

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No. PCT/IB2015/054712	International filing date (day/month/year) 23.06.2015	Priority date (day/month/year) 25.06.2014
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International Patent Classification (IPC) or both national classification and IPC
INV. C07D401/14 A61K31/506 A61P35/00

Applicant
GLAXOSMITHKLINE INTELLECTUAL PROPERTY...

1. This opinion contains indications relating to the following items:
- ☒ Box No. I Basis of the opinion
 - ☒ Box No. II Priority
 - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - ☐ Box No. IV Lack of unity of invention
 - ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
 - ☒ Box No. VI Certain documents cited
 - ☐ Box No. VII Certain defects in the international application
 - ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:  European Patent Office Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Date of completion of this opinion see form PCT/ISA/210	Authorized Officer Frelon, Didier Telephone No. +49 30 25901-0 
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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed.
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
 - a. ☐ forming part of the international application as filed:
 - ☐ in the form of an Annex C/ST.25 text file.
 - ☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
 - ☐ in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	<u>1-27</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	<u>1-27</u>
	No: Claims	
Industrial applicability (IA)	Yes: Claims	<u>1-27</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V.

1. Cited documents

Reference is made to the following documents:

- D1 WO 2014/100719 (intermediate document - Rules 33.1c, 64.3, 70.10 PCT)
D2 WO 2011/079236

2. Novelty

The presently claimed salts are novel in view of the prior art available.

It is noted that document D1, cited by the applicant, is an intermediate document relevant only for novelty in regional (European) phase. D1 discloses *generically* the formation and crystallization of chiral salts of the compounds described therein (paragraphs [0017], [0055], [00231] and [00232]), particularly compound 208 which corresponds to present compound A, the crystalline succinate and benzoate salts of which are now claimed (present compounds B and C, resp.). These salts are not specifically disclosed and consequently, in a regional phase, the presently claimed subject-matter would be considered as a novel selection of D1.

3. Inventive step

3.1 The problem underlying the present application is to provide crystalline succinate and benzoate salts of the title compound.

3.2 In the absence of further relevant document retrieved in relation with the present application, the closest prior art for the present application can be considered to be the same as the prior art taken into consideration for the examination of the compounds of intermediate document D1 which overlaps the present application by disclosing

generically the presently claimed crystalline salts. Like the compounds of D1 which have been acknowledged as patentable, the presently claimed salts do not appear to be directly and unambiguously derivable from the teaching of D2.

Additionally the applicant has provided solubility tests for the claimed salts in examples 2 and 3. It belongs to the general knowledge of the skilled person that crystalline forms of a compound present solubility properties which can be useful for the preservation and/or the administration of the drug. However the specific test results as provided could not be directly and unambiguously derived from the prior art teaching. The succinate and benzoate salts as now identified as novel appear therefore to be also inventive.

Re Item VI.

Publication date	Filing date	Priority date
WO 2014/100719	20.12.2013	21.12.2012 15.03.2013

The intermediate document is relevant for the purposes of Rules 33.1c, 64.3 and 70.10 PCT, but since the priority document(s) is(are) not available at the time of establishing this written opinion, this prior art is not taken into account. It is based on the assumption that all claims enjoy priority rights from the filing date of the priority document(s). If during a subsequent procedure (*e.g.*, EPO examination) it later turns out that this assumption is not correct for some or all the presently claimed subject-matter, the intermediate document(s) may be highly relevant for the assessment of novelty in the regional phase of examination and, depending on the validity of the respective priorities, may also be relevant for the assessment of inventive step.

Re Item VIII.

1. Claims 19 to 23 are directed to methods for treatment of the human or animal body by surgery or therapy. These claims relate to subject-matter considered by the ISA to be covered by the provisions of Art. 17(2)(a)(i) PCT in conjunction with Rule 39.1(iv) PCT. Under the terms of this rule, the ISA is not required to carry out a search of such claims, the search was therefore carried out and based on the alleged effects of the

compounds. Similarly, according to Art. 34(4)(a)(i) PCT in conjunction with Rule 67.1 (iv) PCT, the IPEA is not required to carry out an international preliminary examination of such claims.

In this respect it is noted that no unified criteria exists within the Contracting States of the PCT as to the question whether or not such methods are industrially applicable and accordingly whether or not claims directed to such methods are admissible. The patentability can also be dependent upon the formulation of the claims. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Art. 34(4)(a)(ii) PCT).

The EPO, for example, does not recognize as patentable the subject-matter of claims to the use of a compound in medical treatment or diagnostic method practised on the human or animal body on the ground of lack of industrial applicability, but may allow claims directed to a product, in particular substances or compositions, for use in a first or further medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment. The present written opinion will be based on the alleged effects of the compounds.

This objection also applies to the corresponding passages throughout the description, referring to methods of treatment, which contravene the PCT provisions. These mentions should be removed or reworded to indicate a possible application of the invention.

2. Since examples are, by definition, illustrative of the invention, they normally should not serve any limiting purpose. It is the claims, when appropriately drafted, which define the scope, not the examples. The sentence "the examples are to be construed as merely illustrative and not a limitation of the scope of the invention in any way" is not clear and if it is intended as a precautionary measure on the limits of the invention, it should be avoided since this is superfluous if the invention is clearly defined and appropriately illustrated, as it should be. Furthermore, the examples actually are and should be illustrative of the invention.

Expressions and/or sentences which may also refer to an extent of protection beyond the actual invention are essentially speculative. The insertion of such broadening expressions and/or sentences is therefore also objectionable because it would suggest that the subject-matter is not properly covered by the claimed scope for which a protection is sought. The specification should be clear and sufficient by itself and the claims should find a clear support in the description. Unspecific expressions cannot serve as a support for the invention and, particularly, do not help a skilled person looking for reproducing it.

3. The expression "*incorporated herein by reference*" concerning cited patents and publications gives rise to clarity objections and should be deleted since it is vague and ambiguous which technical features are referred to. Furthermore, it should be noted that this kind of reference contravenes the basic requirement of each application that whenever certain matter in a document is essential to the reproduction of the invention, it should be expressly incorporated in the description. Indeed, a patent specification should, regarding the essential features of the invention, be self-contained, *i.e.* capable of being understood without reference to any other document.