines

Cell Line	Hydrochloride crystal form I of compound of Formula I-1 IC_{50}(nM)
KATO III	0.8
NCI-H716	2.4
SNU-16	3.0
AN3CA	9.9
MFE-296	14.9
SUM52PE	6.2
MFM223	1.0

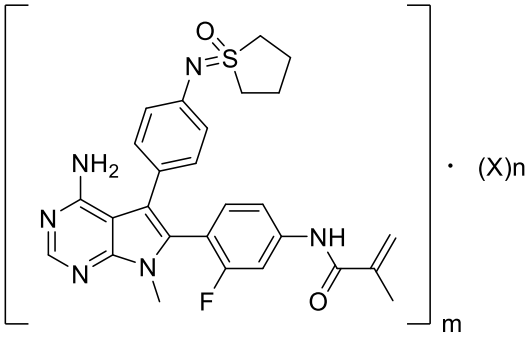
As shown in Table 36, the compounds of the present invention exhibit good inhibitory

effects on cell proliferation of FGFR2 background cells.

All documents mentioned in the present invention are cited herein as references, as if each document were individually cited as a reference. Furthermore, it should be understood that, after reading the description of the present invention, those skilled in the art may make various changes or modifications to the present invention, and such equivalent forms also fall within the scope defined by the appended claims.

Claim

1. A compound of formula (I),



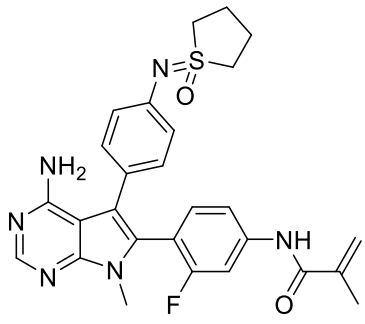
(I)

in an amorphous form or a crystal form or a solvate thereof;

wherein m is 1, 2, 3, 4, 5, 6, 7, 8, or 9;

n is 0, 0.5, 1, 1.5, 2, 2.5, or 3; and X is selected from the group consisting of: hydrochloric acid, hydrobromic acid, hydrofluoric acid, sulfuric acid, nitric acid, or phosphoric acid, formic acid, acetic acid, trifluoroacetic acid, propionic acid, oxalic acid, malonic acid, succinic acid, fumaric acid, maleic acid, lactic acid, malic acid, tartaric acid, citric acid, picric acid, benzoic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, benzenesulfonic acid, naphthalenesulfonic acid, hippuric acid, glycolic acid, or glutaric acid.

2. A crystal form A of the compound of formula (I) according to claim 1, wherein, the compound of formula (I) is I-1, n = 0, and the X-ray powder diffraction pattern of the crystal form A has 2θ angles selected from the group consisting of: 14.16 ± 0.2°, 16.74 ± 0.2°, and 23.01 ± 0.2°,



(I-1).

3. A method for preparing the crystal form A according to claim 2, wherein, the method comprises the following steps:

a. dissolving or dispersing compound I-1 in acetonitrile, an alcoholic solvent, an ester solvent, an ether solvent, or a mixed solvent of the alcoholic solvent and water at a volume ratio of 1-5 times;

b. performing recrystallization or slurrying;

wherein the alcoholic solvent is selected from the group consisting of: methanol, ethanol, isopropanol, or a combination thereof;

the ester solvent is selected from the group consisting of: ethyl acetate, isopropyl acetate, methyl formate, ethyl formate, isopropyl formate, or a combination thereof;

the ether solvent is selected from the group consisting of: methyl tert-butyl ether, tetrahydrofuran, ethylene glycol dimethyl ether, or a combination thereof;

the mixed solvent of the alcoholic solvent and water is selected from the group consisting of: a mixture of methanol and water, a mixture of ethanol and water, or a mixture of isopropanol and water; wherein the volume ratio of the alcoholic solvent to water is 1: (0.1–1.5).

4. A crystal form of the compound of formula (I) according to claim 1, wherein, the compound of formula (I) is a salt formed by compound I-1 and an acid; wherein the acid is an inorganic acid or an organic acid;

preferably, the inorganic acid is selected from the group consisting of: hydrochloric acid, hydrobromic acid, hydrofluoric acid, sulfuric acid, nitric acid, or phosphoric acid;

preferably, the organic acid is selected from the group consisting of: formic acid, acetic acid, trifluoroacetic acid, propionic acid, oxalic acid, malonic acid, succinic acid, fumaric acid, maleic acid, lactic acid, malic acid, tartaric acid, citric acid, picric acid, benzoic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, benzenesulfonic acid, naphthalenesulfonic acid, hippuric acid, glycolic acid, or glutaric acid;

preferably, the molar ratio of compound I-1 to the acid is 1: (0.8–3); more preferably, 1: (0.8–2).

5. The crystal form according to claim 4, wherein, the crystal form is the maleate crystal form A of the compound of formula I-1, the X-ray powder diffraction pattern of the maleate crystal form A has 2θ angles selected from the group consisting of: 15.17 ± 0.2°, 23.02 ± 0.2°, 24.42 ± 0.2°;

the crystal form is the monomaleate crystal form B of the compound of Formula I-1, the X-ray powder diffraction pattern of the monomaleate crystal form B has 2θ angles selected from the group consisting of: 16.57±0.2°, 17.38 ± 0.2°, and 20.39 ± 0.2°;

the crystal form is the fumarate crystal form A of the compound of formula I-1, the X-ray powder diffraction pattern of the fumarate crystal form A has 2θ angles selected from the group consisting of: 5.11±0.2°, 14.23±0.2°, 28.85 ± 0.2°;

the crystal form is the hemifumarate crystal form B of the compound of formula I-1, the X-ray powder diffraction pattern of the hemifumarate crystal form B has 2θ angles selected from the group consisting of: 5.12±0.2°, 14.24±0.2°, 10.20±0.2°;

the crystal form is the monoglycolate crystal form A of the compound of formula I-1, the X-ray powder diffraction pattern of the monoglycolate crystal form A has 2θ angles selected from the group consisting of: 18.22±0.2°, 22.83±0.2°, 26.41±0.2°;

the crystal form is the glycolate crystal form B of the compound of formula I-1, the X-ray powder diffraction pattern of the glycolate crystal form B has 2θ angles selected from the group consisting of: 13.87±0.2°, 17.30±0.2°, 19.49±0.2°, 23.50±0.2°;

the crystal form is of the compound of formula I-1, the X-ray powder diffraction pattern of the mono-L-malate crystal form A has 2θ angles selected from the group consisting of: 17.99±0.2°, 22.58±0.2°, and 24.00±0.2°;

the crystal form is the monosuccinate crystal form A of the compound of formula I-1, the X-ray powder diffraction pattern of the monosuccinate crystal form A has 2θ angles selected from the group consisting of: 18.40±0.2°, 24.09 ± 0.2°, and 24.62 ± 0.2°;

the crystal form is sulfate crystal form A of the compound of formula I-1, the X-ray powder diffraction pattern of sulfate crystal form A has 2θ angles selected from the group consisting of: 14.97±0.2°, 20.21±0.2°, 22.58 ± 0.2°;

the crystal form is the L-tartrate crystal form A of the compound of Formula I-1, the X-ray powder diffraction pattern of the L-tartrate crystal form A has 2θ angles selected from the group consisting of: 5.53±0.2°, 16.95±0.2°, 20.79±0.2°;

the crystal form is the hippurate crystal form A of the compound of Formula I-1, the X-ray powder diffraction pattern of the hippurate crystal form A has 2θ angles selected from the group consisting of: 6.17±0.2°, 12.30 ± 0.2°, and 18.78 ± 0.2°;

the crystal form is the glutarate crystal form A of the compound of Formula I-1, the X-ray powder diffraction pattern of the glutarate crystal form A has 2θ angles selected from the group consisting of: 17.82±0.2°, 23.20 ± 0.2°, and 24.47 ± 0.2°;

the crystal form is the p-toluenesulfonate crystal form A of the compound of Formula I-1, the X-ray powder diffraction pattern of the p-toluenesulfonate crystal form A has 2θ angles

selected from the group consisting of: 19.12±0.2°, 20.11 ± 0.2°, and 20.53 ± 0.2°;

the crystal form is the p-toluenesulfonate crystal form B of the compound of formula I-1, the X-ray powder diffraction pattern of p-toluenesulfonate crystal form B has 2θ angles selected from the group consisting of: 13.95±0.2°, 19.52 ± 0.2°, and 25.40 ± 0.2°;

the crystal form is the methanesulfonate crystal form A of the compound of formula I-1, the X-ray powder diffraction pattern of the methanesulfonate crystal form A has 2θ angles selected from the group consisting of: 19.57±0.2°, 14.27±0.2°, 24.99±0.2°;

the crystal form is the hydrochloride crystal form C1 of the compound of Formula I-1, the X-ray powder diffraction pattern of the hydrochloride crystal form C1 has 2θ angles selected from the group consisting of: 7.73±0.2°, 19.57±0.2°, 19.78 ± 0.2°;

the crystal form is the hydrochloride crystal form C2 of the compound of formula I-1, the X-ray powder diffraction pattern of the hydrochloride crystal form C2 has 2θ angles selected from the group consisting of: 7.79±0.2°, 19.66±0.2°, 19.82 ± 0.2°;

the crystal form is the hydrochloride crystal form D of the compound of formula I-1, the X-ray powder diffraction pattern of the hydrochloride crystal form D has 2θ angles selected from the group consisting of: 15.93±0.2°, 20.09±0.2°, 20.41 ± 0.2°;

the crystal form is the hydrochloride crystal form E1 of the compound of formula I-1, the X-ray powder diffraction pattern of the hydrochloride crystal form E1 has 2θ angles selected from the group consisting of: 7.90±0.2°, 14.06 ± 0.2 °, 20.19 ± 0.2 °;

the crystal form is the hydrochloride crystal form E2 of the compound of formula I-1, the X-ray powder diffraction pattern of the hydrochloride crystal form E2 has 2θ angles selected from the group consisting of: 7.88±0.2°, 14.14±0.2°, 19.75 ± 0.2°;

the crystal form is the hydrochloride crystal form F of the compound of Formula I-1, wherein the X-ray powder diffraction pattern of the hydrochloride crystal form F has 2θ angles selected from the group consisting of: 7.65±0.2°, 11.47 ± 0.2°, and 13.93 ± 0.2°;

the crystal form is the hydrochloride crystal form G of the compound of formula I-1, the X-ray powder diffraction pattern of the hydrochloride crystal form G has 2θ angles selected from the group consisting of: 15.52±0.2°, 16.77 ± 0.2°, and 23.04 ± 0.2°;

the crystal form is the hydrochloride crystal form H of the compound of formula I-1, the X-ray powder diffraction pattern of the hydrochloride crystal form H has 2θ angles selected from the group consisting of: 5.83±0.2°, 16.67±0.2°, 18.40 ± 0.2°;

the crystal form is hydrochloride crystal form I, the X-ray powder diffraction pattern of the hydrochloride crystal form I has 2θ angles selected from the group consisting of: 6.68 ± 0.2°, 13.34 ± 0.2°, and 21.42 ± 0.2°;

the crystal form is hydrochloride crystal form J1, the X-ray powder diffraction pattern of hydrochloride crystal form J1 comprises 2θ angles selected from the group consisting of: 6.80±0.2°, 14.87±0.2°, and 20.41±0.2°;

the crystal form is hydrochloride crystal form J2, the X-ray powder diffraction pattern of hydrochloride crystal form J2 has 2θ angles selected from the group consisting of: 14.69 ± 0.2°, 18.89 ± 0.2°, and 22.23 ± 0.2°;

the crystal form is hydrochloride crystal form K, the X-ray powder diffraction pattern of the hydrochloride crystal form K has 2θ angles selected from the group consisting of: 14.93 ± 0.2°, 16.08 ± 0.2°, and 23.68 ± 0.2°;

the crystal form is hydrochloride crystal form L, the X-ray powder diffraction pattern of hydrochloride crystal form L has 2θ angles selected from the group consisting of: 16.89 ± 0.2°, 21.69 ± 0.2°, and 22.60 ± 0.2°;

the crystal form is hydrochloride crystal form M, the X-ray powder diffraction pattern of hydrochloride crystal form M has 2θ angles selected from the group consisting of: 14.17 ± 0.2°, 20.82 ± 0.2°, and 22.60 ± 0.2°;

the crystal form is hydrochloride crystal form N, the X-ray powder diffraction pattern of hydrochloride crystal form N has 2θ angles selected from the group consisting of: 16.19 ±

0.2°, 20.10 ± 0.2°, and 28.42 ± 0.2°; or

the crystal form is hydrochloride crystal form O, the X-ray powder diffraction pattern of hydrochloride crystal form O has 2θ angles selected from the group consisting of: 15.51 ± 0.2°, 18.36 ± 0.2°, and 20.17 ± 0.2°.

6. The crystal form according to claim 5, wherein, the X-ray powder diffraction pattern of the maleate crystal form A further comprises one or more 2θ angles selected from the group consisting of: 5.82±0.2°, 9.86±0.2°, 11.06 ± 0.2 °, 11.29 ± 0.2 °, 11.64 ± 0.2 °, 11.90 ± 0.2 °, 12.72 ± 0.2 °, 13.04 ± 0.2 °, 15.66 ± 0.2°, 16.36±0.2°, 17.70±0.2°, 17.88±0.2°, 18.11±0.2°, 18.35±0.2°, 18.61±0.2°, 19.41±0.2°, 20.16±0.2°, 20.38±0.2°, 20.69±0.2°, 21.32±0.2°, 21.62±0.2°, 22.28±0.2°, 22.71±0.2°, 25.00±0.2°, 25.34±0.2°, 26.24±0.2°, 26.77±0.2°, 29.85±0.2°, 34.09±0.2°;

the monomaleate crystal form B further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the monomaleate crystal form B further has one or more 2θ angles selected from the group consisting of: 7.98±0.2°, 8.29±0.2°, 10.27±0.2°, 11.61 ± 0.2 °, 13.21 ± 0.2 °, 13.99 ± 0.2 °, 14.52 ± 0.2 °, 15.25 ± 0.2 °, 15.95 ± 0.2 °, 16.89 ± 0.2°, 18.06±0.2°, 20.61±0.2°, 21.25±0.2°, 21.61±0.2°, 22.17±0.2°, 23.31±0.2°, 23.54±0.2°, 23.98±0.2°, 24.70±0.2°, 24.93±0.2°, 25.32±0.2°, 25.91±0.2°, 26.55±0.2°, 27.24±0.2°, 28.23±0.2°, 28.54±0.2°, 29.00±0.2°, 29.47±0.2°, 29.71±0.2°, 32.64±0.2°, 35.12±0.2°;

b. the differential scanning calorimetry curve of the monomaleate crystal form B has the onset of the endothermic peak at 213.92°C ± 2°C;

c. the thermogravimetric analysis curve of the monomaleate crystal form B has two weight loss steps at 24.00°C ± 2°C and 180.00°C ± 2°C, and decomposition begins above 250.00°C ± 2°C;

the X-ray powder diffraction pattern of the fumarate crystal form A further has one or more 2θ angles selected from the group consisting of: 7.26±0.2°, 10.20±0.2°, 10.51 ± 0.2 °, 14.47 ± 0.2 °, 14.93 ± 0.2°, 16.17 ± 0.2°, 17.03 ± 0.2°, 17.90 ± 0.2°, 18.79 ± 0.2°, 19.44±0.2°, 20.19±0.2°, 20.80±0.2°, 22.48±0.2°, 23.07±0.2°, 23.74±0.2°, 24.07±0.2°, 27.06±0.2°, 27.85±0.2°, 28.30±0.2°, 29.46±0.2°, 38.24±0.2°;

the hemifumarate crystal form B further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hemifumarate crystal form B further comprises one or more 2θ angles selected from the group consisting of: 7.27±0.2°, 7.48±0.2°, 8.77 ± 0.2°, 9.18 ± 0.2°, 9.74 ± 0·2°, 10.53 ± 0.2°, 14.96 ± 0.2°, 16.09 ± 0.2°, 16.99 ± 0.2°, 17.61±0.2°, 17.95±0.2°, 18.81±0.2°, 19.45±0.2°, 20.22±0.2°, 20.43±0.2°, 20.84±0.2°, 22.51±0.2°, 23.11±0.2°, 23.76±0.2°, 24.19±0.2°, 25.24±0.2°, 27.04±0.2°, 27.90±0.2°, 28.25±0.2°, 28.75±0.2°, 29.73±0.2°, 30.14±0.2°, 30.77±0.2°, 31.28±0.2°, 33.95±0.2°, 34.52±0.2°, 37.07±0.2°, 38.26±0.2°;

b. the differential scanning calorimetry curve of the hemifumarate crystal form B has the onsets of the endothermic peaks at 21.34°C ± 2°C, 172.21°C ± 2°C, and 234.34°C ± 2°C;

c. the thermogravimetric analysis curve of the hemifumarate crystal form B has three weight loss steps at 31.90°C ± 2°C, 90.00°C ± 2°C, and 190.00°C ± 2°C, and decomposition begins above 270.00°C ± 2°C;

the monoglycolate crystal form A further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the monoglycolate crystal form A also has one or more 2θ angles selected from the group consisting of: 6.37±0.2°, 10.37±0.2°, 11.09 ± 0.2°, 11.70 ± 0.2°, 12.69 ± 0.2°, 13.55 ± 0.2°, 14.06 ± 0.2°, 15.97 ± 0.2°, 17.34 ± 0.2°, 18.47±0.2°, 19.09±0.2°, 20.41±0.2°, 20.71±0.2°, 21.25±0.2°, 22.06±0.2°, 22.43±0.2°, 23.49±0.2°, 24.09±0.2°, 24.79±0.2°, 25.21±0.2°, 27.23±0.2°, 28.00±0.2°, 29.59±0.2°, 30.44±0.2°, 30.96±0.2°, 38.67±0.2°;

b. the differential scanning calorimetry curve of the monoglycolate crystal form A has the onsets of the endothermic peaks at 109.66°C ± 2°C and 198.83°C ± 2°C;

c. the thermogravimetric analysis curve of the monoglycolate crystal form A has three weight loss steps at 33.00°C ± 2°C, 100.00°C ± 2°C, and 165.00°C ± 2°C, and decomposition begins above 200.00°C ± 2°C;

the X-ray powder diffraction pattern of the glycolate crystal form B further has one or more 2θ angles selected from the group consisting of: 5.95±0.2°, 11.06±0.2°, 12.20 ± 0.2°, 15.01 ± 0.2°, 15.79 ± 0.2°, 15.97 ± 0.2°, 16.44 ± 0.2°, 16.63 ± 0.2°, 16.79±0.2°, 17.90±0.2°, 18.33±0.2°, 18.91±0.2°, 21.59±0.2°, 22.18±0.2°, 22.80±0.2°, 23.16±0.2°, 23.93±0.2°, 24.49±0.2°, 25.13±0.2°, 26.68±0.2°, 27.95±0.2°, 30.49±0.2°, 31.62±0.2°, 32.27±0.2°;

the mono-L-malate crystal form A further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the mono-L-malate crystal form A also has one or more 2θ angles selected from the group consisting of: 6.01±0.2°, 10.06±0.2°, 11.04 ± 0.2°, 11.98 ± 0.2°, 12.66 ± 0.2°, 12.86 ± 0.2°, 13.39 ± 0.2°, 15.15 ± 0.2°, 15.62 ± 0.2°, 16.46±0.2°, 17.27±0.2°, 18.58±0.2°, 19.53±0.2°, 19.77±0.2°, 20.25±0.2°, 21.01±0.2°, 21.57±0.2°, 22.04±0.2°, 23.67±0.2°, 24.50±0.2°, 25.00±0.2°, 27.34±0.2°, 28.54±0.2°, 28.91 ± 0.2 °, 29.40 ± 0.2 °, 29.89 ± 0.2 °, 30.53 ± 0.2°, 31.33 ± 0.2°, 33.67 ± 0.2°, 36.16 ± 0.2°;

b. the differential scanning calorimetry curve of the mono-L-malate crystal form A has the onset of the endothermic peak at 204.74°C ± 2°C;

c. the thermogravimetric analysis curve of the mono-L-malate crystal form A has two weight loss steps at 33.00°C ± 2°C and 185.00°C ± 2°C, and decomposition begins at 250.00°C ± 2°C;

the monosuccinate crystal form A further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the monosuccinate crystal form A also has one or more 2θ angles selected from the group consisting of: 6.15±0.2°, 9.64±0.2°, 9.95 ± 0.2°, 11.19 ± 0.2°, 12.26 ± 0.2°, 12.70 ± 0.2°, 13.30 ± 0.2°, 14.95 ± 0.2°, 15.25 ± 0.2°, 16.18±0.2°, 17.59±0.2°, 18.89±0.2°, 19.11±0.2°, 19.73±0.2°, 20.28±0.2°, 20.90±0.2°, 21.27±0.2°, 21.64±0.2°, 22.12±0.2°, 23.12±0.2°, 23.83±0.2°, 24.35±0.2°, 24.93±0.2°, 25.17±0.2°, 26.05±0.2°, 27.00±0.2°, 28.27±0.2°, 28.72±0.2°, 30.12±0.2°, 31.20±0.2°, 33.57±0.2°, 34.13±0.2°, 34.58±0.2°, 35.60±0.2°, 38.23±0.2°;

b. the differential scanning calorimetry curve of the monosuccinate crystal form A has the onsets of the endothermic peaks at 72.75°C ± 2°C, 146.41°C ± 2°C, and 175.72°C ± 2°C;

c. the thermogravimetric analysis curve of the monosuccinate crystal form A has three weight loss steps at 33.00°C ± 2°C, 90.00°C ± 2°C, and 160.00°C ± 2°C, and decomposition begins above 260.00°C ± 2°C;

the X-ray powder diffraction pattern of the sulfate crystal form A further comprises one or more 2θ angles selected from the group consisting of: 6.74±0.2°, 9.56±0.2°, 12.89 ± 0.2°, 13.78 ± 0.2°, 14.68 ± 0.2°, 15.49 ± 0.2°, 15.70 ± 0.2°, 16.41 ± 0.2°, 16.90 ± 0.2°, 18.47±0.2°, 18.68±0.2°, 18.86±0.2°, 19.33±0.2°, 19.87±0.2°, 20.70±0.2°, 21.54±0.2°, 21.76±0.2°, 22.25±0.2°, 23.75±0.2°, 24.11±0.2°, 24.50±0.2°, 25.25±0.2°, 25.86±0.2°, 26.10±0.2°, 26.71±0.2°, 26.96±0.2°, 27.73±0.2°, 28.41±0.2°, 28.90±0.2°, 29.70±0.2°, 30.21±0.2°, 30.99±0.2°;

the X-ray powder diffraction pattern of L-tartarate crystal form A further has one or more 2θ angles selected from the group consisting of: 8.90±0.2°, 9.35±0.2°, 11.05±0.2°, 12.54±0.2°, 12.90±0.2°, 14.35±0.2°, 14.64±0.2°, 18.70±0.2°, 19.45±0.2°, 19.74±0.2°, 20.38±0.2°, 21.45±0.2°, 21.94±0.2°, 22.88±0.2°, 23.80±0.2°, 25.01±0.2°, 25.77±0.2°, 27.33±0.2°, 27.80±0.2°, 28.65±0.2°, 29.41±0.2°, 30.00±0.2°, 31.09±0.2°;

the X-ray powder diffraction pattern of the hippurate crystal form A further has one or more 2θ angles selected from the group consisting of: 6.52±0.2°, 8.77±0.2°, 10.74±0.2°,

11.16±0.2°, 14.18±0.2°, 14.70±0.2°, 15.62±0.2°, 16.06±0.2°, 16.78±0.2°, 17.64±0.2°, 20.42±0.2°, 21.15±0.2°, 21.29±0.2°, 21.79±0.2°, 23.03±0.2°, 24.05±0.2°, 24.42±0.2°, 25.32±0.2°, 26.45±0.2°, 26.87±0.2°, 28.85±0.2°;

the X-ray powder diffraction pattern of the glutarate crystal form A further has one or more 2θ angles selected from the group consisting of: 9.86±0.2°, 10.97±0.2°, 11.82 ± 0.2°, 12.29 ± 0.2°, 12.75 ± 0.2°, 13.19 ± 0.2°, 14.87 ± 0.2°, 15.10 ± 0.2°, 15.37 ± 0.2°, 16.33±0.2°, 17.10±0.2°, 18.35±0.2°, 19.17±0.2°, 19.75±0.2°, 20.14±0.2°, 20.70±0.2°, 21.14±0.2°, 22.23±0.2°, 24.26±0.2°, 24.86±0.2°, 25.28±0.2°, 29.92±0.2°;

the X-ray powder diffraction pattern of the p-toluenesulfonate crystal form A further has one or more 2θ angles selected from the group consisting of: 7.08±0.2°, 8.00±0.2°, 9.39 ± 0.2°, 10.23 ± 0.2°, 13.36 ± 0.2 °, 14.16 ± 0.2°, 14.81 ± 0.2°, 15.77 ± 0.2°, 16.21±0.2°, 17.77±0.2°, 18.10±0.2°, 18.90±0.2°, 20.91±0.2°, 21.29±0.2°, 22.49±0.2°, 23.11±0.2°, 24.41±0.2°, 25.51±0.2°, 26.77±0.2°, 28.28±0.2°, 28.81±0.2°, 29.22±0.2°, 29.95±0.2°, 30.98±0.2°, 35.22±0.2°;

the X-ray powder diffraction pattern of the p-toluenesulfonate crystal form B further has one or more 2θ angles selected from the group consisting of: 8.27 ± 0.2°, 12.59 ± 0.2°, 13.69 ± 0.2°, 14.63 ± 0.2°, 16.15 ± 0.2°, 17.72 ± 0.2°, 18.68 ± 0.2°, 20.75 ± 0.2°, 21.05±0.2°, 21.92±0.2°, 22.45±0.2°, 23.23±0.2°, 23.91±0.2°, 27.33±0.2°, 29.25±0.2°;

the X-ray powder diffraction pattern of the methanesulfonate crystal form A further comprises one or more 2θ angles selected from the group consisting of: 6.70±0.2°, 9.10±0.2°, 9.81 ± 0.2°, 10.16 ± 0.2°, 13.34 ± 0.2°, 13.87 ± 0.2°, 15.37 ± 0.2°, 15.79 ± 0.2°, 17.21 ± 0.2°, 18.75±0.2°, 21.16±0.2°, 22.09±0.2°, 23.31±0.2°, 23.86±0.2°, 24.30±0.2°, 27.18±0.2°, 28.04±0.2°, 28.83±0.2°;

the hydrochloride crystal form C1 further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hydrochloride crystal form C1 also has one or more 2θ angles selected from the group consisting of: 7.47±0.2°, 9.63±0.2°, 11.46±0.2°, 12.25 ± 0.2°, 13.18 ± 0.2°, 13.51 ± 0.2°, 14.96 ± 0.2°, 15.46 ± 0.2°, 16.79 ± 0.2°, 17.04 ± 0.2°, 17.31±0.2°, 17.72±0.2°, 18.56±0.2°, 19.34±0.2°, 20.01±0.2°, 20.41±0.2°, 20.76±0.2°, 22.60±0.2°, 23.09±0.2°, 23.80±0.2°, 24.36±0.2°, 25.63±0.2°, 26.47 ± 0.2°, 27.51 ± 0.2°, 29.09 ± 0.2°, 30.76 ± 0.2°, 31.99 ± 0.2°, 36.24 ± 0.2°;

b. the differential scanning calorimetry curve of the hydrochloride crystal form C1 has the onsets of the endothermic peaks at 39.76°C ± 2°C and 153.80°C ± 2°C;

c. the thermogravimetric analysis curve of the hydrochloride crystal form C1 has three weight loss steps at 26.03°C ± 2°C, 100.00°C ± 2°C, and 150.00°C ± 2°C, and decomposition begins at 214.75°C ± 2°C;

the hydrochloride crystal form C2 further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hydrochloride crystal form C2 further has one or more 2θ angles selected from the group consisting of: 7.56±0.2°, 9.65±0.2°, 11.48±0.2°, 12.32 ± 0.2°, 13.21 ± 0.2°, 13.63 ± 0.2°, 15.10 ± 0.2°, 15.56 ± 0.2°, 16.86 ± 0.2°, 17.16 ± 0.2°, 17.41±0.2°, 17.77±0.2°, 18.58±0.2°, 19.36±0.2°, 20.32±0.2°, 20.91±0.2°, 22.71±0.2°, 23.21±0.2°, 23.80±0.2°, 24.35±0.2°, 25.71±0.2°, 26.56±0.2°, 27.53±0.2°, 27.80±0.2°, 28.20±0.2°, 29.15±0.2°, 30.74±0.2°, 32.06±0.2°, 36.30±0.2°, 38.22±0.2°;

b. the differential scanning calorimetry curve of the hydrochloride crystal form C2 has the onsets of the endothermic peaks at 33.27°C ± 2°C and 155.72°C ± 2°C;

c. the thermogravimetric analysis curve of the hydrochloride crystal form C2 has three weight loss steps at 28.19°C ± 2°C, 115.00°C ± 2°C, and 150.00°C ± 2°C, and decomposition begins at 212.45°C ± 2°C;

the hydrochloride crystal form D further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hydrochloride crystal form D also has one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) 2θ angles selected from the group consisting of: 6.60±0.2°, 7.26 ± 0.2 °, 7.79 ± 0.2 °, 8.48 ± 0.2 °, 9.84 ± 0.2 °, 11.18 ± 0.2 °, 13.31 ± 0.2°, 13.89±0.2°, 14.64±0.2°, 14.98±0.2°, 15.23±0.2°, 16.27±0.2°, 17.04±0.2°, 18.21±0.2°, 19.33±0.2°, 21.23±0.2°, 21.80±0.2°, 23.49±0.2°, 24.79±0.2°, 28.43±0.2°;

b. the differential scanning calorimetry curve of the hydrochloride crystal form D has the onsets of the endothermic peaks at 55.20°C ± 2°C and 164.37°C ± 2°C,

c. the thermogravimetric analysis curve of the hydrochloride crystal form D has two weight loss steps at 36.24°C ± 2°C and 110.00°C ± 2°C, and decomposition begins at 211.35°C ± 2°C;

the hydrochloride crystal form E1 further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hydrochloride crystal form E1 further has one or more 2θ angles selected from the group consisting of: 6.15±0.2°, 7.66±0.2°, 8.41 ± 0.2°, 9.49 ± 0.2°, 9.91 ± 0.2°, 10.88 ± 0.2°, 11.42 ± 0.2°, 13.06 ± 0.2°, 13.66 ± 0.2°, 14.69 ± 0.2 °, 15.32 ± 0.2 °, 15.52 ± 0.2 °, 15.88 ± 0.2 °, 16.25 ± 0.2 °, 16.81 ± 0.2 °, 17.35 ± 0.2°, 18.37±0.2°, 19.01±0.2°, 19.75±0.2°, 21.15±0.2°, 21.51±0.2°, 21.81±0.2°, 22.50±0.2°, 22.87±0.2°, 23.56±0.2°, 24.95±0.2°, 25.18±0.2°, 25.63±0.2°, 26.71±0.2°, 27.10±0.2°, 27.91±0.2°, 28.47±0.2°, 29.30±0.2°, 29.81±0.2°, 30.12±0.2°, 32.93±0.2°, 34.96±0.2°;

b. the differential scanning calorimetry curve of the hydrochloride crystal form E1 has the onsets of the endothermic peaks at 13.36°C ± 2°C and 174.06°C ± 2°C;

c. The thermogravimetric analysis curve of the hydrochloride crystal form E1 has three weight loss steps at 25.81°C ± 2°C, 120.00°C ± 2°C, and 160.00°C ± 2°C, and decomposition begins at 211.29°C ± 2°C;

the hydrochloride crystal form E2 further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hydrochloride crystal form E2 also has one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) 2θ angles selected from the group consisting of: 9.51±0.2°, 10.90±0.2°, 11.49±0.2°, 13.10±0.2°, 13.64±0.2°, 14.76±0.2°, 15.39±0.2°, 15.75±0.2°, 16.30±0.2°, 16.93±0.2°, 19.01±0.2°, 20.69±0.2°, 21.54±0.2°, 21.84±0.2°, 22.19±0.2°, 22.57±0.2°, 23.01±0.2°, 23.63±0.2°, 24.96±0.2°, 25.90±0.2°, 26.32±0.2°, 26.78±0.2°, 27.19±0.2°, 27.48±0.2°, 27.94±0.2°, 28.68±0.2°, 29.07±0.2°, 29.50±0.2°, 29.91±0.2°, 31.74±0.2°, 32.96±0.2°, 33.66±0.2°;

b. the differential scanning calorimetry curve of the hydrochloride crystal form E2 has the onsets of the endothermic peaks at 14.99°C ± 2°C and 174.19°C ± 2°C;

c. the thermogravimetric analysis curve of the hydrochloride crystal form E2 has three weight loss steps at 33.18°C ± 2°C, 90.00°C ± 2°C, and 140.00°C ± 2°C, and decomposition begins at 213.17°C ± 2°C;

the hydrochloride crystal form F further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hydrochloride crystal form F also has one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) 2θ angles selected from the group consisting of: 6.85±0.2°, 10.21±0.2°, 10.70±0.2°, 14.80 ± 0.2°, 15.25 ± 0.2°, 16.60 ± 0.2°, 16.88 ± 0.2 °, 17.84 ± 0.2 °, 19.00 ± 0.2 °, 19.16 ± 0.2 °, 19.84 ± 0.2° , 20.09 ± 0.2°, 20.34 ± 0.2°, 21.51±0.2°, 22.35±0.2°, 23.22±0.2°, 23.86±0.2°, 25.06±0.2°, 25.31±0.2°, 25.63±0.2°, 26.68 ± 0.2 °, 28.10 ± 0.2 °, 28.87 ± 0.2 °, 30.53 ± 0.2 °, 32.45 ± 0.2 °, 33.59 ± 0.2°;

b. the differential scanning calorimetry curve of the hydrochloride crystal form F has the onsets of the endothermic peaks at 36.03°C ± 2°C and 172.45°C ± 2°C;

c. the thermogravimetric analysis curve of the hydrochloride crystal form F has three weight loss steps at 33.35°C ± 2°C, 100.00°C ± 2°C, and 150.00°C ± 2°C, and decomposition begins at 212.66°C ± 2°C;

the hydrochloride crystal form G further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hydrochloride crystal form G also has one or more 2θ angles selected from the group consisting of: 5.83±0.2°, 7.18±0.2°, 9.97±0.2°, 11.63 ± 0.2°, 12.00 ± 0.2°, 12.35 ± 0.2°, 13.26 ± 0.2°, 13.58 ± 0.2°, 14.17 ± 0.2° , 14.60 ± 0.2°, 17.64±0.2°, 18.37±0.2°, 18.81±0.2°, 19.14±0.2°, 19.80±0.2°, 20.27±0.2°, 20.48±0.2°, 21.35±0.2°, 21.82±0.2°, 22.65±0.2°, 23.35±0.2°, 24.43±0.2°, 25.47±0.2°, 26.24±0.2°, 26.54±0.2°, 26.84±0.2°, 27.92±0.2°, 28.94±0.2°, 29.31±0.2°, 30.18±0.2°;

b. the differential scanning calorimetry curve of the hydrochloride crystal form G has the onsets of the endothermic peaks at 59.42°C ± 2°C, 151.02°C ± 2°C, and 166.01°C ± 2°C;

c. the thermogravimetric analysis curve of the hydrochloride crystal form G has three weight loss steps at 26.28°C ± 2°C, 120.00°C ± 2°C, and 150.00°C ± 2°C;

the hydrochloride crystal form H further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hydrochloride crystal form H further has one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) 2θ angles selected from the group consisting of: 7.16±0.2°, 10.02±0.2°, 11.64±0.2°, 12.35 ± 0.2 °, 13.23 ± 0.2 °, 13.59 ± 0.2 °, 14.58 ± 0.2 °, 15.51 ± 0.2 °, 15.97 ± 0.2 °, 17.63 ± 0.2°, 18.62±0.2°, 19.11±0.2°, 20.23±0.2°, 20.54±0.2°, 21.40±0.2°, 22.07±0.2°, 22.62±0.2°, 22.78±0.2°, 23.36±0.2°, 24.73±0.2°, 24.98±0.2°, 26.23±0.2°, 26.57±0.2°, 26.91±0.2°, 27.88±0.2°, 29.01±0.2°, 29.30±0.2°, 29.61±0.2°, 30.21±0.2°, 31.21±0.2°, 32.12±0.2°, 34.66±0.2°;

b. the differential scanning calorimetry curve of the hydrochloride crystal form H has the onsets of the endothermic peaks at 51.49°C ± 2°C and 153.61°C ± 2°C;

c. the thermogravimetric analysis curve of the hydrochloride crystal form H has three weight loss steps at 26.12°C ± 2°C, 110.00°C ± 2°C, and 150.00°C ± 2°C, and decomposition begins at 211.73°C ± 2°C;

the hydrochloride crystal form I further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hydrochloride crystal form I also has one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) 2θ angles selected from the group consisting of: 9.50±0.2°, 12.31±0.2°, 12.54 ± 0.2°, 14.05 ± 0.2°, 14.96 ± 0.2°, 15.38 ± 0.2° , 17.18 ± 0.2°, 17.92 ± 0.2°, 19.03 ± 0.2°, 19.74±0.2°, 19.99±0.2°, 20.96±0.2°, 21.62±0.2°, 21.99±0.2°, 22.98±0.2°, 23.52±0.2°, 23.80±0.2°, 24.38±0.2°, 25.92±0.2°, 26.81±0.2°, 27.21±0.2°, 27.60±0.2°, 27.78±0.2°, 28.26±0.2°, 28.74±0.2°, 30.07±0.2°, 31.00±0.2°, 32.69±0.2°, 34.02±0.2°, 34.83±0.2°;

b. the differential scanning calorimetry curve of the hydrochloride crystal form I has the onsets of the endothermic peaks at 18.15°C ± 2°C and 194.49°C ± 2°C;

c. the thermogravimetric analysis curve of the hydrochloride crystal form I has three weight loss steps at 28.31°C ± 2°C, 70.00°C ± 2°C, and 173.00°C ± 2°C, and decomposition begins at 215.51°C ± 2°C;

the hydrochloride crystal form J1 further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hydrochloride crystal form J1 also has one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) 2θ angles selected from the group consisting of: 7.82±0.2°, 7.95±0.2°, 10.08±0.2°, 11.69 ± 0.2°, 12.30 ± 0.2°, 12.60 ± 0.2°, 13.60 ± 0.2°, 15.98 ± 0.2°, 16.25 ± 0.2°, 18.05 ± 0.2°, 18.60±0.2°, 18.79±0.2°, 19.49±0.2°, 20.82±0.2°, 21.55±0.2°, 21.70±0.2°, 22.06±0.2°, 22.88±0.2°, 23.69±0.2°, 24.92±0.2°, 25.13±0.2°, 26.19±0.2°, 26.57 ± 0.2 °, 29.07 ± 0.2 °, 30.16 ± 0.2 °, 31.85 ± 0.2 °, 32.80 ± 0.2 °;

b. the differential scanning calorimetry curve of the hydrochloride crystal form J1 has the onsets of the endothermic peaks at 70.82°C ± 2°C and 165.48°C ± 2°C;

c. the thermogravimetric analysis curve of the hydrochloride crystal form J1 has two

weight loss steps at 33.94°C ± 2°C and 110.00°C ± 2°C, and decomposition begins at 212.96°C ± 2°C;

the hydrochloride crystal form J2 further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hydrochloride crystal form J2 also has one or more 2θ angles selected from the group consisting of: 6.78±0.2°, 7.96±0.2°, 8.31±0.2°, 11.59 ± 0.2°, 12.24 ± 0.2°, 13.56 ± 0.2°, 16.44 ± 0.2°, 16.63 ± 0.2°, 17.45 ± 0.2° , 18.12 ± 0.2°, 19.51±0.2°, 20.12±0.2°, 20.35±0.2°, 20.49±0.2°, 21.28±0.2°, 21.46±0.2°, 22.75±0.2°, 23.27±0.2°, 24.09±0.2°, 24.86±0.2°, 24.99±0.2°, 25.37±0.2°, 25.65±0.2°, 26.54±0.2°, 27.62±0.2°, 28.61±0.2°, 29.00±0.2°, 30.43±0.2°, 32.10±0.2°, 33.01±0.2°, 36.96±0.2°;

b. the differential scanning calorimetry curve of hydrochloride crystal form J2 has the onsets of the endothermic peaks at 77.60°C ± 2°C and 163.47°C ± 2°C;

c. the thermogravimetric analysis curve of the hydrochloride crystal form J2 has two weight loss steps at 28.73°C ± 2°C and 120.00°C ± 2°C, and decomposition begins at 211.78°C ± 2°C;

the hydrochloride crystal form K further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hydrochloride crystal form K also has one or more 2θ angles selected from the group consisting of: 6.79±0.2°, 7.83 ± 0.2°, 8.04 ± 0.2 °, 10.00 ± 0.2 °, 10.74 ± 0.2 °, 11.61 ± 0.2 °, 12.25 ± 0.2 °, 12.64 ± 0.2°, 13.57±0.2°, 18.05±0.2°, 18.63±0.2°, 19.43±0.2°, 20.15±0.2°, 20.49±0.2°, 20.64±0.2°, 21.52±0.2°, 21.72±0.2°, 21.93±0.2°, 23.27±0.2°, 24.73±0.2°, 25.19±0.2°, 26.25±0.2°, 26.57±0.2°, 27.42±0.2°, 28.02±0.2°, 28.67±0.2°, 29.13±0.2°, 29.91±0.2°, 32.56±0.2°;

b. the differential scanning calorimetry curve of the hydrochloride crystal form K has the onsets of the endothermic peaks at 80.73°C ± 2°C and 171.74°C ± 2°C;

c. the thermogravimetric analysis curve of the hydrochloride crystal form K has three weight loss steps at 33.39°C ± 2°C, 125.00°C ± 2°C, and 155.00°C ± 2°C, and decomposition begins at 211.42°C ± 2°C;

the hydrochloride crystal form L further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hydrochloride crystal form L further has one or more 2θ angles selected from the group consisting of: 7.70±0.2°, 8.15±0.2°, 8.82±0.2°, 9.85 ± 0.2 °, 11.25 ± 0.2 °, 12.72 ± 0.2 °, 13.59 ± 0.2 °, 14.68 ± 0.2 °, 15.07 ± 0.2 °, 15.56 ± 0.2°, 16.60±0.2°, 17.56±0.2°, 18.53±0.2°, 18.98±0.2°, 19.74±0.2°, 20.29±0.2°, 20.52±0.2°, 21.30±0.2°, 22.79±0.2°, 24.38±0.2°, 25.57±0.2°, 26.21±0.2°, 26.50±0.2°, 26.97±0.2°, 27.48±0.2°, 28.17±0.2°, 28.60±0.2°, 29.54±0.2°, 29.80±0.2°, 31.17±0.2°, 33.28±0.2°;

b. the differential scanning calorimetry curve of the hydrochloride crystal form L has an onset of an endothermic peak at 180.17°C ± 2°C;

c. the thermogravimetric analysis curve of the hydrochloride crystal form L has two weight loss steps at 33.53°C ± 2°C and 140.00°C ± 2°C, and decomposition begins at 212.43°C ± 2°C;

the hydrochloride crystal form M further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hydrochloride crystal form M also has one or more 2θ angles selected from the group consisting of: 6.84±0.2°, 7.21 ± 0.2 °, 8.92 ± 0.2 °, 10.07 ± 0.2 °, 10.69 ± 0.2 °, 10.89 ± 0.2°, 11.24 ± 0.2 °, 13.23 ± 0.2 °, 14.90 ± 0.2 °, 15.59 ± 0.2 °, 16.74 ± 0.2 °, 17.67 ± 0.2 °, 18.29 ± 0.2°, 18.94±0.2°, 19.46±0.2°, 19.71±0.2°, 19.96±0.2°, 21.49±0.2°, 21.83±0.2°, 23.14±0.2°, 23.54±0.2°, 24.17±0.2°, 25.17±0.2°, 25.45±0.2°, 26.10±0.2°, 27.17±0.2°, 27.61±0.2°, 28.09±0.2°, 28.88±0.2°, 29.42±0.2°, 30.12±0.2°, 32.48±0.2°, 35.22±0.2°;

b. the differential scanning calorimetry curve of the hydrochloride crystal form M has

the onsets of the endothermic peaks at 31.74°C ± 2°C and 150.05°C ± 2°C;

c. the thermogravimetric analysis curve of the hydrochloride crystal form M has two weight loss steps at 32.98°C ± 2°C and 115.00°C ± 2°C, and decomposition begins at 215.09°C ± 2°C;

the hydrochloride crystal form N further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hydrochloride crystal form N also has one or more 2θ angles selected from the group consisting of: 6.61±0.2°, 7.80±0.2°, 9.75±0.2°, 11.19 ± 0.2°, 12.53 ± 0.2°, 13.17 ± 0.2°, 14.61 ± 0.2°, 15.24 ± 0.2°, 16.02 ± 0.2°, 18.51 ± 0.2°, 19.36 ± 0.2°, 21.57 ± 0.2°, 21.95 ± 0.2°, 23.47 ± 0.2°, 25.60 ± 0.2°, 27.32 ± 0.2°, 29.12 ± 0.2°;

b. the differential scanning calorimetry curve of the hydrochloride crystal form N has the onsets of the endothermic peaks at 47.38°C ± 2°C and 167.91°C ± 2°C;

c. the thermogravimetric analysis curve of the hydrochloride crystal form N has three weight loss steps at 33.22°C ± 2°C, 75.00°C ± 2°C, and 150.00°C ± 2°C, and decomposition begins at 212.57°C ± 2°C;

the hydrochloride crystal form O further comprises one or more of the following characteristics:

a. the X-ray powder diffraction pattern of the hydrochloride crystal form O also has one or more 2θ angles selected from the group consisting of: 6.14±0.2°, 8.39±0.2°, 9.90±0.2°, 11.28 ± 0.2 °, 13.19 ± 0.2 °, 13.54 ± 0.2 °, 14.40 ± 0.2 °, 15.33 ± 0.2 °, 15.87 ± 0.2 °, 16.79 ± 0.2°, 17.32±0.2°, 19.03±0.2°, 19.38±0.2°, 19.84±0.2°, 20.39±0.2°, 21.14±0.2°, 21.82±0.2°, 22.51±0.2°, 22.84±0.2°, 23.77±0.2°, 24.59±0.2°, 25.28±0.2°, 26.21±0.2°, 26.82±0.2°, 27.07±0.2°, 27.93±0.2°, 28.45±0.2°, 29.24±0.2°, 29.70±0.2°, 30.12±0.2°, 30.91±0.2°, 31.32±0.2°, 32.02±0.2°, 32.81±0.2°, 33.99±0.2°, 35.51±0.2°, 37.27±0.2°;

b. the differential scanning calorimetry curve of the hydrochloride crystal form O has the onsets of the endothermic peaks at 12.36°C ± 2°C and 174.87°C ± 2°C;

c. the thermogravimetric analysis curve of the hydrochloride crystal form O has three weight loss steps at 27.70°C ± 2°C, 115.00°C ± 2°C, and 160.00°C ± 2°C, and decomposition begins at 212.00°C ± 2°C.

7. A method for preparing a crystal form of a pharmaceutically acceptable salt of the compound of formula (I) according to any one of claims 4-6, wherein, the method comprises the following steps:

a. dissolving or dispersing the compound of formula (I) and an acid at a molar ratio of 1: (0.8–3) into 1-20 times of solvent A;

b. performing suspension, recrystallization, or slurrying treatment;

wherein the acid is not selected from hydrochloric acid (preferably, the acid is selected from the group consisting of: maleic acid, fumaric acid, glycolic acid, L-malic acid, succinic acid, sulfuric acid, L-tartaric acid, hippuric acid, glutaric acid, p-toluenesulfonic acid, or methanesulfonic acid);

wherein solvent A is selected from the group consisting of: acetonitrile, dichloromethane, tetrahydrofuran, or a combination thereof;

or the acid is hydrochloric acid or hydrogen chloride in dioxane; and the solvent A is selected from the group consisting of: ethyl acetate, 2-methyl-4-hydroxyfuran, butanone, ethanol, acetone, ethyl acetate, acetonitrile, tetrahydrofuran, methyl isobutyl ketone, trifluoroethanol, water, methanol, tert-butyl methyl ether, toluene, isopropanol, dimethyl sulfoxide, isopropyl acetate, dichloromethane, or combinations thereof.

8. A method for preparing a crystal form of a pharmaceutically acceptable salt of the compound of formula (I) according to any one of claims 4-6, wherein, the method is a crystal form transformation by converting one crystal form of a pharmaceutically acceptable salt of the compound of formula (I) into another crystal form thereof;

wherein the method of crystal form transformation comprises the following steps:

a. dissolving or dispersing a crystal form of a pharmaceutically acceptable salt of the compound of formula (I) in 1-20 times of solvent A;

b. performing suspension treatment;

c. centrifuging the resulting suspension through a 0.4 to 0.5 μm filter membrane at a speed of 12,000 to 16,000 rpm;

wherein the solvent A is selected from the group consisting of: ethanol, acetone, ethyl acetate, acetonitrile, tetrahydrofuran, methyl isobutyl ketone, trifluoroethanol, methanol, 2-methyl-tetrahydrofuran, methyl tert-butyl ether, toluene, isopropanol, dimethyl sulfoxide, isopropyl acetate, dimethyl sulfoxide, methanol, dichloromethane, water, or a combination thereof.

9. A pharmaceutical composition comprising the compound of formula (I) according to any one of claims 1-2, the crystal form A according to claim 3, or the crystal form of the compound of formula (I) according to any one of claims 4-6;

and

one or more pharmaceutically acceptable carriers, excipients, adjuvants, ingredients, and/or diluents.

10. A use of the compound of formula (I) according to any one of claims 1-2, the crystal form A according to claim 3, the crystal forms of the compound of formula (I) according to any one of claims 4-6, and the pharmaceutical composition according to claim 9 in preparing a medicament for the prevention and/or treatment of diseases associated with increased activity or expression of FGFR2.