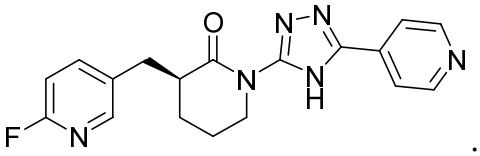
inhibiting both axonal degeneration and heightened pain sensitivity that develops after chemotherapeutic vincristine treatment (Geisler et al, *Brain*, 2016, 139, 3092-3108).

[0004] WO 2022/046606 A1 discloses certain inhibitors of SARM1, including (S)-3-((6-fluoropyridin-3-yl)methyl)-1-(5-(pyridin-4-yl)-4H-1,2,4-triazol-3-yl)piperidin-2-one free base (Compound I-23-a as described therein):



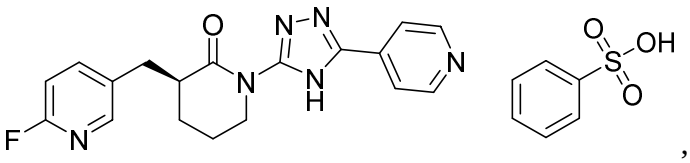
Compound I-23-a

SUMMARY

[0005] Early form and stability work on Compound I-23-a as obtained through the synthetic methods disclosed in WO 2022/046606 A1 revealed that the material is subject to the formation of several polymorphs and solvates, including a monohydrate form which is readily generated by subjecting the anhydrous form to standard room humidity conditions. Furthermore, it was later determined that a number of salt forms of the compound present with the same issues as the free base and additional unfavorable properties, such as poor crystallinity and dissociation in water. For these reasons it was concluded that neither the free base nor the specific salt forms would be suitable for further development into a commercial active pharmaceutical ingredient (API).

[0006] Among all the salts tested, (S)-3-((6-fluoropyridin-3-yl)methyl)-1-(5-(pyridin-4-yl)-4H-1,2,4-triazol-3-yl)piperidin-2-one benzenesulfonate was initially obtained as a mixture of two forms as detected by X-ray powder diffraction (XRPD). Further synthetic and characterization work allowed the isolation of a single form of the benzenesulfonate salt, which was surprisingly found to be highly crystalline, high melting, non-hygroscopic and stable under a variety of conditions.

[0006a] In an aspect, there is provided a compound of the formula:



or a hydrate or solvate thereof.

[0006b] In another aspect, there is provided a pharmaceutical composition comprising a compound as described herein with one or more pharmaceutically acceptable carriers, diluents, or excipients.

[0006c] In another aspect, there is provided a compound as described herein, or the pharmaceutical composition as described herein for use in inhibiting SARM1.

[0006d] In another aspect, there is provided use of a compound as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for treating or preventing a disease associated with SARM1 activation.

[0006e] In another aspect, there is provided use of a compound as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for treating or preventing a disease associated with axonal degeneration.

[0006f] In another aspect, there is provided use of a compound as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for treating or preventing a disease selected from amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), diabetic neuropathy and chemotherapy-induced peripheral neuropathy (CIPN).

[0006g] In another aspect, there is provided a compound as described herein for use in therapy.

[0006h] In another aspect, there is provided a compound as described herein for use in the treatment or prevention of a disease associated with SARM1 activation.

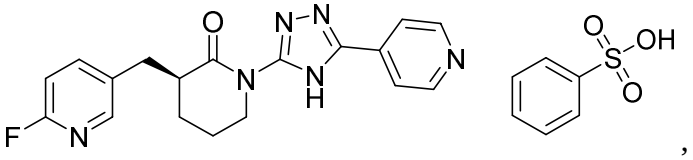
[0006i] In another aspect, there is provided a compound as described herein for use in the treatment or prevention of a disease associated with axonal degeneration.

[0006j] In another aspect, there is provided a compound as described herein for use in the treatment of a disease selected from amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), diabetic neuropathy and chemotherapy-induced peripheral neuropathy (CIPN).

CLAIMS

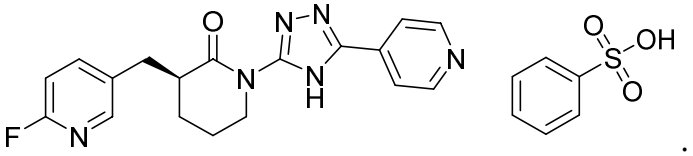
What is claimed is:

1. A compound of the formula:



or a hydrate or solvate thereof.

2. The compound according to claim 1, which is:



3. The compound according to claim 1 or 2, which is crystalline.
4. The compound according to any one of claims 1 to 3, which is crystalline, and which is characterized by an X-ray powder diffraction pattern using CuKα radiation comprising a peak at diffraction angle 2θ of 16.6˚, and one or more peaks at 5.7˚, 21.7˚ or 22.9˚ (±0.2˚ respectively).
5. A pharmaceutical composition comprising a compound according to any one of claims 1 to 4 with one or more pharmaceutically acceptable carriers, diluents, or excipients.
6. A compound according to any one of claims 1 to 4, or the pharmaceutical composition according to claim 5 for use in inhibiting SARM1.
7. Use of a compound according to any one of claims 1 to 4, or the pharmaceutical composition according to claim 5 in the manufacture of a medicament for treating or preventing a disease associated with SARM1 activation.
8. Use of a compound according to any one of claims 1 to 4, or the pharmaceutical composition according to claim 5 in the manufacture of a medicament for treating or preventing a disease associated with axonal degeneration.
9. Use of a compound according to any one of claims 1 to 4, or the pharmaceutical composition according to claim 5 in the manufacture of a medicament for treating

or preventing a disease selected from amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), diabetic neuropathy and chemotherapy-induced peripheral neuropathy (CIPN).

10. A compound according to any one of claims 1 to 4 for use in therapy.
11. A compound according to any one of claims 1 to 4 for use in the treatment or prevention of a disease associated with SARM1 activation.
12. A compound according to any one of claims 1 to 4 for use in the treatment or prevention of a disease associated with axonal degeneration.
13. A compound according to any one of claims 1 to 4 for use in the treatment of a disease selected from amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), diabetic neuropathy and chemotherapy-induced peripheral neuropathy (CIPN).