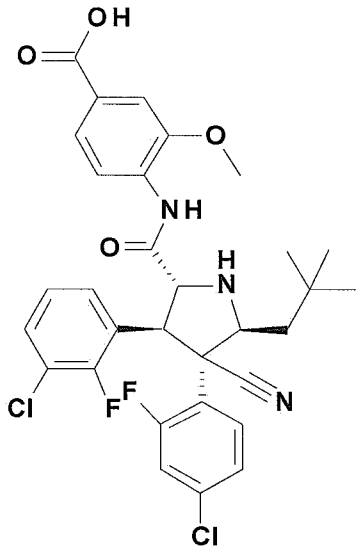
induces cell cycle arrest and/or apoptosis in a variety of tumor types expressing wild-type p53 in vitro and in vivo. Compound (1) belongs to a novel class of MDM2 inhibitors having potent anti-cancer therapeutic activity, in particular in leukemia such as acute myeloid leukemia (AML) and solid tumors such as for example head and neck, non-small cell lung, breast and colorectal cancers, as well as sarcoma.

The above-identified international patent application and US Patent describe Compound A in crystalline form and is herein incorporated by reference in its totality. The crystalline form of the compound has an on-set melting point of approximately 277 °C. The crystalline forms have relatively low aqueous solubility (<0.05 μg/mL in water) at physiological pHs (which range from pH1.5-8.0) and consequently less than optimal bioavailability (high variability). It is thus desirable to obtain a form of the compound which has improved solubility/dissolution rate and bioavailability.

Active pharmaceutical ingredients (API's) may be prepared in a variety of different forms, such as for example salts, solvates, hydrates, co-crystals. API's may also be in their amorphous state or one or several crystalline forms (polymorphs). Depending on the form, the physicochemical properties of an API may change, leading to e.g. different solubility, thermodynamic stability, density or melting point of different forms. Such physicochemical properties therefore may have significant influence of the efficacy or bioavailability of a known API.

SUMMARY

The present disclosure provides solid forms of compound (1)



selected from the group consisting of,

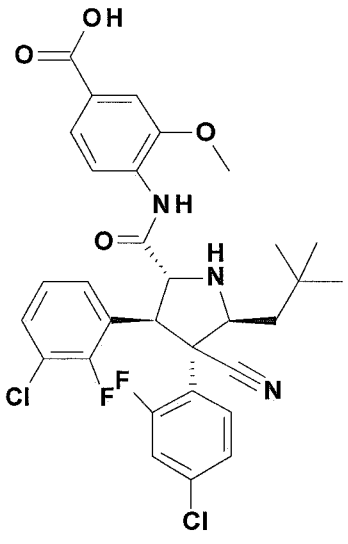
a) a substantially amorphous form of compound (1);

b) a hemi-hydrate, hydrate, hemi-solvate or solvate of compound (1);

c) a polymorph of compound (1); or

d) a pharmaceutically acceptable salt of compound (1).

In one aspect, there is provided a solid form of compound (1)



(1),

selected from

a) an amorphous form of compound (1);

b) a hemi-hydrate, hydrate, hemi-solvate or solvate of compound (1); or

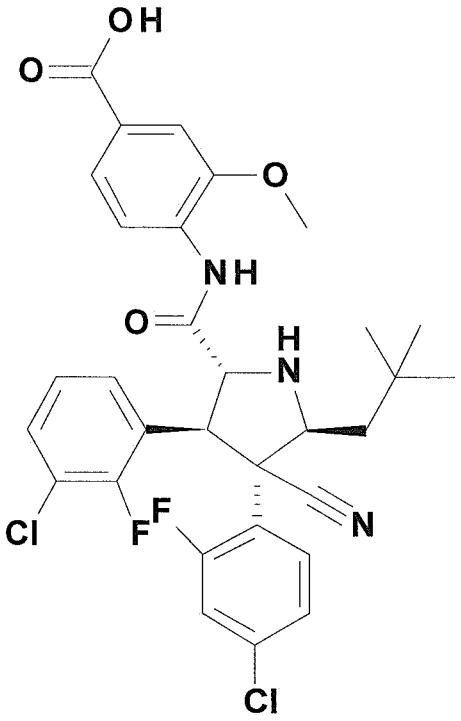
c) a polymorph of compound (1); or

d) a pharmaceutically acceptable salt of compound (1).

In one particular embodiment, said solid form is selected from a hemi-hydrate or -solvate designated form IV, V, VI, VII of compound (1).

CLAIMS

1. A solid form of compound (1)



(1),

selected from

a) an amorphous form of compound (1);

b) a hemi-hydrate, hydrate, hemi-solvate or solvate of compound (1); or

c) a polymorph of compound (1); or

d) a pharmaceutically acceptable salt of compound (1).

2. A solid form according to claim 1, characterized in that said solid form is a polymorph, hydrate, hemi-hydrate, solvate, hemi-solvate or pharmaceutically acceptable salt.

3. A solid form according to claim 1, characterized in that it is the amorphous form.

4. A solid form according to claim 1 or 2, characterized by the XRPD patterns obtained using Cu K • radiation at 2-theta values of 4.9, 6.9, 7.7, 9.1, 10.9, 13.5, 14.5, 17.2, 20.4, 22.3 and 25.5.

5. A solid form according to claim 1 or 2, characterized by the XRPD patterns obtained using Cu K • radiation at 2-theta values of 4.1, 5.0, 5.7, 6.3, 6.9, 7.9, 8.1, 9.0, 10.0, 14.3 and 19.5.

6. A solid form according to claim 1 or 2, characterized by the XRPD patterns obtained using Cu K • radiation at 2-theta values of 5.9, 8.3, 9.5, 10.1, 11.3, 14.2, 15.8, 17.6, 19.0, 19.4, 19.8, 20.3 and 25.5.

7. A solid form according to claim 1 or 2, characterized by the XRPD patterns obtained using Cu K • radiation at 2-theta values of 5.1, 8.0, 8.3, 8.8, 9.3, 10.0, 10.3, 13.7, 14.3, 18.7, 20.2, 20.8 and 27.6.

8. A solid form according to claim 1 or 2, characterized by the XRPD patterns obtained using Cu K • radiation at 2-theta values of 3.9, 7.8, 8.7, 9.1, 13.7, 14.5, 18.2 and 20.3.

9. A solid form according to claim 1 or 2, characterized by the XRPD patterns obtained using Cu K • radiation at 2-theta values of 5.5, 7.4, 14.5, 14.8, 15.6, 16.9, 17.8, 18.6, 19.9, 20.5, 24.8 and 26.7.

10. A solid form according to claim 1 or 2, characterized by the XRPD patterns obtained using Cu K • radiation at 2-theta values of 6.6, 10.7, 14.6, 15.7, 16.0, 16.4, 18.9, 19.8, 21.4, 22.0, 25.3 and 26.1.

11. A solid form according to claim 3, characterized by the FTIR wavenumbers, in cm^{-1}, of 1705, 1687, 1600, 1587, 1525, 1483, 1409, 1367, 1343, 1299, 1276, 1250, 1230, 1221, 1178, 1128, 1086, 1034, 902, 885, 817, 778, 765 and 729.

12. A pharmaceutical composition comprising one ore several solid forms according to any one of claims 1 to 11, together with pharmaceutically acceptable adjuvants or excipients.

***