PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.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.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2015/061350	22.05.2015	23.05.2014

International Patent Classification (IPC) or both national classification and IPC
INV. C07D487/04 A61K31/519 A61P11/06 A61P29/00

Applicant
F. HOFFMANN-LA ROCHE AG

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 43*bis*.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 notifed the International Bureau under Rule 66.1*bis*(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:	Date of completion of this opinion	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Fax: +49 89 2399 - 4465	see form PCT/ISA/210	Gettins, Marc Telephone No. +49 89 2399-0

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 43*bis*.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 13*ter*.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 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.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. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-13, 25
	No:	Claims	1, 14-24, 26-35
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-35
Industrial applicability (IA)	Yes:	Claims	1-35
	No:	Claims	

2. Citations and explanations

see separate sheet

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

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Relevant prior art is provided by:

D1 WO 2011/003065 cited in the application

D2 WO 2012/129258

1.1 The Applicant should explain the reason for the proviso found in claim 1. If it is intended to exclude some unacknowledged prior art known to the Applicant the said prior art should be cited (Rule 5.1 (a) (ii) PCT).

2 Claims 25-28, 30 and 32-34 relate to a subject-matter considered by this Authority to be covered by the provision of Rule 39.1(iv) /67.1(iv) PCT. The patentability can be dependent upon the formulation of the claims. The EPO, for example, does not recognise as patentable claims to the use of a compound in medical treatment, but may allow claims to a product, in particular substances or compositions for use in a first or further medical treatment. The patentability can be dependent upon the formulation of the claims. The EPO, for example, does not recognise as patentable claims to the use of a compound in medical treatment, but may allow claims to a product, in particular substances or compositions for use in a first or further medical treatment.

3 The current application is novel vis-à-vis D2 on account of the points of attachment on the Q ring. The current application overlaps with D1. The specific examples in D1 (examples 18, 124 and 460) which anticipate the current application have been excluded by means of a proviso. However, document D1 not only discloses the excluded example compounds, but also discloses a generic formula illustrated by examples. In the present case, there

is a novelty destroying area of overlap between present claim 1 and the generic formula of claim 11 of D1. The overlap is considered to be novelty destroying.

4 The current application and the closest prior art D1 are both JAK inhibitors. The currently claimed matter overlaps with the said prior art and is only novel vis-à-vis specific examples in D1 on account of a proviso. In such a case the problem underlying the invention must be considered to be the provision of improved JAK inhibitors. Any such improvement can only be shown by means of comparative data. There does not appear to be any such data on file and accordingly it is considered that the problem has not been demonstrably solved.

4.1 The Applicant is asked to demonstrate that the problem underlying the current application has in fact been solved. In order to be fully convincing any comparative tests used to demonstrate this must be carried out against the structurally closest prior art i.e. D1, examples 18, 124 and 460 and should be representative for the whole scope of the claims.

Re Item VIII

Certain observations on the international application

1 Claim 25 which refers to Table 1 is not allowable under Rule 6.2 PCT.

2 The omnibus claim 35 is both superfluous and unclear in scope. It should be deleted.

3 All "incorporated by reference" passages(see e.g. p1, line 8 should be deleted.

4 There is an unacceptable discrepancy between the claims and the description since the description (see e.g. page 19 indicates that various substituents such as alkyl can be substituted even when this has not been specified. The skilled person would not have been aware of this from a reading of the claims

since the skilled person would assume that standard IUPAC nomenclature was being used. In the current case, however, the Applicant has obviously seen fit to use non-standard interpretations of standard nomenclature. The intended scope of the claims cannot be understood without referring to the description which contravenes (Rule 6 PCT). The claims and description should be fully harmonised so that their scope is the same and so that the claims are fully clear in their own right.

5 "A" and "an" only means one and doe snot mean "more". Page 44, lines 19-20 should be deleted.

6 The paragraph bridging pages 249-250 (spirit and scope) merely blurs the intended scope of the invention and should be deleted.

7 The reference on page 85, line 4 to D1 is unclear in scope. the Applicant should make it specifically clear how the current application differs from D1 and should not simply give a broad statement that any compound(s) of D1 is excluded.