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/EP2013/075876	09.12.2013	10.12.2012

International Patent Classification (IPC) or both national classification and IPC
INV. C07C311/16 C07C311/21 C07C311/29 C07C311/39 C07C311/44 A61K31/18 A61P29/00 A61P37/00

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 P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Fax: +31 70 340 - 3016	see form PCT/ISA/210	Fitz, Wolfgang Telephone No. +31 70 340-4359

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 filed or furnished:

   a. (means)

   ☐ on paper

   ☐ in electronic form

   b. (time)

   ☐ in the international application as filed

   ☐ together with the international application in electronic form

   ☐ subsequently to this Authority for the purposes of search

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 in 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	4, 6, 8, 10, 12-18, 20-27
	No:	Claims	1-3, 5, 7, 9, 11, 19, 28
Inventive step (IS)	Yes:	Claims	4, 6, 8, 10, 12-18, 20-27
	No:	Claims	1-3, 5, 7, 9, 11, 19, 28
Industrial applicability (IA)	Yes:	Claims	1-28
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

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

D1 DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 6 July 2005 (2005-07-06), Database accession no. 851689-54-8

D2 DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 19 December 2003 (2003-12-19), Database accession no. 627841-51-4

D3 WO 2012/158784 A2

D4 KUMAR N ET AL: "Probe Reports from the NIH Molecular Libraries Program, Campaign to identify novel modulators of the Retinoic acid receptor-related Orphan Receptors (ROR)", PROBE REPORTS FROM THE NIH MOLECULAR LIBRARIES PROGRAM, pages 1-22, XP002686345, Retrieved from the Internet: URL:http://www.ncbi.nlm.nih.gov/books/NBK56239/ [retrieved on 2012-10-30]

Re Item V

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

1. Claims 23 and 25 relate to subject-matter considered by this Authority to be covered by the provisions 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.

2. D1 (abstract) discloses a compound which falls in the scope of claims 1-3, 5, 7, 9, 11 and 28. D2 (abstract) discloses a compound which falls in the scope of claims 1-3, 5, 9, 11, 19 and 28.

The subject-matter of claims 1-3,5,7,9,11,19 and 28 is consequently not new, Art. 33 (2) PCT.

3. No inventive step can be acknowledged for subject matter which is not new. The subject-matter of claims 1-3,5,7,9,11,19 and 28 consequently lacks an inventive step, Art. 33(3) PCT.

Each of D3 or D4 can be regarded as being the prior art closest to the subject-matter of claims 1-28. D3 and D4 disclose benzenesulfonamide derivatives, which are useful as RORc modulators.

The main difference between the compounds of present claim 1 and the compounds of D2 and D3 is that the former contain two rings in the sulfonic acid part of the sulfonamide.

There is no improved technical effect demonstrated with regard to the difference to the closest prior art.

The problem underlying the present application is seen as providing alternative RORc modulators.

The solution proposed in claims 1-28 of the present application, as far as new and not too broadly claimed (see below), is considered as involving an inventive step (Article 33(3) PCT), because the present compounds are structurally rather remote from the compounds of D3 and D4.

Re Item VII

Certain defects in the international application

4. Contrary to the requirements of Rule 5.1 (a)(ii) PCT, the relevant background art disclosed in D3 and D4 is not mentioned in the description, nor are these documents identified therein.

Re Item VIII

Certain observations on the international application

5. The formulae Ia and Ib in claim 1 are broader than justified by the support which is available in the description, in particular when considering the limited diversity in the structures of the compounds in the examples, Art. 6 PCT.

The scope of the claim should be in balance with the support, so that it is reasonable to assume that substantially all claimed compounds are indeed useful as RORc modulators.

6. Claim 28 is vague, Art. 6 PCT.

7. The following issues might also have to be addressed in the European phase: general statements ("spirit of the invention", "but not limited", "and the like" etc.) should be deleted. References to methods of treatment in the description should be reformulated, see also point 1 above.