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Declarations under Rule 4.17:

— of inventorship (Rule 4.17(iv))

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 amendments (Rule 48.2(h))  
— with sequence listing part of description (Rule 5.2(a))

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

29 September 2022 (29.09.2022)

(54) Title: EXTRACELLULAR VESICLE-NLRP3 ANTAGONIST

(57) Abstract: The present disclosure relates to extracellular vesicles, e.g. exosomes, comprising an NLRP3 antagonist. In some aspects, the NLRP3 antagonist comprises an antisense oligonucleotide (ASO). Also provided herein are methods for producing the exosomes and methods for using the exosomes to treat and/or prevent diseases or disorders, such as, for example, a peripheral neuropathy.



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**INTERNATIONAL SEARCH REPORT**

International application No  
**PCT/US2022/016828**

**A. CLASSIFICATION OF SUBJECT MATTER**  
**INV. A61K38/20 A61K31/341 A61K31/7125 A61P29/00 A61K31/145**  
**A61K31/164 A61K47/00 A61K35/12 A61P25/02**

**ADD.**  
 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)  
**A61K A61P**

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**

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
<b>X</b>	<b>US 2018/028600 A1 (HONG YEON-SUN [KR] ET AL) 1 February 2018 (2018-02-01)</b>  <b>paragraph [0044]; claims 1,5,6,11</b> -----	<b>1-4, 10-13, 42-73</b>
<b>Y</b>	<b>WO 2017/173034 A1 (UNIV NORTH CAROLINA CHAPEL HILL [US]) 5 October 2017 (2017-10-05)</b> <b>paragraphs [0121], [0122]; example 1</b> -----	<b>1-4,10, 11,42-73</b>
<b>Y</b>	<b>WO 2017/161010 A1 (CODIAK BIOSCIENCES INC [US]) 21 September 2017 (2017-09-21)</b>  <b>paragraph [0044]; claims 1-5,38,</b> -----  -/--	<b>1-4, 10-13, 42-73</b>

Further documents are listed in the continuation of Box C.       See patent family annex.

\* Special categories of cited documents :

<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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</p> <p>"&amp;" document member of the same patent family</p>
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Date of the actual completion of the international search  <b>14 June 2022</b>	Date of mailing of the international search report  <b>19/08/2022</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>Greif, Gabriela</b>
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## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2022/016828

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	XINGYI CHEN ET AL: "Exosome-like Nanoparticles from Ginger Rhizomes Inhibited NLRP3 Inflammasome Activation", MOLECULAR PHARMACEUTICS, vol. 16, no. 6, 30 April 2019 (2019-04-30), pages 2690-2699, XP055740853, US ISSN: 1543-8384, DOI: 10.1021/acs.molpharmaceut.9b00246 page 39, right-hand column; figures 4,5 -----	1-4, 10-13, 42-73
X	WO 2018/102397 A1 (PURETECH HEALTH LLC [US]) 7 June 2018 (2018-06-07) -----	1-4, 10, 11, 67-73
Y	paragraphs [0564], [0686]; claims 1, 2, 24 -----	42-66
Y	WO 2020/101740 A1 (CODIAK BIOSCIENCES INC [US]) 22 May 2020 (2020-05-22) the whole document -----	42-66
Y	MOHAMED LAMKANFI ET AL: "'Glyburide inhibits the Cryopyrin/Nalp3 inflammasome'", THE JOURNAL OF CELL BIOLOGY, vol. 187, no. 1, 5 October 2009 (2009-10-05), pages 61-70, XP055296717, DOI: 10.1161/CIRCULATIONAHA.108.793869 the whole document -----	10
Y	BO-ZONG SHAO ET AL: "NLRP3 inflammasome and its inhibitors: a review", FRONTIERS IN PHARMACOLOGY, vol. 6, 5 November 2015 (2015-11-05), XP055627432, DOI: 10.3389/fphar.2015.00262 page 4, left-hand column, paragraph 2 - page 6, left-hand column, paragraph 1; table 1 -----	10-13
Y	YANG YANG ET AL: "Recent advances in the mechanisms of NLRP3 inflammasome activation and its inhibitors", CELL DEATH & DISEASE, vol. 10, no. 2, 1 February 2019 (2019-02-01), XP055626877, DOI: 10.1038/s41419-019-1413-8 table 1 -----	10-13

# INTERNATIONAL SEARCH REPORT

International application No.

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## Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out 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).
2.  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.
3. Additional comments:

# INTERNATIONAL SEARCH REPORT

International application No.  
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## 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.:  
**10-13 (completely); 1-4, 42-73 (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: 10-13 (completely); 1-4, 42-73 (partially)

An extracellular vesicle comprising an exogenous NLRP3 antagonist, wherein the exogenous NLRP3 antagonist is a small molecule, related methods and uses.

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2. claims: 5-9, 14-41 (completely); 1-4, 42-73 (partially)

An extracellular vesicle comprising an exogenous NLRP3 antagonist, wherein the exogenous NLRP3 antagonist is a siRNA, SHRNA, an antisense oligonucleotide, a protein, and related methods and uses.

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2022/016828

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