

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/US2020/056676

International filing date (day/month/year)
21.10.2020

Priority date (day/month/year)
22.10.2019

International Patent Classification (IPC) or both national classification and IPC
INV. C07K16/28 A61P25/28 A61K39/395 C07K16/18

Applicant
BIOGEN MA INC.

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
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

Durrenberger, Anne
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	
	No: Claims	<u>1-59</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-59</u>
Industrial applicability (IA)	Yes: Claims	<u>1-59</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 1-59 relate to subject-matter considered by this Authority to be covered by the provision of Rule 39.1(iv)/64.1(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 a medical treatment, but may allow claims to a product, in particular substances or compositions for use in a first or further medical treatment.

Prior art

- 2 Reference is made to the following documents:
- D1 WO 2017/211827 A1 (BIOGEN INT NEUROSCIENCE GMBH [CH]) 14
 December 2017 (2017-12-14)
- D2 WO 2016/087944 A2 (BIOGEN INTERNAT NEUROSCIENCE GMBH [CH])
 9 June 2016 (2016-06-09)

Unless indicated otherwise reference is made to the relevant passages emphasized in the search report.

Novelty

- 3 *Preliminary remark:* the features related to tau in claims 31 to 59 are not considered as making any difference over the general treatment of Alzheimer's disease. In particular, these features do not define groups of patients distinguishable from the main group of Alzheimer's disease patients. In detail:
- the presence of "p-tau tangles, p-tau threads, and/or p-tau neuritic plaques" (independent claim 31) is a common feature of all Alzheimer's disease patients;
 - "reducing tau" (independent claims 37 and 38) does not change anything to the way the physician will treat a patient having Alzheimer's disease.
- 4 In view of the above remark, any prior art disclosing the use of aducanumab or variants thereof comprising SEQ ID NOs: 3 to 8 in the treatment of Alzheimer's disease (e.g. D1 and D2) anticipates the subject-matter of claims 37 to 47.

- 5 D1 and D2 further anticipate the subject-matter of claims 7-9, 11-37 and 48-59 as they disclose the intravenous administration of aducanumab with the claimed protocols, the treatment being continued if the patient has a mild asymptomatic ARIA.
- 6 D1 further discloses a multiple doses protocol wherein at least 15 doses at 10mg/kg are administered, thereby anticipating also the subject-matter of claims 1 to 6 and 10.

Inventive step

- 7 In case an independent claim overcoming the novelty objection is filed at a later stage, D1 would possibly be the closest prior art, as it addresses the same problem of reducing ARIA incidence. This problem is solved in D1 by the same dosage regimen as the ones claimed and exemplified in the present application, as well as in D2 by very similar dosage regimens.

The application does not appear to make any inventive contribution to the teaching of D1 taken alone or in combination with D2.

Re Item VIII

Certain observations on the international application

- 8 Although claims 1, 7, 13, 20, 31, 37 and 38 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought and/or in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.