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- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(88) Date of publication of the international search report:

18 April 2019 (18.04.2019)

(54) Title: COMPOUNDS, SALTS THEREOF AND THEIR USE IN THE TREATMENT OF DISEASES

(57) Abstract: The present disclosure relates to compounds according to Formulae disclosed herein, useful for treating diseases.



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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2018/000353

A. CLASSIFICATION OF SUBJECT MATTER INV. C07D403/12 C07D413/12 C07D451/04 C07D471/08 C07D471/18 C07D487/18 C07D205/04 C07D265/06 C07D205/12 C07D207/06 C07D209/44 C07D209/52 C07D223/06 C07D241/04 C07D487/04		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) C07D		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, WPI Data, CHEM ABS Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2008/280886 A1 (GANT THOMAS G [US] ET AL) 13 November 2008 (2008-11-13) claims; examples -----	1,5, 7-10, 22-33, 35-37, 39-44, 46-71
X	WO 2017/015272 A1 (ACADIA PHARM INC [US]) 26 January 2017 (2017-01-26) claims; examples ----- -/-	1,5, 7-10, 22-33, 35-37, 39-44, 46-71
☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search	Date of mailing of the international search report	
23 January 2019	22/03/2019	
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Beyss-Kahana, Ellen	

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2018/000353

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NUTT, D. ET AL.: "Inverse agonists - What do they mean for psychiatry?", EUROPEAN NEUROPSYCHOPHARMACOLOGY, vol. 27, January 2017 (2017-01), pages 87-90, XP029884877, DOI: 10.1016/j.euroneuro.2016.11.013 abstract -----	1,5, 7-10, 22-33, 35-37, 39-44, 46-71
X	EP 1 965 805 A1 (PROSKELIA SAS [FR]) 10 September 2008 (2008-09-10) paragraph [0101]; examples 1-100, 120, 121, 125, 126 -----	1,5-7, 10,25, 26, 28-34, 39-53, 55-57, 59-64, 69-71

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/000353

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1, 5-71(all partially)
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
62-64(completely); 1, 5-61, 65-71(partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 62-64(completely); 1, 5-61, 65-71(partially)

A compound according to Formula (I) wherein E means N and A means C(=X)-C, C(=S)-S, C(=X)-O and C(=X)-NH

2. claims: 1, 5-61, 65-71(all partially)

A compound according to Formula (I) wherein E means N and A means C(=S)-C-NH

3. claims: 1-4, 6-59, 61, 65-71(all partially)

A compound according to Formula (I) wherein E means N and A means a heteroaryl moiety

4. claims: 1-60, 65-71(all partially)

A compound according to Formula (I) wherein E means CH

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 1, 5-71(all partially)

The present claims 1, 5-71 of invention 1 relates to an extremely large number of possible compounds, pharmaceutical compositions and uses thereof, due to the fact that formula (I) of claim 1 accordingly contains so many options, variables and possible permutations. Support and disclosure within the meaning of Articles 5 and 6 PCT are to be found, however, for only a very small proportion of the compounds claimed, see especially the examples.

Non-compliance with the substantive provisions is such that a meaningful search of the whole claimed subject-matter of invention 1 could not be carried out.

The Search Division considers the subject-matter of claim 1, wherein R1 means a halogen atom and R2 means O-alkyl or CN and wherein R1a, R1b, R1c, R1d, R2a, R2b, R2c, R2d mean a hydrogen atom, to represent a subject-matter on which a meaningful search could be performed since it represents a legitimated scope of protection in view of the examples and biological results put forward.

It is furthermore stressed that, the initial phase of the search of invention 1 revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of claim 1 according to invention 1 may be said to define subject-matter for which protection might legitimately be sought. For these reasons, a meaningful search of the whole claimed subject-matter of invention 1 could not be carried out. The extent of the search was consequently restricted to those claimed compounds, which appear to be supported and to a generalisation of its structural formula, namely compounds of formula (I) wherein:

- R1 means a halogen atom,
-
- R2 means O-alkyl or CN,
- R1a, R1b, R1c, R1d, R2a, R2b, R2c, R2d mean a hydrogen atom.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2018/000353

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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