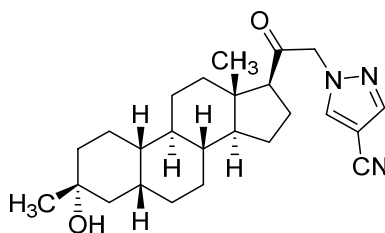


CNS-related diseases. Crystalline forms of such a steroid described herein are directed toward this end.

SUMMARY

[0005] The present disclosure relates, in part, to novel forms (for example, certain crystalline forms described herein) of a 19-nor (i.e., C19 desmethyl) compound. Generally, a solid compound's efficacy as a drug can be affected by the properties of the solid it comprises.

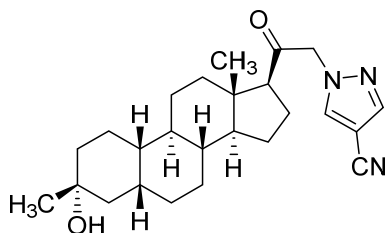
[0006] The present disclosure provides a crystalline compound of Formula (I):



Formula (I)

also referred to herein as “Compound 1.”

[0006a] In one aspect of the present disclosure, there is provided a crystalline solid form of Compound 1:

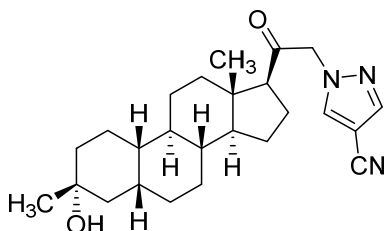


Compound 1,

having an XRPD pattern comprising peaks between and including 16.8 to 17.2 degrees in 2θ and between and including 20.5 to 20.9 degrees in 2θ .

[0006b] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising a crystalline compound disclosed herein, and a pharmaceutically acceptable excipient.

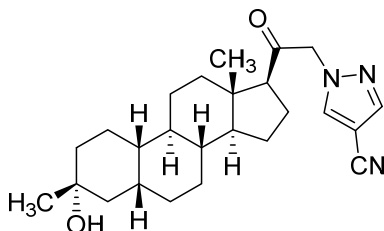
[0006c] In another aspect of the present disclosure, there is provided a crystalline solid form of Compound 1:



Compound 1,

having an XRPD pattern comprising peaks: 11.8, 14.4 and 21.5 degrees in 2 θ .

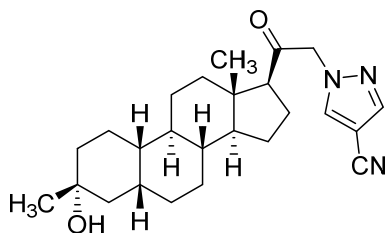
[0006d] In a further aspect of the present disclosure, there is provided a crystalline solid form of Compound 1:



Compound 1,

having an XRPD pattern comprising peaks between and including 9.7 to 10.1 degrees in 2 θ , between and including 11.6 to 12.0 degrees in 2 θ , between and including 13.2 to 13.6 degrees in 2 θ , between and including 14.2 to 14.6 degrees in 2 θ , between and including 14.6 to 15.0 degrees in 2 θ , between and including 16.8 to 17.2 degrees in 2 θ , between and including 20.5 to 20.9 degrees in 2 θ , between and including 21.3 to 21.7 degrees in 2 θ , between and including 21.4 to 21.8 degrees in 2 θ , and between and including 22.4 to 22.8 degrees in 2 θ .

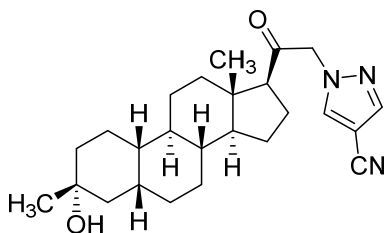
[0006e] In another aspect of the present disclosure, there is provided a crystalline solid form of Compound 1:



Compound 1,

having an XRPD pattern comprising peaks between and including 9.7 to 10.1 degrees in 2θ , between and including 14.6 to 15.0 degrees in 2θ , between and including 16.8 to 17.2 degrees in 2θ , between and including 20.5 to 20.9 degrees in 2θ , between and including 21.3 to 21.7 degrees in 2θ .

[0006f] In a further aspect of the present disclosure, there is provided a crystalline solid form of Compound 1:



Compound 1,

having an XRPD pattern comprising peaks at 9.9 degrees in 2 θ , 14.8 degrees in 2 θ , 17.0 degrees in 2 θ , 20.7 degrees in 2 θ , and 21.5 degrees in 2 θ .

[0007] In some embodiments, a solubilized form of the crystalline form of Compound 1 is converted to a different crystalline form of Compound 1 by slow evaporation, anti-solvent addition, slow-cooling, solution vapor diffusion, solid vapor diffusion, fast evaporation, reverse anti-solvent addition, and water activity experiments.

[0008] In some embodiments, a crystalline form of Compound 1 is converted to a different crystalline form of Compound 1 by slurry conversion.

In some embodiments, physical or chemical parameters of a solid form of Compound 1 are evaluated from one or more of the following analytical techniques: X-ray powder diffraction (XRPD) analysis, e.g., variable-temperature XRPD (VT-XRPD) analysis, single-crystal X-ray crystallography, thermogravimetric analysis (TGA), differential scanning calorimetry (DSC), nuclear magnetic resonance (NMR) spectroscopy or solid-state NMR spectroscopy, Raman spectroscopy, or dynamic vapor sorption (DVS).

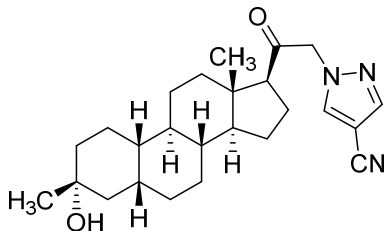
[0009] In embodiments, each solid form is characterized and identified with parameters obtained from one or more of the aforementioned analytical methods:

X-ray diffraction patterns presented with degrees 2-theta (2 θ) as the abscissa and peak intensity as the ordinate as determined by analysis with XRPD. These patterns are also referred to herein as XRPD patterns;

CLAIMS

What is claimed is:

1. A crystalline solid form of Compound 1:



Compound 1,

having an XRPD pattern comprising peaks between and including 16.8 to 17.2 degrees in 2θ and between and including 20.5 to 20.9 degrees in 2θ .

2. The crystalline solid form of claim 1, wherein the peak between and including 16.8 to 17.2 is 17.0 degrees in 2θ and the peak between and including 20.5 to 20.9 is 20.7 degrees in 2θ .
3. The crystalline solid form of claim 1, having an XRPD pattern further comprising a peak between and including 9.7 to 10.1 degrees in 2θ .
4. The crystalline solid form of claim 3, wherein the peak between and including 9.7 to 10.1 is 9.9 degrees in 2θ .
5. The crystalline solid form of claim 1, having an XRPD pattern substantially as depicted in FIG. 3A.
6. The crystalline solid form of claim 1, wherein the crystalline solid form is characterized by the following crystallographic unit cell parameters:

Unit Cell dimensions	a= 9.6642(8) Å	$\alpha = 90^\circ$
	b = 9.8676(8) Å	$\beta = 90^\circ$
	c = 23.9408(19) Å	$\gamma = 90^\circ$
Volume	2283.1(3) Å ³	
Z	4	
Density	1.192 mg/m ³	

7. A pharmaceutical composition comprising the crystalline solid form of claim 1, and a pharmaceutically acceptable excipient.

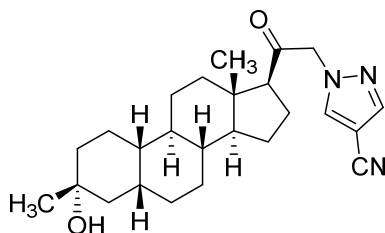
8. The crystalline solid form of claim 2, further comprising peaks at 9.9, 11.8, 13.4, 14.8, 17.0 and 21.5 degrees in 2 θ .

9. The crystalline solid form of claim 1, having an XRPD pattern comprising peaks as indicated in Table 5:

Table 5

2 θ (degrees)	d-spacing ($\text{\AA}$)	Relative Intensity (%)
22.60955	3.93279	26.76
20.65623	4.30006	27.84
13.36358	6.62573	28.42
14.81188	5.98097	33.78
21.50066	4.12963	36.7
21.54634	4.12439	36.94
9.889125	8.94443	41.85
11.79075	7.50579	65.73
14.41313	6.14552	65.89
16.99542	5.21715	100

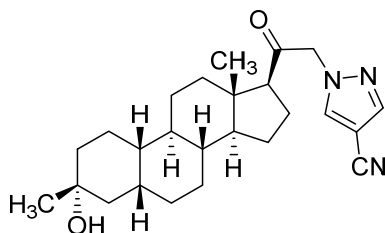
10. A crystalline solid form of Compound 1:



Compound 1,

having an XRPD pattern comprising peaks: 11.8, 14.4 and 21.5 degrees in 2 θ .

11. A crystalline solid form of Compound 1:

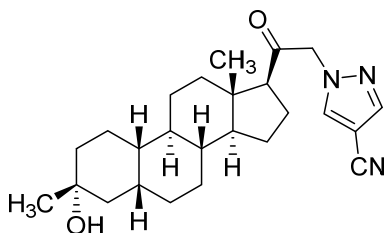


Compound 1,

having an XRPD pattern comprising peaks between and including 9.7 to 10.1 degrees in 2θ , between and including 11.6 to 12.0 degrees in 2θ , between and including 13.2 to 13.6 degrees in 2θ , between and including 14.2 to 14.6 degrees in 2θ , between and including 14.6 to 15.0 degrees in 2θ , between and including 16.8 to 17.2 degrees in 2θ , between and including 20.5 to 20.9 degrees in 2θ , between and including 21.3 to 21.7 degrees in 2θ , between and including 21.4 to 21.8 degrees in 2θ , and between and including 22.4 to 22.8 degrees in 2θ .

12. The crystalline solid form of claim 11, wherein the peak between and including 9.7 to 10.1 is 9.9 degrees in 2θ , the peak between and including 11.6 to 12.0 is 11.8 degrees in 2θ , the peak between and including 13.2 to 13.6 is 13.4 degrees in 2θ , the peak between and including 14.2 to 14.6 is 14.4 degrees in 2θ , the peak between and including 14.6 to 15.0 degrees is 14.8 in 2θ , the peak between and including 16.8 to 17.2 is 17.0 degrees in 2θ , the peak between and including 20.5 to 20.9 is 20.7 degrees in 2θ , the peak between and including 21.3 to 21.7 is 21.5 degrees in 2θ , the peak between and including 21.4 to 21.8 is 21.6 degrees in 2θ , and the peak between and including 22.4 to 22.8 is 22.6 degrees in 2θ .

13. A crystalline solid form of Compound 1:

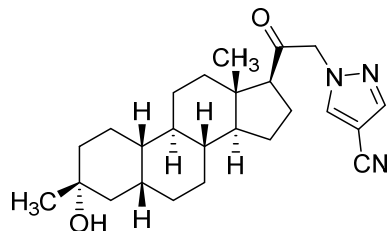


Compound 1,

having an XRPD pattern comprising peaks between and including 9.7 to 10.1 degrees in 2θ , between and including 14.6 to 15.0 degrees in 2θ , between and including 16.8 to 17.2 degrees in 2θ , between and including 20.5 to 20.9 degrees in 2θ , between and including 21.3 to 21.7 degrees in 2θ .

14. The crystalline solid form of claim 13, wherein the peak between and including 9.7 to 10.1 is 9.9 degrees in 2θ , the peak between and including 14.6 to 15.0 is 14.8 degrees in 2θ , the peak between and including 16.8 to 17.2 is 17.0 degrees in 2θ , the peak between and including 20.5 to 20.9 is 20.7 degrees in 2θ , and the peak between and including 21.3 to 21.7 is 21.5 degrees in 2θ .

15. A crystalline solid form of Compound 1:



Compound 1,

having an XRPD pattern comprising peaks at 9.9 degrees in 2 θ , 14.8 degrees in 2 θ , 17.0 degrees in 2 θ , 20.7 degrees in 2 θ , and 21.5 degrees in 2 θ .