

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

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/EP2020/072377

International filing date (day/month/year)
10.08.2020

Priority date (day/month/year)
12.08.2019

International Patent Classification (IPC) or both national classification and IPC
INV. A61P35/00 C07D487/04 C07D519/00

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 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

Authorized Officer

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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>1-10, 12</u>
	No: Claims	<u>11</u>
Inventive step (IS)	Yes: Claims	<u>1-10, 12</u>
	No: Claims	<u>11</u>
Industrial applicability (IA)	Yes: Claims	<u>1-12</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

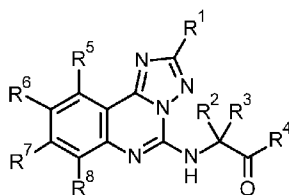
2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

ITEM V

Concerning present claim 8, 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.

The present subject matter is directed towards compound of formula (I)



(I)

which inhibit the Aryl Hydrocarbon Receptor (AHR).

Reference is made to the following documents:

- D1 FRANCIS J E ET AL: "STRUCTURE-ACTIVITY PROFILE OF A SERIES OF NOVEL TRIAZOLOQUINAZOLINE ADENOSINE ANTAGONISTS", JOURNAL OF MEDICAL CHEMISTRY,, vol. 31, 1 January 1988 (1988-01-01), pages 1014-1020, ISSN: 0022-2623, DOI: 10.1021/JM00400A022
- D2 MAGDY M GINEINAH ET AL: "Synthesis And Antiinflammatory Evaluation Of New 2- And 3-Substituted 1,2,4-Triazolo[4,3-C] And [1,5-C]Quinazoline Derivatives", MEDICINAL CHEMISTRY RESEARCH, BIRKHAUSER, BOSTON, US, vol. 10, no. 4, 1 January 2000 (2000-01-01), pages 243-252, XP009523573, ISSN: 1054-2523
- D3 WO 2010/059401 A2 (IRM LLC; SCRIPPS RESEARCH INST [US] ET AL.) 27 May 2010 (2010-05-27)
- D4 WO 2012/015914 A2 (UNIV BOSTON [US]; UNIV NORTHEASTERN [US] ET AL.) 2 February 2012 (2012-02-02)cited in the application

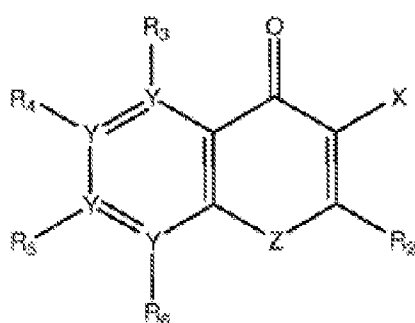
NOVELTY (Article 33(2) PCT)

D1 (compound 2) and D2 (compounds 26 and 27) specifically disclose compounds falling within the scope of claim 11. The said claim is therefore not novel over D1 and D2.

None of the documents cited disclose compounds falling within the scope of the compound of formula (I) as defined in present claim 1.

INVENTIVE STEP (Article 33(3) PCT)

D4 is the closest prior art and discloses AHR inhibitors of formula:



wherein Z can be O, S or NH.

The problem to be solved by the present subject matter vis-à-vis D4 may be regarded as being the provision of further AHR inhibitors.

As solution to this problem, the present subject matter proposes the compound of formula (I) above, characterised by the [1,2,4]triazolo[1,5-c]quinazolin-5-amine core structure.

Having regarded the data on file (cf. tables 1 and 2) it is reasonable to assume that the whole of the scope claimed represents a solution to the given problem.

It remain to assess whether the proposed solution involve an inventive step.

AHR inhibitors are also disclosed in D3 (cf, e.g. [0084]). However, neither D4 nor the combined teaching of D4 and D3 appear to disclose or even to suggest that the [1,2,4] triazolo[1,5-c]quinazoline derivatives may have the required activity. An inventive step is therefore acknowledged for the subject matter of present claims 1-10 and 12 and for the novel part of present claim 11.

ITEM VI

The present subject matter appears to be entitled to the claimed priority. Thus, it appears that WO 2020/102506 (D5, cited in the search report) should not be considered as prior art for the present subject matter within the meaning of Rule 64.1 PCT.