

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

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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/IB2019/000716

International filing date (day/month/year)
08.07.2019

Priority date (day/month/year)
09.07.2018

International Patent Classification (IPC) or both national classification and IPC
INV. A61K38/10 A61K47/02 A61K9/20 A61P1/00

Applicant
ABBOTT LABORATORIES GMBH

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:



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Date of completion of
this opinion

see form
PCT/ISA/210

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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>4, 5, 7-10, 14-34, 37, 40, 41</u>
	No: Claims	<u>1-3, 6, 11-13, 35, 36, 38, 39</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-41</u>
Industrial applicability (IA)	Yes: Claims	<u>1-41</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item V

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

1 Prior art:

Reference is made to the following documents:

- D1 US 2012/237593 A1 (COMISKEY STEPHEN [US] ET AL) 20 September 2012 (2012-09-20)
- D2 WO 2014/088623 A1 (FOREST LAB HOLDINGS LTD; SANGHVI RITESH [US] ET AL.) 12 June 2014 (2014-06-12)
- D3 WO 2016/097030 A1 (SYNTHON BV [NL]) 23 June 2016 (2016-06-23)
- D4 US 2012/088774 A1 (GRAHEK ROK [SI] ET AL) 12 April 2012 (2012-04-12)

If not indicated otherwise the relevant passages are those mentioned in the search report.

With regard to claims 39 and 41 it is noted that 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 Novelty (Art. 33 (1) and (2) PCT):

2.1 Document D1 discloses compositions comprising a GCC agonist peptide like linacotide falling in the scope of the sequence of claim 1 and a carrier wherein the peptide is applied to the carrier like calcium phosphate (see §[0044]) thus forming a peptide-coated carrier (see claim 26). The composition is formulated as a tablet or a capsule.

Document D2 discloses oral pharmaceutical dosage forms, e.g. tablets or capsules, comprising linaclotide having a sequence of SEQ ID NO:3 which is applied to a carrier.

Although, documents D1-D2 do not use the term adsorbate it seems that the coating or the application of a linaclotide peptide to a carrier would result in an adsorbate as claimed. Therefore, it is considered that claim 1 is anticipated by the disclosure of D1-D2. The dependent claims 2-3, 6 and 11-13 also appear to lack novelty in view of D1 and D2.

- 2.2 Document D1 and D2 disclose tablets or capsules dosage forms thus anticipating claims 35 and 36.
- 2.3 Claims 38 and 39 lack novelty in view of D1 and D2.

Claims 1-3, 6, 11-13, 35-36 and 38-39 do not meet the requirements of Art. 33(1) (2) PCT.

3 Inventive step (Art. 33 (1) and (3) PCT):

- 3.1 Document D1 which is the closest prior art discloses a method wherein a GCC agonist peptide is applied by spray coating (see examples) to a carrier thus forming a peptide-coated carrier (see claim 26). Claim 29 differs in that the mixture of the aqueous solution of the peptide is combined with a carrier and dried at 30 to 50°C under reduced pressure. The problem to be solved is defined as to provide an alternative process for coating a carrier with a peptide as claimed. D1 discloses the spray coating of the carrier with a peptide at 50°C and dried until the temperature reached 36°C (see e.g. example 6). A skilled person would consider to use such a process for coating a carrier with linaclotide. Claim 29 does not involve an inventive step. The dependent claims 30-34 relate to obvious modifications of the process of D1. Claims 29-34 do not involve an inventive step.
- 3.2 Claims 40-41 differ from D1-D2 in that the peptide is combined with a probiotic or a prebiotic. The problem to be solved is defined as to provide an improved treatment for GI disorders. There is no evidence provided of an unexpected technical effect due to the combination. It would be obvious for a skilled person to combine linaclotide with a probiotic or prebiotic in order to solve the problem. An inventive step is not acknowledged for said claims.

- 3.3 The dependent claims 4-5, 7-10, 14-34 and 37 appear not to be inventive for the following reasons:
- 3.3.1 The use of a modified peptide as in claim 4 would be obvious for a skilled person,
- 3.3.2 Claim 10 relates to a particular amount of carrier which cannot be readily assessed since *mg per weight* is not clear with regard to a composition. However a selection of a ratio of the peptide and carrier (claim 9) or an amount of carrier (claim 10) does not confer inventive step to said claims.
- 3.3.3 Claims 5, 7-8 and 14-28 are directed to alternative carriers i.e. porous metal oxides like silicon dioxide, having defined surface area and particle size. The problem to be solved is defined as to provide an improved composition of linaclotide. The application does not provide any evidence of an unexpected technical effect over the closest prior art due to the particular carrier of surface area and particle size. The problem is thus redefined as to provide alternative compositions of linaclotide. Documents D3 and D4 disclose adsorbates of drugs on a carrier composed of porous silicon dioxide. It would be obvious for a skilled person to use a carrier as disclosed in D3 or D4 in order to solve the problem. The subject-matter of said claims is obvious in view of D1 and D3-D4.
- 3.3.4 The dosage form of claim 37 is obvious in view of D1-D2.

Claims 4, 5, 7-10, 14-34 and 37 do not meet the requirements of Art. 33(1) (3) PCT.