

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/IB2016/055336	International filing date (day/month/year) 07.09.2016	Priority date (day/month/year) 09.09.2015
International Patent Classification (IPC) or both national classification and IPC INV. C07K16/24 A61K9/00 A61P11/06 A61P37/08		
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 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 P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Fax: +31 70 340 - 3016	Date of completion of this opinion see form PCT/ISA/210	Authorized Officer Le Flao, Katell Telephone No. +31 70 340-0	
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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. 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>1-53</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-53</u>
Industrial applicability (IA)	Yes: Claims	<u>1-53</u>
	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 Claims 33 and 37-45 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 Reference is made to the following documents:
 - D1 WO 2011/056772 A1 (SCHERING CORP [US]; PRESTA LEONARD G [US]) 12 May 2011
 - D2 WO 2007/096149 A1 (NOVARTIS AG [CH]; NOVARTIS PHARMA GMBH [AT]; BARDROFF MICHAEL [DE]; ED) 30 August 2007
 - D3 GAUVREAU GAIL M ET AL: "Effects of an anti-TSLP antibody on allergen-induced asthmatic responses", NEW ENGLAND JOURNAL OF MEDICINE, vol. 370, no. 22, 24 May 2014, pages 2102-2110, XP009189903, ISSN: 1533-4406
 - D4 WO 2007/112146 A2 (IRM LLC; DONG LIQUN [US]; NASOFF MARC [US]) 4 October 2007
 - D5 EP 1 797 902 A2 (ADVANCED INHALATION RES INC [US]) 20 June 2007
 - D6 US 2006/039910 A1 (COMEAU MICHAEL R [US] ET AL) 23 February 2006
 - D7 EDWARDS M J: "Therapy directed against thymic stromal lymphopoietin", DRUG NEWS AND PERSPECTIVES, vol. 21, no. 6, 1 January 2008, pages 312-316, XP001539393, ISSN: 0214-0934, DOI: 10.1358/DNP.2008.21.6.1246830
- 3 The present application does not meet the criteria of Article 33(3) PCT, because the subject-matter of claim 1 does not involve an inventive step.
 - 3.1 D1 may be regarded as being the prior art closest to the subject-matter of claim 1, and discloses humanized anti human TSLP mAB 23B12 neutralizing activity of TSLP (claims 1-37 and examples 1-7).

- 3.2 The subject-matter of claim 1 therefore differs from this known neutralizing antibody in that the structure of the antibody is defined by referring to either the CDR sequences (alternatives a) and b)) or the VH and VL sequences (alternatives c), d) and e)) or in that the molecule is defined by its paratope (alternative f)).
- 3.3 The problem to be solved by the present invention may therefore be regarded as the provision of an alternative molecule binding TSLP.
- 3.4 The solution proposed in claim 1 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons: providing a mere alternative antibody is considered to be a matter of routine for the skilled person that does not require any inventive skills.
- 3.5 The same applies to independent claims 2 and 28, to claims 33-45 related to the use of these molecule, and to claims 46-53.
- 3.6 The same applies when taking any of Documents D2 to D4 as closest prior art. In all these documents is disclosed the preparation, isolation and characterisation of anti TSLP antibodies suitable for treating asthma or allergic diseases (see the relevant passages cited in the search report).
- 3.7 None of the dependent claims seems to contain a features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, see Document D5 disclosing the preparation of particles for inhalation including dry-powders (claims 1-10).

Re item VIII

The application does not meet the requirements of Article 6 PCT, because claims 1-53 are not clear.

The binding molecule referred to in claims 1-3, if not an antibody, is unclear and technically not supported by the description. The claims have therefore been interpreted as limited to antibody.

An antibody is structurally made of two light and two heavy chains and the combination of the heavy and light chain variable regions confers the antigen-binding properties such as antigen specificity and affinity. The antigen-binding specificity is considered to be defined by the six CDRs, whereas affinity is not only determined by

the CDRs, but also by the relative disposition of the CDRs. Therefore, to define the antigen-binding specificity and properties of the exemplified antibodies the sequences of the full heavy and light chain variable regions of the antibody should be specified. However, the antibodies of claims xxxxx are defined by less than six CDRs/ one variable region/arbitrary combinations of six CDRs/arbitrary combinations of VH and VL regions. Since the molecule defined in alternatives a), b) and f) of claim 1 as well as the molecule defined in claim 2 are not clearly defined, claims 1-53 do not meet the requirements of Article 6 PCT.