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/IB2015/052552	08.04.2015	10.04.2014

International Patent Classification (IPC) or both national classification and IPC
INV. A61K9/16 A61K9/20 A61K9/28 A61K31/397

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 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	Giménez Miralles, J Telephone No. +49 89 2399-0

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IB2015/052552

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	1, 14, 15
	No:	Claims	2-13
Inventive step (IS)	Yes:	Claims	1, 14, 15
	No:	Claims	2-13
Industrial applicability (IA)	Yes:	Claims	1-15
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

1. The relevant prior art documents are referred to as D1 to D2 as in the order of appearance in the International Search Report (ISR). Unless otherwise indicated, reference is made to the passages of said documents cited in the ISR.

2. Citations and explanations supporting the statement with regard to novelty (N), inventive step (IS) and industrial applicability (IA) (Rule 43*bis*.1(a)(i) and (b) PCT):

(N) The subject-matter of independent claim 2 is not novel because it is anticipated by the prior art (Article 33(2) PCT).

D1 and D2 disclose a tablet containing 0.294 wt.% siponimod, 7 wt.% moisture protective agent (glyceryl behenate), and 92.7 wt.% of other pharmaceutical excipients. D1 and D2 further disclose the additional features defined in present claims 3-13. Accordingly, D1 and D2 are prejudicial to claims 2-13.

However, none of D1 or D2 anticipates a process for producing a dosage form comprising siponimod wherein the active agent is first pre-blended with a moisture protective agent to form agglomerates which are then further processed into the final dosage form, nor a dosage form (tablet) having the characteristics deriving from said manufacturing process. Therefore, the subject-matter of independent claims 1, 14 and 15 is novel.

(IS) The subject-matter of independent claims 1, 14 and 15 is considered to involve an inventive step (Article 33(3) PCT) for the following reasons.

The closest prior art is any of D1 or D2 disclosing a tablet containing 0.294 wt.% siponimod, 7 wt.% moisture protective agent (glyceryl behenate), and 92.7 wt.% of other pharmaceutical excipients, wherein the glyceryl behenate is admixed as a lubricant excipient for tableting. The difference of present claims 1, 14 and 15 is that the active agent is first pre-blended with the glyceryl behenate as moisture protective agent to form agglomerates, which are then further processed into the final dosage form. The comparative examples provided in the patent application (examples 5-6) demonstrate an improvement of the long-term storage stability of the active ingredient

as a consequence of the pre-blending with the moisture protective agent before admixture of the remaining excipients. Based on said unexpected effect, an inventive step can be recognized.

(IA) The subject-matter of claims 1-15 is considered to be industrially applicable (Article 33(4) PCT). The possibility of industrial application is beyond any doubt.