

**PATENT COOPERATION TREATY**

**PCT**

**INTERNATIONAL SEARCH REPORT**

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 130197-00320	<b>FOR FURTHER ACTION</b> see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2020/030884	International filing date ( <i>day/month/year</i> ) 30 April 2020 (30-04-2020)	(Earliest) Priority Date ( <i>day/month/year</i> ) 30 April 2019 (30-04-2019)
Applicant  CHONDRIAL THERAPEUTICS, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 7 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the **language**, the international search was carried out 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))

b.  This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).

c.  With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2.  **Certain claims were found unsearchable** (See Box No. II)

3.  **Unity of invention is lacking** (see Box No III)

4. With regard to the **title**,

- the text is approved as submitted by the applicant
- the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- the text is approved as submitted by the applicant
- the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_
  - as suggested by the applicant
  - as selected by this Authority, because the applicant failed to suggest a figure
  - as selected by this Authority, because this figure better characterizes the invention
- b.  none of the figures is to be published with the abstract

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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:

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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.:  
6, 50, 55, 72, 77, 82(completely); 1-5, 7, 13, 19, 20, 22-49, 51-54, 56, 62  
68-71, 73-76, 78-81, 83(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.

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A. CLASSIFICATION OF SUBJECT MATTER  
INV. C12Q1/6809 C12Q1/6883  
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)  
C12Q  
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, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	VIJAYENDRAN CHANDRAN ET AL: "Inducible and reversible phenotypes in a novel mouse model of Friedreich's Ataxia", ELIFE, vol. 6, 19 December 2017 (2017-12-19), XP055715118, DOI: 10.7554/eLife.30054 page 18; figures 7a, 7b (and supplements 1-6) 8 (with supplement 1) page 21 - page 24 ----- -/--	1-7,13, 19,20, 22-56, 62,68

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	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search <b>17 July 2020</b>	Date of mailing of the international search report <b>14/09/2020</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>Costa Roldán, Nuria</b>
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## INTERNATIONAL SEARCH REPORT

International application No

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HUMMERT C ET AL: "Creation and Comparison of Different Chip Definition Files for Affymetrix Microarrays", 2011 INTERNATIONAL CONFERENCE ON BIOINFORMATICS & COMPUTATIONAL BIOLOGY. BIOCOMP 2011, 18-21 JULY 2011, LAS VEGAS NV, USA,, vol. 1, 1 January 2011 (2011-01-01), pages 16-22, XP009186218, ISBN: 978-1-60132-170-1 abstract -----	69-83
X	PILARKSY CHRISTIAN P ET AL: "Expression of the extracellular matrix signalling molecule Cyr61 is downregulated in prostate cancer", PROSTATE, WILEY-LISS, NEW YORK, NY, US, vol. 36, no. 2, 1 July 1998 (1998-07-01), pages 85-91, XP009521728, ISSN: 0270-4137, DOI: 10.1002/(SICI)1097-0045(19980701)36:2<85::AID-PROS3>3.3.CO;2-X abstract -----	69-83
X	SAKAMOTO S ET AL: "Increased expression of CYR61, an extra cellular matrix signaling protein, in human benign prostatic hyperplasia and its regulation by lysophosphatidic acid", ENDOCRINOLOGY, THE ENDOCRINE SOCIETY, US, vol. 45, no. 6, 1 June 2004 (2004-06-01), pages 2929-2940, XP002981701, ISSN: 0013-7227, DOI: 10.1210/EN.2003-1350 abstract -----	69-83
A	JIUN-I LAI ET AL: "Transcriptional profiling of isogenic Friedreich ataxia neurons and effect of an HDAC inhibitor on disease signatures", JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 294, no. 6, 8 February 2019 (2019-02-08), pages 1846-1859, XP055715112, US ISSN: 0021-9258, DOI: 10.1074/jbc.RA118.006515 abstract page 1853 - page 1854 ----- -/--	1-7,13, 19,20, 22-56, 62,68

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International application No  
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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>JILL SERGESKETTER NAPIERALA ET AL:  "Comprehensive analysis of gene expression patterns in Friedreich's ataxia fibroblasts by RNA sequencing reveals altered levels of protein synthesis factors and solute carriers",  DISEASE MODELS &amp; MECHANISMS,  vol. 10, no. 11,  1 November 2017 (2017-11-01), pages 1353-1369, XP055715105,  GB  ISSN: 1754-8403, DOI: 10.1242/dmm.030536  abstract</p>	1-7,13, 19,20, 22-56, 62,68
A	<p>-----</p> <p>NAPIERALA J ET AL: "Upregulation of mitochondrial aldehyde dehydrogenase activity inhibits lipid peroxidation in friedreich's ataxia cells",  NEUROLOGY : OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF NEUROLOGY, LIPPINCOTT WILLIAMS &amp; WILKINS, US,  vol. 90, no. 15, Supplement 1,  22 April 2018 (2018-04-22), XP009521707,  ISSN: 1526-632X  [retrieved on 2018-04-09]  the whole document</p>	1-7,13, 19,20, 22-56, 62,68
A	<p>-----</p> <p>ABRAHAO AGESSANDRO ET AL: "Gene Expression Profile in Peripheral Blood Cells of Friedreich Ataxia Patients",  CEREBELLUM, TAYLOR AND FRANCIS, GB,  vol. 15, no. 3, 15 July 2015 (2015-07-15),  pages 306-313, XP035959447,  ISSN: 1473-4222, DOI:  10.1007/S12311-015-0700-X  [retrieved on 2015-07-15]  abstract</p> <p>-----</p>	1-7,13, 19,20, 22-56, 62,68

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

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

1. claims: 6, 50, 55, 72, 77, 82(completely); 1-5, 7, 13, 19, 20, 22-49, 51-54, 56, 62, 68-71, 73-76, 78-81, 83(partially)

Methods for evaluating effectiveness of Frataxin (FXN) replacement therapy comprising:

- (a) determining an FXN replacement expression profile for at least FXN-sensitive genomic marker (FSGMs) CYR61 in a sample from an FXN deficient patient following treatment with FXN replacement therapy;
- (b) comparing the patient FXN replacement expression profile with a baseline FXN(-) expression profile; and
- (c) using the comparison to determine effectiveness of the FXN replacement therapy.

Compositions, panels, kits thereto.

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2. claims: 1-5, 7-49, 51-54, 56-71, 73-76, 78-81, 83(all partially)

Methods for evaluating effectiveness of Frataxin (FXN) replacement therapy wherein invention 2 is defined by the first marker as depicted in Table 2, namely ABCE1.

Compositions, panels, kits thereto.

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- 3-85. claims: 1-5, 7-49, 51-54, 56-71, 73-76, 78-81, 83(all partially)

concerns methods for evaluating effectiveness of Frataxin (FXN) replacement therapy wherein inventions 3-85 are defined by the markers as depicted consecutively in Table 2 (with the exception of CYR61 which is sorted to the first invention), namely marker ADAMTS1 for invention 3, ADNP marker for invention 4 and so on until marker TMEM126a for invention 85. Compositions, kits, panels thereto.

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