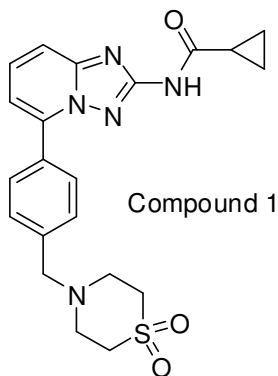


SUMMARY OF THE INVENTION

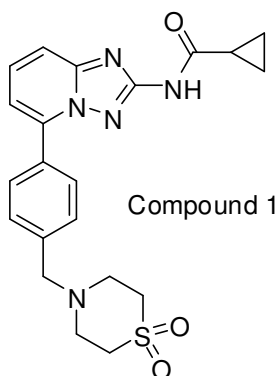
[0037] The present disclosure is based on the identification of novel salts and crystalline forms of Compound 1, useful in the treatment and/or prophylaxis of inflammatory conditions, autoimmune diseases, proliferative diseases, allergy, transplant rejection, diseases involving degradation and/or disruption of cartilage homeostasis, congenital cartilage malformations, and/or diseases associated with hypersecretion of IL6 or interferons. In particular, the salts of the disclosure may act as inhibitors of JAK, and in more particularly of JAK1. The present disclosure also provides methods for the production of these salts, pharmaceutical compositions comprising these salts and methods for the treatment and/or prophylaxis of inflammatory conditions, autoimmune diseases, proliferative diseases, allergy, transplant rejection, diseases involving degradation and/or disruption of cartilage homeostasis, congenital cartilage malformations, and/or diseases associated with hypersecretion of IL6 or interferons by administering the salts of the disclosure.

[0038] Also disclosed is a salt of a compound according to Formula (I) below (hereafter also named Compound 1):



wherein said salt is formed with hydrobromic acid, hydrochloric acid, sulfuric acid, toluenesulfonic acid, benzenesulfonic acid, oxalic acid, maleic acid, naphthalene-2-sulfonic acid, naphthalene-1,5-disulfonic acid, 1-2-ethane disulfonic acid, methanesulfonic acid, 2-hydroxy ethanesulfonic acid, phosphoric acid, ethane sulfonic acid, malonic acid, 2-5-dihydroxybenzoic acid, or L-Tartaric acid.

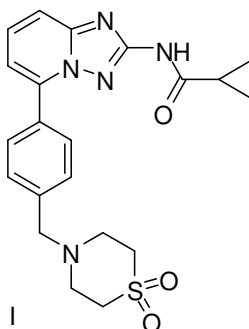
[0039] Accordingly, in one aspect the present invention provides a salt of a compound according to Formula (I) below (hereafter also named Compound 1):



wherein said salt is formed with hydrochloric acid, or a maleic acid salt, and wherein the salt is in a crystalline form.

CLAIMS

- 1) A pharmaceutically acceptable salt of a compound according to Formula (I):



wherein the salt is an hydrochloric acid, or a maleic acid salt, and

wherein the salt is in a crystalline form.

- 2) A pharmaceutically acceptable salt according to claim 1, wherein the salt is a 1:1 free base/hydrochloric acid salt.
- 3) A pharmaceutically acceptable salt according to claim 1, wherein the salt is a 1:1 free base/maleic acid salt.
- 4) A pharmaceutically acceptable salt according to any one of claim 1-2, wherein the salt is a pharmaceutically acceptable solvate of the salt.
- 5) A pharmaceutically acceptable salt according to any one of claim 1-2, wherein the salt is a hydrate of the salt.
- 6) A pharmaceutically acceptable salt according to claim 5, wherein the hydrate of the salt is a 1:1:3 Free Base/HCl/H₂O adduct.
- 7) A pharmaceutically acceptable salt or pharmaceutically acceptable hydrate of a salt according to claims 6, wherein the hydrate of the salt is in a crystalline form.
- 8) A pharmaceutically acceptable hydrate of a salt according to claim 7, wherein the 1:1:3 Free Base/HCl/H₂O hydrate of the salt is characterized at least by a powder X-ray diffraction peak at any one or more of the following positions: 7.25, 8.31, 8.78, 10.69, 11.96, 12.25, 13.17, 13.74, 16.23, 16.71, 19.26, 19.64, 20.15, 20.57, 20.95, 21.38, 21.69, 22.77, 23.37, 25.14, 25.71, 25.89, 27.66, 28.57, 28.81, 29.17, 29.58, 30.63, 30.94, 32.06, 32.63, 34.14, 36.22, 36.67, and 37.12° 2θ ± 0.2° 2θ.
- 9) A pharmaceutically acceptable hydrate of a salt according to claim 7, wherein the 1:1:3 Free Base/HCl/H₂O hydrate of the salt characterized by the following diffraction parameters:

Molecular formula	C ₂₁ H ₂₄ N ₅ O ₃ S.Cl ₃ (H ₂ O)				
Molecular weight	516.02				
Crystal system	Monoclinic				
Space group	P2 _{1/n}	a	13.1388(4) Å	α	102.089(2)°
		b	8.9437(3) Å	β	
		c	21.6376(9) Å	γ	
V	2486.24(15) Å ³				
Z	4				
Dc	1.379 mg / m ³				
μ	0.284 mm ⁻¹				

Source	Mo-K α , 0.71073 Å
F(000)	1088
T	120(2) K
Crystal	colourless prism, 0.39 x 0.16 x 0.12 mm
θ range for data collection	2.982 – 27.483°
Completeness	99.3%
Reflections	21028
Unique reflections	5649
R _{int}	0.0307

- 10) A pharmaceutical composition comprising a pharmaceutically acceptable hydrate of a salt according to any one of claims 1-9, and a pharmaceutically acceptable carrier, excipient or diluent.
- 11) A pharmaceutical composition according to claim 10, comprising a further therapeutic agent.
- 12) A pharmaceutically acceptable salt according to any one of claims 1-9, or a pharmaceutical composition according to 10 or 11 for use in medicine.
- 13) A pharmaceutically acceptable salt according to any one of claims 1-9, or a pharmaceutical composition according to 10 or 11 for use in the prophylaxis and/or treatment of inflammatory conditions, autoimmune diseases, proliferative diseases, allergy, transplant rejection, diseases involving degradation and/or disruption of cartilage homeostasis, congenital cartilage malformations, and/or diseases associated with hypersecretion of IL6 or interferons.
- 14) The use according to claim 12 or 13, wherein the pharmaceutically acceptable salt according to any one of claims 1-9, or the pharmaceutical composition according to 10 or 11 is to be administered in combination with another therapeutic agent.
- 15) The pharmaceutical composition according to claim 11, or the use according to claim 14, wherein the further therapeutic agent is an agent for the prophylaxis and/or treatment of inflammatory conditions, autoimmune diseases, proliferative diseases, allergy, transplant rejection, diseases involving degradation and/or disruption of cartilage homeostasis, congenital cartilage malformations, and/or diseases associated with hypersecretion of IL6 or interferons.
- 16) A method for preparing a [Compound according to Formula I:HCl:3H₂O] adduct in a solid crystalline form comprising the steps of:
 - i) mixing the compound of Formula I suspended in DCM, with MeOH at 35°C,
 - ii) adding water under stirring at 35°C for at least 15 min,
 - iii) separating the organic layer,
 - iv) adding a 10% w/w solution of HCl in MeOH to the organic layer obtained in the previous step iii),
 - v) separating the resulting solid by filtration obtained in the previous step iv),
 - vi) drying said resulting solid obtained in the previous step v),
 - vii) adding the solid obtained in the previous step vi) to a 1.6/0.4 formic acid/water solution, under stirring at 55°C
 - viii) adding water to the solution obtained in the previous step vii),
 - ix) separating by filtration the resulting solid obtained in the previous step viii), and