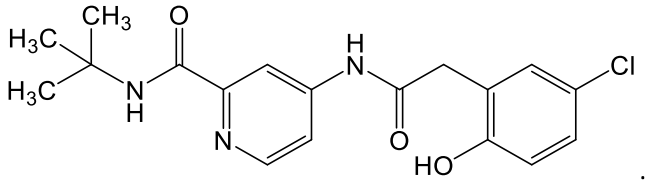
activity is independent of CFTR function, TMEM16A positive modulators have the potential to deliver clinical benefit to all CF patients and non-CF respiratory diseases characterised by mucus congestion including chronic bronchitis and severe asthma.

TMEM16A modulation has been implicated as a therapy for dry mouth (xerostomia), resultant from salivary gland dysfunction in Sjorgen's syndrome and radiation therapy, dry eye, cholestasis and gastrointestinal motility disorders.

The present inventors have developed novel compounds, and novel forms of these compounds, which are positive modulators of TMEM16A and which are therefore of use in the treatment of diseases and conditions in which TMEM16A plays a role, particularly respiratory diseases and conditions. These compounds were described for the first time in our earlier application WO2019/145726, the contents of which are hereby incorporated by reference in their entirety. In particular, WO2019/145726 discloses N-tert-Butyl-4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 1), which has the following structural formula:

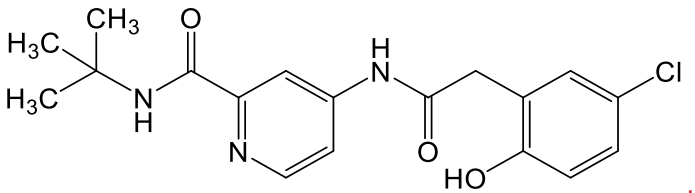


.

Summary ~~of the invention~~

The inventors have now developed novel forms of Compound 1.

In an aspect, there is provided a compound which is N-tert-Butyl-4-[[2-(5-chloro-2-hydroxy-phenyl)acetyl]amino]pyridine-2-carboxamide (Compound 1), having the following structural formula:



.

in the form of its Form A anhydrous solid crystalline polymorph, for example a form having an XRPD diffractogram substantially as shown in Figure 1; or in the form of its Form B hydrate solid crystalline polymorph, for example a form having an XRPD diffractogram substantially as shown in Figure 4; or in amorphous form.

In another aspect, there is provided a process for the preparation of a compound as defined above comprising crystallising Compound 1 from a solvent selected from acetone, butanol, ethanol, ethyl formate, isopropyl acetate, methyl acetate, nitromethane, 2-propanol, propionitrile and acetonitrile.

In another aspect, there is provided a process for the preparation of a compound as defined above, comprising crystallising Compound 1 from an aqueous solvent such as water or water mixed with acetonitrile.

In a first ~~aspect~~ example of the disclosure~~invention~~ there is provided Compound 1 in the form of its Form A anhydrous solid crystalline polymorph.

In a second ~~aspect~~ example of the disclosure~~invention~~ there is provided Compound 1 in the form of its Form B hydrate solid crystalline polymorph, in particular the Form B(I) hydrate solid crystalline pseudopolymorph or the Form B(II) hydrate solid crystalline pseudopolymorph.

In a third ~~aspect~~ example of the ~~invention~~ disclosure there is provided anhydrous solid amorphous Compound 1.

Brief description of the figures

Figure 1a is an XRPD diffractogram of solid crystalline polymorphic form A of Compound 1 in the range of 5 to 60 2-theta, step size 0.02 s (reflection mode, offset 500 counts).