

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

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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/EP2020/067828

International filing date (day/month/year)
25.06.2020

Priority date (day/month/year)
27.06.2019

International Patent Classification (IPC) or both national classification and IPC
INV. C07D417/12 C07D417/14 A61P13/00 A61P25/00 A61P29/00 A61P31/00 A61K31/427

Applicant
BAYER AKTIENGESELLSCHAFT

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:



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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>1-16</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-16</u>
Industrial applicability (IA)	Yes: Claims	<u>1-16</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Item V

1. PRIOR ART

Reference is made to the following documents:

- D1 WO 2016/091776 A1 (EVOTEC AG [DE]) 16 June 2016 (2016-06-16)
- D2 US 2018/072713 A1 (DAVENPORT ADAM JAMES [GB] ET AL) 15 March 2018 (2018-03-15)

2. NOVELTY

The subject-matter of the claims is considered to be novel (Article 33(2) PCT): It forms an overlapping part with the ones from D1 and D2. The presently claimed subject matter represents a novel selection from said documents on account of more specific definitions (see R2). None of the examples disclosed in said documents fall under the overlapping part.

3. INVENTIVE STEP

The subject-matter of the claims does not appear to fulfil the requirements of Article 33(3) PCT for the following reasons:

The present application relates to 1,3-thiazol-2-yl substituted benzamide compounds which inhibit the p2x3 receptor and which are useful in the treatment or prophylaxis of diseases such as neurogenic disorders.

The closest prior art is represented by D1. As already stated under item novelty, the presently claimed compounds represent a selection, only.

Thus, the mere provision of further 1,3-thiazol-2-yl substituted benzamide compounds which inhibit the p2x3 receptor and which are useful in the treatment or prophylaxis of diseases such as neurogenic disorders encompassed by the general teaching of D1 has to be seen as obvious.

Therefore the problem of the present application has to be seen in the provision of further 1,3-thiazol-2-yl substituted benzamide compounds having surprisingly superior qualities in relation to the range disclosed.

In the case where comparative tests are envisaged in order to support an inventive step, these must be carried in such a manner that the effect is shown to have its origins in the distinguishing feature of the claimed invention. Moreover, the effect has to be present for the whole scope of the claims.

Starting from p. 51 comparative data in relation to compound 11 of D1 are disclosed which describe superior qualities concerning solubility and metabolic stability for current examples 1-3 in relation to example 11. Said comparative data appear to justify an effect only over a part of the scope of current claim 1 (namely for the case if OH is an compulsory substituent of the heterocycloalkyl moiety). No effect has however been justified for entities where R2 represents a linear entity substituted by two OH in relation to examples from D1 with one OH substituent. In the absence of further comparative data, inventive step can only be acknowledged for part of claim 1 as well as the respective dependent claims.

Therefore, inventive step cannot be acknowledged.

Item VI

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| D3 | WO 2019/219674 A1 (BAYER AG [DE]; BAYER PHARMA AG [DE]) 21 November 2019 (2019-11-21) |
| D4 | WO 2019/219672 A1 (BAYER AG [DE]; BAYER PHARMA AG [DE]) 21 November 2019 (2019-11-21) |

D3 and D4 are published between the presently claimed priority date and filing date. The presently claimed priority appears to be validly claimed.

The presently claimed subject matter forms an overlapping part with the ones from D3 and D4. It represents a novel selection from said documents on account of more specific definitions (see R2). None of the examples disclosed in said documents fall under the overlapping part.

