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Datasheet for the decision of 25 July 2024

Case Number: T 1206/22 - 3.3.02

Application Number: 16704896.6

Publication Number: 3256472

IPC: C07D471/04, A61P11/00, A61P11/06

Language of the proceedings: EN

Title of invention:
SALT OF A PYRIMIDO[6,1-A]ISOQUINOLIN-4-ONE COMPOUND

Applicant:
Verona Pharma PLC

Relevant legal provisions:
EPC Art. 123(2), 84, 83, 54, 56

Keyword:
Amendments
Clarity
Sufficiency of disclosure
Novelty
Inventive step

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Case Number: T 1206/22 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 25 July 2024

Appellant: (Applicant)	Verona Pharma PLC One Central Square Cardiff CF10 1FS (GB)
Representative:	J A Kemp LLP 80 Turnmill Street London EC1M 5QU (GB)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 1 December 2021 refusing European patent application No. 16704896.6 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	M. O. Müller
Members:	A. Lenzen
	L. Bühler

Summary of Facts and Submissions

I. This decision concerns the appeal filed by the applicant (appellant) against the examining division's decision (decision under appeal) to refuse European patent application No. 16 704 896.6 (application).

II. The decision under appeal is based on a single claim request. The examining division considered that the subject-matter of claim 1 was not novel over the following document:

D1 WO 2012/020016 A1

With regard to inventive step, the examining division expressed a positive opinion in an *obiter dictum* on the subject-matter of claim 3.

III. In the statement of grounds of appeal, the appellant pursued, *inter alia*, the request on which the decision under appeal is based.

IV. In preparation for the oral proceedings, which had been arranged at the appellant's request, the board issued a communication pursuant to Article 15(1) RPBA. In it, the board agreed with the examining division's novelty objection based on D1. The board also provided comments on clarity, sufficiency and inventive step.

V. The oral proceedings before the board were held by videoconference on 25 July 2024 in the presence of the appellant. During the oral proceedings, the appellant filed the following document:

D5 L. G. Franciosi et al., Lancet Respir. Med. vol. 1(9), 2013, 714-27

It also filed a set of claims of a replacement first auxiliary request. In view of the board's favourable opinion on this request, the appellant made it its main request. At the end of the oral proceedings, the chair announced the order of the present decision.

VI. The appellant requested that the decision under appeal be set aside and that a patent be granted based on the set of claims of the main request, filed during the oral proceedings before the board as replacement first auxiliary request.

Reasons for the Decision

Main request

1. The independent claims 1 and 3 to 5 of the main request read as follows:

Claim 1

"*A pharmaceutically acceptable acid addition salt of:*

(i) 9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)-3-(N-carbamoyl-2-aminoethyl)-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one (RPL554); and
(ii) ethane-1,2-disulfonic acid,

or a solvate thereof, wherein the pharmaceutically acceptable acid addition salt or solvate thereof is a solid."

Claim 3

"*A pharmaceutical composition which is a dry powder comprising a pharmaceutically acceptable acid addition salt as defined in claim 1 or 2 and a pharmaceutically acceptable excipient or carrier.*"

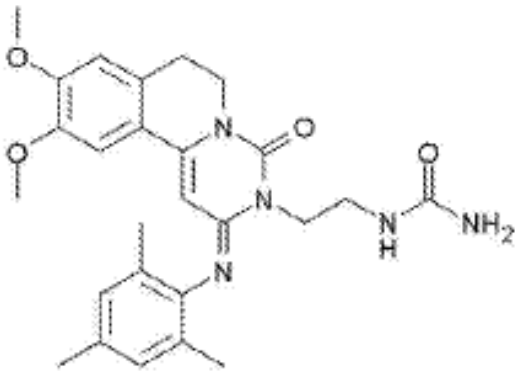
Claim 4

"*A pharmaceutically acceptable acid addition salt as defined in claim 1 or 2 for use in the treatment of the human or animal body.*"

Claim 5

"*A pharmaceutically acceptable acid addition salt as defined in claim 1 or 2 for use in the treatment or prevention of a disease or condition selected from asthma and chronic obstructive pulmonary disease (COPD).*"

2. Thus, the independent claims essentially relate to the solid acid addition salt of RPL554, i.e.



,

with ethane-1,2-disulfonic acid (claim 1), a pharmaceutical dry powder composition comprising it (claim 3), and its first (claim 4) and second medical use (claim 5).

3. Amendments (Article 123(2) EPC)

3.1 The subject-matter of claim 1 of the main request is based on the following parts of the application as filed: page 2, lines 13 to 15; page 4, line 26 to page 5, line 2; and claim 1. Based on the disclosure of these parts, the subject-matter of claim 1 of the main request is the result of a single selection of ethane-1,2-disulfonic acid as the acid component of the pharmaceutically acceptable acid addition salt. This single selection does not result in subject-matter which extends beyond the content of the application as filed.

3.2 Compared to claim 19 as filed, which recites a plurality of diseases/conditions, claim 5 of the main request relates only to asthma and COPD. By referring back to claim 1, the subject-matter of claim 5 of the main request is therefore the result of a double selection, namely ethane-1,2-disulfonic acid as the acid component of the pharmaceutically acceptable acid addition salt and asthma and COPD as diseases/ conditions. The board considers such a double selection to be allowable in the case at hand since there are pointers in the application as filed indicating a preference for the respective selections (page 11, line 10; page 23, lines 8 to 10; page 44, lines 11 to 12).

3.3 The subject-matter of claims 2, 3, 4 and 6 of the main request is based on claims 3, 10 and 12, 18, and 20 of the application as filed, respectively.

3.4 Thus, the claimed subject-matter of the main request meets the requirements of Article 123(2) EPC.

4. Sufficiency (Article 83 EPC)

4.1 The set of claims on which the decision under appeal is based contains a second medical use claim directed to a plurality of diseases/conditions. In its communication, the board did not consider it credible that each of these diseases/conditions could be treated/prevented with the compound in question, i.e. the pharmaceutically acceptable acid addition salt of claim 1 above (Article 83 EPC).

4.2 In the second medical use claim of the main request, these conditions have been restricted to asthma and COPD (see the wording of claim 5 above).

4.3 According to the application as filed (page 1, last paragraph), RPL554 is a dual PDE3/PDE4 inhibitor and as such has both anti-inflammatory and bronchodilatory activity. It is useful in the treatment of respiratory disorders such as asthma and COPD. This disclosure of the application as filed is confirmed by D5 (page 714, last paragraph of the summary) and is, therefore, not just a mere assertion.

Against this background, the board considers it credible that the pharmaceutically acceptable acid addition salt of claim 1 is suitable for the treatment and prevention of asthma and COPD. Therefore, the

board's objection under Article 83 EPC raised in the communication under Article 15(1) RPBA is now moot.

5. Clarity (Article 84 EPC)

The set of claims of the main request is clear. The board's objections under Article 84 EPC raised in the communication under Article 15(1) RPBA have been rendered moot due to the deletion of the corresponding claims.

6. Novelty (Article 54 EPC)

Claim 1 of the set of claims on which the decision under appeal is based relates not only to a pharmaceutically acceptable acid addition salt of RPL554 and ethane-1,2-disulfonic acid but also to salts formed between RPL554 and other acids, namely ethanesulfonic acid, methanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, hydrobromic acid, phosphoric acid and sulfuric acid. The examining division objected to this claim 1 as not being novel only for some of these other acids. It considered the acid addition salt formed between RPL554 and ethane-1,2-disulfonic acid to be novel.

The board agrees. D1 does not disclose ethane-1,2-disulfonic acid or salts derived from it.

Thus, the subject-matter of claim 1, the other independent claims 3 to 5, and the dependent claims 2 and 6 is novel over the cited prior art.

7. Inventive step (Article 56 EPC)

7.1 The board agrees with the view expressed by the examining division in its *obiter dictum* that D1 represents the closest prior art.

7.2 D1 (e.g. claim 1) relates to RPL554 and its solid forms.

7.3 The subject-matter of claim 1 is distinguished from solid RPL554 as disclosed in D1 in that it relates to a salt of RPL554 with ethane-1,2-disulfonic acid.

7.4 The application (table 6) discloses that RPL554 ethane-1,2-disulfonate has a much higher solubility in 0.7 w/w% and 0.9 w/w% saline than RPL554. Of the numerous RPL554 salts tested (phosphate, methane sulfonate, ethane-1,2-disulfonate, hydrochloride, sulfate, benzenesulfonate, ethanesulfonate, hydrobromide, p-toluenesulfonate, naphthalene-2-sulfonate and naphthalene-1,5-disulfonate), RPL554 ethane-1,2-disulfonate has the third and second highest solubility in 0.7 w/w% and 0.9 w/w% saline, respectively.

The application (tables 14 and 22) also evaluates the performance of RPL554 and various salts of it in a dry powder inhaler. To this end, RPL554 and its salts were micronised to a degree required for formulation as a respiratory product (D(0.9) < 5 µm) and mixed with lactose, and the formulations were aerosolised. The formulation containing RPL554 ethane-1,2-disulfonate had a significantly higher percentage of fine particles (< 5 µm) in the aerosol output (fine particle fraction, FPF) than that containing RPL554 alone (RPL554 ethane-1,2-disulfonate, 40.39%; RPL554, 35.20%). Of the

numerous RPL554 salts tested (methane sulfonate, ethane-1,2-disulfonate, hydrochloride, sulfate, benzenesulfonate, ethanesulfonate, hydrobromide and p-toluenesulfonate), RPL554 ethane-1,2-disulfonate had the second highest FPF.

7.5 The appellant argued that a high FPF was beneficial as it allowed more of the formulation to penetrate deep into the lungs. Furthermore, 0.7 w/w% and 0.9 w/w% saline used for the solubility tests were representative of the physiological conditions in the lungs. A high solubility in these media indicated a high solubility in the lung tissue. RPL554 ethane-1,2-disulfonate not only imparted a high FPF to the dry powder formulation containing it but also had a high solubility in 0.7 w/w% and 0.9 w/w% saline. In terms of these two aspects, it was not only better than RPL554 but also than most other salts of it tested in the application. Thus, RPL554 ethane-1,2-disulfonate had a beneficial combination of properties that made it more suitable for the treatment of respiratory diseases with a dry powder formulation.

7.6 The board saw no reason to object to the appellant's arguments. Therefore, starting from RPL554 as disclosed in D1, the objective technical problem is to provide a form of RPL554 that makes it more suitable for the treatment of respiratory diseases with a dry powder formulation.

7.7 Even if the skilled person had contemplated the formation of the ethane-1,2-disulfonate of RPL554 to increase its solubility in general and in various salt solutions (0.7 w/w% and 0.9 w/w% saline), the skilled person would not have had a reasonable expectation of obtaining in this way a form of RPL554 with such a

beneficial combination of properties as shown in the application, i.e. in terms of solubility and FPF.

This reasoning applies *mutatis mutandis* also to the subject-matter of the other independent claims 3 to 5 and the dependent claims 2 and 6.

7.8 Therefore, the subject-matter of the main request involves an inventive step. The main request is allowable.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the examining division with the order to grant a patent with the following claims and a description to be possibly adapted thereto:

   claims 1 to 6 of the main request filed during the oral proceedings as replacement first auxiliary request dated 25 July 2024

The Registrar: The Chairman:

H. Jenney M. O. Müller

Decision electronically authenticated