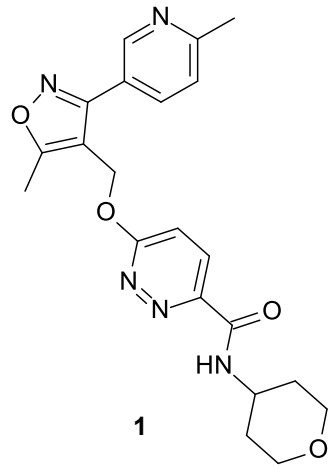
alogabat, i.a. due to use of toxic solvents, such as DMF, the need for silica gel chromatography, formation of side products, and low yields.

Accordingly, there is a high unmet need for new processes for manufacturing alogabat, in order to be able to provide patients with this new treatment option for ASD.

Summary

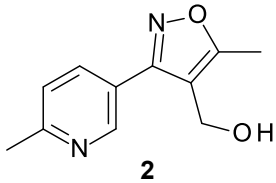
The present disclosure provides improved processes for manufacturing alogabat (**1**), which overcome the problems outlined above.

In one aspect, the present disclosure provides a process for manufacturing alogabat (**1**), or a pharmaceutically acceptable salt thereof,



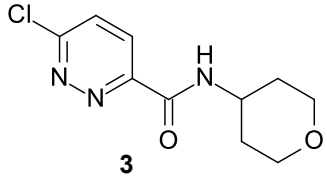
1

comprising reacting [5-methyl-3-(6-methyl-3-pyridyl)isoxazol-4-yl]methanol (**2**)



2

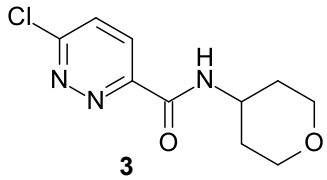
with 6-chloro-N-tetrahydropyran-4-yl-pyridazine-3-carboxamide (**3**)



3

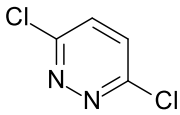
in the presence of a base, to afford said alogabat (**1**).

In another aspect, the present disclosure provides a process for manufacturing 6-chloro-N-tetrahydropyran-4-yl-pyridazine-3-carboxamide (**3**),



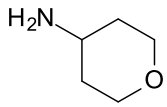
3

comprising reacting 3,6-dichloropyridazine (**4**)



4

with tetrahydro-2H-pyran-4-amine (**5**)

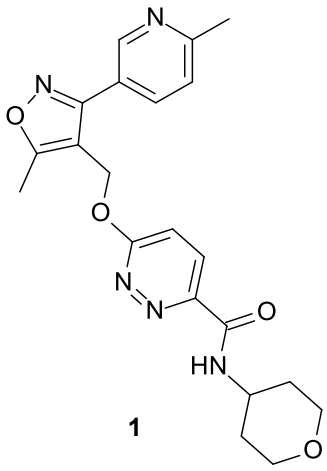


5

and carbon monoxide in the presence of a base and a palladium catalyst to afford said 6-chloro-N-tetrahydropyran-4-yl-pyridazine-3-carboxamide (**3**).

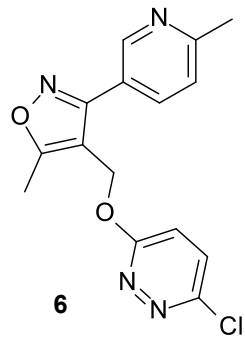
In another aspect, the present disclosure provides use of the process as described herein in the manufacture of alogabat (**1**).

In another aspect, the present disclosure provides a process for manufacturing alogabat (**1**), or a pharmaceutically acceptable salt thereof,



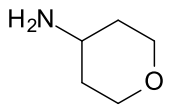
1

comprising reacting 4-[(6-chloropyridazin-3-yl)oxymethyl]-5-methyl-3-(6-methyl-3-pyridyl)isoxazole (**6**)



6

with tetrahydropyran-4-amine (**7**)



7

and carbon monoxide in the presence of a base and a palladium catalyst to afford said alogabat (**1**).

Detailed Description of the Invention

Definitions

Features, integers, characteristics, compounds, chemical moieties or groups described in conjunction with a particular aspect, embodiment or example of the invention are to be understood to be applicable to any other aspect, embodiment or example described herein, unless incompatible therewith. All of the features disclosed in this specification (including any accompanying claims and the abstract), and/or all of the steps of any method or process so disclosed, may be combined in any combination, except combinations where at least some of such features and/or steps are mutually exclusive. The invention is not restricted to the details of any foregoing embodiments. The invention extends to any novel one, or any novel combination, of the features disclosed in this specification (including any accompanying claims and the abstract), or to any novel one, or any novel combination, of the steps of any method or process so disclosed.

The term "pharmaceutically acceptable salt" refers to those salts which retain the biological effectiveness and properties of the free bases or free acids, which are not biologically or otherwise undesirable. The salts are formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, in particular hydrochloric acid, and organic acids such as acetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid, N-acetylcystein and the like. In addition these salts may be prepared by addition of an inorganic base or an organic base to the free acid. Salts derived from an inorganic base include, but are not limited to,