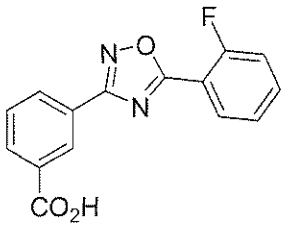
diesease ameliorated by modulation of premature translation termination or nonsense-mediated mRNA decay. The present invention provides such novel crystalline forms, for example, crystalline forms of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid.

[005] Citation of any reference in Section 2 of this application is not to be construed as an admission that such reference is prior art to the present application.

3. SUMMARY

[006] The ~~invention~~disclosure provides novel crystalline forms of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid, which has the following chemical structure (I):



[007]

[008] (I)

[008a] In a first aspect, there is provided a crystal form of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid comprising Form B crystals having 1-butyl acetate in the crystal lattice and characterized by X-ray powder diffraction pattern peak positions (shifted 1):

Position (°2θ)	d-spacing	I	I/Io°
6.42	13.75	214	34
7.00	12.63	23	4
7.89	11.20	98	15
10.85	8.15	97	15
12.61	7.01	117	18
12.92	6.85	29	5
13.47	6.57	208	33
13.97	6.33	558	88
15.81	5.60	635	100
16.45	5.38	143	23
17.12	5.18	320	50
20.05	4.42	544	86
21.05	4.22	66	10
23.92	3.72	110	17
24.28	3.66	21	3

27.00	3.30	48	8
27.39	3.25	126	20
27.84	3.20	32	5
28.04	3.18	68	11
28.94	3.08	90	14
31.10	2.87	35	6
32.58	2.75	42	7
36.11	2.49	89	14
37.71	2.38	19	3
38.15	2.36	20	3
38.61	2.33	52	8

[008b] In a second aspect, there is provided a crystal form of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid comprising Form B crystals having a 1/1 mixture of tetrahydrofuran and heptane in the crystal lattice and characterized by X-ray powder diffraction pattern peak positions (shifted 2):

Position (°2θ)	d-spacing	I	I/Io[c]
6.10	14.48	155	3
6.38	13.84	1068	23
6.54	13.50	1371	29
7.10	12.44	270	6
8.02	11.02	653	14
10.91	8.11	376	8
12.71	6.96	195	4
13.50	6.55	601	13
13.62	6.50	404	9
13.86	6.38	702	15
14.10	6.27	4633	99
15.56	5.69	158	3
15.70	5.64	402	9
15.91	5.57	3422	73
16.55	5.35	673	14
16.96	5.22	283	6
17.22	5.15	1639	35
17.50	5.06	150	3
19.82	4.48	242	5
20.08	4.42	1950	42
20.34	4.36	209	4
21.15	4.20	718	15
23.78	3.74	208	4
23.93	3.72	508	11
24.38	3.65	412	9
24.56	3.62	184	4
26.88	3.31	198	4
27.16	3.28	219	5

27.48	3.24	4657	100
27.88	3.20	231	5
28.04	3.18	183	4
28.78	3.10	353	8
29.02	3.07	948	20
32.71	2.74	233	5
36.01	2.49	639	14
38.10	2.36	253	5
38.56	2.33	216	5
39.38	2.29	179	4

[008c] In a third aspect, there is provided a crystal form of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid comprising Form B crystals having dimethoxyether in the crystal lattice and characterized by X-ray powder diffraction pattern peak positions:

Position (°2θ)	d-spacing	I	I/Io[c]
6.22	14.20	356	8
6.51	13.57	1332	30
7.13	12.39	171	4
8.17	10.81	727	17
10.91	8.11	484	11
12.87	6.87	355	8
13.80	6.41	930	21
14.12	6.27	4251	97
14.28	6.20	2569	59
15.78	5.61	172	4
16.23	5.46	4368	100
16.54	5.36	684	16
17.15	5.17	1377	32
20.33	4.36	1057	24
21.22	4.18	475	11
21.36	4.16	290	7
23.94	3.71	578	13
24.30	3.66	201	5
27.30	3.26	217	5
27.58	3.23	303	7
28.00	3.18	262	6
28.74	3.10	239	5
28.96	3.08	327	7
32.70	2.74	224	5
36.74	2.44	265	6
38.18	2.36	175	4
38.38	2.34	227	5
38.52	2.34	160	4
39.31	2.29	142	3

[008d] In a fourth aspect, there is provided a crystal form of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid comprising Form B crystals having dioxane in the crystal lattice and characterized by X-ray powder diffraction pattern peak positions shifted:

Position (°2θ)	d-spacing	I	I/Io[c]
6.04	14.62	102	5
6.49	13.61	2151	100
7.91	11.17	240	11
10.92	8.10	252	12
12.61	7.01	304	14
12.92	6.85	263	12
13.10	6.75	71	3
13.42	6.59	103	5
13.82	6.40	177	8
13.99	6.32	565	26
15.40	5.75	99	5
15.76	5.62	1580	73
16.51	5.37	516	24
17.15	5.17	334	16
19.92	4.45	606	28
20.04	4.43	624	29
21.01	4.23	101	5
23.92	3.72	80	4
24.28	3.66	285	13
24.48	3.63	81	4
26.77	3.33	161	7
27.14	3.28	259	12
27.40	3.25	1413	66
27.74	3.21	175	8
28.09	3.17	122	6
28.82	3.10	165	8
28.99	3.08	488	23
31.03	2.88	118	5
32.58	2.75	271	13
35.64	2.52	155	7
35.85	2.50	329	15
37.48	2.40	72	3
37.66	2.39	89	4
38.62	2.33	84	4

[009] In particular, crystalline forms of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid are useful for the treatment, prevention or management of diseases ameliorated by modulation of premature translation termination or nonsense-mediated mRNA decay, as described in U.S. Patent No. 6,992,096 B2, issued January 31, 2006,

which is incorporated herein by reference in its entirety. In addition, the present disclosure provides a crystalline form of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid which is substantially pure, i.e., its purity greater than about 90%.

[010] Certain embodiments of the ~~invention~~disclosure provide pharmaceutical dosage forms and compositions comprising a crystalline form of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid and a pharmaceutically-acceptable diluent, excipient or carrier. The ~~invention~~disclosure further provides methods of their use for the treatment, prevention or management of diseases ameliorated by modulation of premature translation termination or nonsense-mediated mRNA decay. In certain embodiments, the ~~invention~~disclosure provides methods of making, isolating and/or characterizing the crystalline forms of the ~~invention~~disclosure. The crystalline forms of the ~~invention~~disclosure are useful as active pharmaceutical ingredients for the preparation of formulations for use in animals or humans. Thus, the present ~~invention~~disclosure

encompasses the use of these crystalline forms as a final drug product. The crystalline forms and final drug products of the ~~invention~~disclosure are useful, for example, for the treatment, prevent or management of the diseases described herein.

4. DETAILED DESCRIPTION OF THE INVENTION

4.1 Brief Description of the Drawings

[011] **FIG. 1** provides an X-ray powder diffraction (XRPD) pattern of a sample comprising Form A of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid.

[012] **FIG. 2** provides differential scanning calorimetry (DSC) and thermogravimentric analysis (TGA) thermograms of a sample comprising Form A of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid.

[013] **FIG. 3** provides a dynamic vapor sorption (DVS) isotherm of a sample comprising Form A of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid.

[014] **FIG. 4** provides a solid-state ^{13}C NMR spectrum of a sample comprising Form A of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid.

[015] **FIG. 5** provides a XRPD pattern of a sample comprising Form B of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid.

[016] **FIG. 6** provides DSC and TGA thermograms of a sample comprising Form B of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid.

[017] **FIG. 7** provides a DVS isotherm of a sample comprising Form B of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid.

[018] **FIG. 8** provides an overlay of experimental XRPD patterns showing a characteristic peak set of Form A (Top) with respect to several samples comprising Form B (second from top to bottom) of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid, illustrating peak shift among certain Form B samples.

[019] **FIG. 9** provides crystal packing diagram of Form A of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid, viewed down the crystallographic *b* axis and showing an outline of the unit cell.

[020] **FIG. 10** provides a XRPD pattern of Form A of 3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid simulated from a single-crystal X-ray diffraction crystal structure obtained from a representative single crystal of Form A.