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CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO,  
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HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP,  
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OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA,  
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Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a  
patent (Rule 4.17(ii))*

Published:

— *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  
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contained color or greyscale and is available for download  
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(88) Date of publication of the international search report:

01 August 2019 (01.08.2019)

(54) Title: PYRAZOLO PIPERIDINE AND PYRAZOLO PYRIMIDINE DERIVATIVES FOR THE TREATMENT OF NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

(57) Abstract: The present invention relates to the use of certain pyrazolo piperidine derivatives in the treatment of diseases and conditions associated with the interaction of the toll like receptor. More particularly, the said treatment pertains to the treatment of NPSLE.



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# INTERNATIONAL SEARCH REPORT

International application No PCT/IB2018/060309
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<b>A. CLASSIFICATION OF SUBJECT MATTER</b> INV. A61K31/437    A61K31/519    A61K31/5377    A61K45/06    A61P25/00 A61P37/00 ADD. According to International Patent Classification (IPC) or to both national classification and IPC
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<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) A61K A61P Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
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Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, BIOSIS, CHEM ABS Data, EMBASE, WPI Data
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C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2015/057655 A1 (EISAI R&D MAN CO LTD [JP]; HAWKINS LYNN [US]) 23 April 2015 (2015-04-23)	1
Y	paragraphs [0002], [0011], [0036] - [0039], [0242], [0249], [0250], [0260] claims 1,6,7,13  -----  -/--	1-5,10, 12,14

<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.	<input checked="" type="checkbox"/> See patent family annex.
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* 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
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Date of the actual completion of the international search  <b>29 April 2019</b>	Date of mailing of the international search report  <b>04/07/2019</b>
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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   <b>Bazzanini, Rita</b>
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## INTERNATIONAL SEARCH REPORT

International application No  
PCT/IB2018/060309

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WANG H P ET AL: "Cystamine attenuates the expressions of NOS- and TLR-associated molecules in the brain of NZB/W F1 mice", EUROPEAN JOURNAL OF PHARMACOLOGY, ELSEVIER SCIENCE, NL, vol. 607, no. 1-3, 1 April 2009 (2009-04-01), pages 102-106, XP026007773, ISSN: 0014-2999, DOI: 10.1016/J.EJPHAR.2009.02.039 [retrieved on 2009-03-04]</p>	1
Y	<p>abstract page 103, left-hand column, paragraph 2 page 105, left-hand column, paragraph 2 page 105, right-hand column, paragraph 4</p> <p>-----</p>	1-5,10, 12,14
X,P	<p>WO 2018/047081 A1 (NOVARTIS AG [CH]) 15 March 2018 (2018-03-15) cited in the application</p>	1-5,10, 12,14
Y,P	<p>page 1, line 5 - page 3, line 5 page 6, lines 16-22 Formula (IIa) examples 8,9 compounds 9,141 page 150, line 35 - page 151, line 7 table 7 claims 4,23</p> <p>-----</p>	1-5,10, 12,14
A	<p>ALLISON R. BIALAS ET AL: "Microglia-dependent synapse loss in type I interferon-mediated lupus", NATURE, 14 June 2017 (2017-06-14), XP055476303, GB ISSN: 0028-0836, DOI: 10.1038/nature22821 cited in the application abstract page 539, left-hand column, paragraph 1 - right-hand column, paragraph 1 last four lines; page 540, right-hand column page 541, left-hand column, paragraph 1 - page 542, left-hand column, paragraph 1 page 543, left-hand column, paragraph 1</p> <p>-----</p> <p style="text-align: center;">-/--</p>	1-5,10, 12,14

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/IB2018/060309

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>CÉSAR MAGRO-CHECA ET AL: "Management of Neuropsychiatric Systemic Lupus Erythematosus: Current Approaches and Future Perspectives", DRUGS, vol. 76, no. 4, 26 January 2016 (2016-01-26), pages 459-483, XP055476422, NZ ISSN: 0012-6667, DOI: 10.1007/s40265-015-0534-3 abstract -----</p>	1-5,10, 12,14

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IB2018/060309

## 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.:  
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:
  
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.:

1-5, 10, 12, 14

### 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: 1-5, 10, 12, 14

A compound of Formula (II) or a pharmaceutically acceptable salt thereof, for use in the treatment and/or prevention of NPSLE.

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2. claims: 6-9, 11, 13, 15

A compound of Formula (I) or a pharmaceutically acceptable salt thereof, for use in the treatment and/or prevention of NPSLE.

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/IB2018/060309
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
WO 2015057655	A1	23-04-2015	AU 2014334551 A1	25-02-2016
			CA 2920791 A1	23-04-2015
			CN 105636945 A	01-06-2016
			CN 107935988 A	20-04-2018
			EP 3057948 A1	24-08-2016
			ES 2670550 T3	30-05-2018
			JP 6483666 B2	13-03-2019
			JP 2016539079 A	15-12-2016
			KR 20160068775 A	15-06-2016
			RU 2016118624 A	17-11-2017
			US 2016176841 A1	23-06-2016
			WO 2015057655 A1	23-04-2015
			-----	
WO 2018047081	A1	15-03-2018	AU 2017323584 A1	31-01-2019
			CA 3031585 A1	15-03-2018
			CL 2019000588 A1	10-05-2019
			CN 109641899 A	16-04-2019
			CO 2019003397 A2	19-06-2019
			DO P2019000055 A	31-05-2019
			EP 3510033 A1	17-07-2019
			KR 20190039809 A	15-04-2019
			SG 11201900482S A	28-03-2019
			WO 2018047081 A1	15-03-2018
			-----	