

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.
PCT/IB2015/055006

International filing date (day/month/year)
02.07.2015

Priority date (day/month/year)
02.07.2014

International Patent Classification (IPC) or both national classification and IPC
INV. C07D401/14 C07D401/10 C07D401/12 A61K31/445 A61P27/06

Applicant
NOVARTIS 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 notified 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:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0
Fax: +49 89 2399 - 4465

Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Götz, Gerhard

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 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. 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. 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

- D1 WO 2008/073452 A1 (REVIVA PHARMACEUTICALS INC [US]; MOHAPATRA PRABHU PRASAD [US]; BHAT LA) 19 June 2008 (2008-06-19)
- D2 WO 2010/099054 A2 (MERCK SHARP & DOHME [US]; KIM RONALD M [US]; PARMEE EMMA R [US]; SINZ) 2 September 2010 (2010-09-02)

Re Item V

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

- 1 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.
Claims 23 to 27 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 39.1(iv) / 67.1(iv) PCT.
- 2 D1 discloses indanone-derivatives which are used in the treatment of glaucoma (see claim 18).
The compounds of D1 differ structurally from the claimed ones:
D1 discloses indanone-derivatives whereas in present claims 1 to 20 indane- and indoline-derivatives are claimed. Additionally the pyrazolyl-pyridine- or pyrazolyl-phenyl-substituent is missing in the compounds of D1.
- D2 discloses guanylate cyclase activators, however, the indane- or indoline-structure is missing (see table 5).
- The present application does thus meet the criteria of Article 33(1) PCT,

because the subject-matter of claims 1 to 27 is new in the sense of Article 33 (2) PCT.

- 3 Having regard to the disclosure of in particular D2 the underlying problem is defined by the provision of further guanylate cyclase activators which are used in the treatment of glaucoma.

The proposed solution which are the compounds according to present claims 1 to 20 are considered to be based on an inventive step:

The performed biological tests as demonstrated in present example 1 and table 1 prove that this underlying problem has been credibly solved.

Furthermore, the claimed compounds are not rendered obvious from any of the prior art documents: the structure of the claimed compounds shows major structural differences to the compounds of D1 and/or D2. Due to these structural differences an inventive step is accepted.

The present application meets therefore the criteria of Article 33(1) PCT, because the subject-matter of claims 1 to 27 involves an inventive step in the sense of Article 33(3) PCT.

- 4 The requirements of Article 33(3) PCT are met.

Re Item VII

Certain defects in the international application

- 1 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in D1 and D2 is not mentioned in the description, nor are these documents identified therein.