

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 30170	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2022/081334	International filing date (<i>day/month/year</i>) 12 December 2022 (12-12-2022)	(Earliest) Priority Date (<i>day/month/year</i>) 13 December 2021 (13-12-2021)
Applicant ELI LILLY AND COMPANY		

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.
 - b. ☐ furnished subsequent to the international filing date for the purposes of international search (Rule 13*ter*.1(a)).

☐ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.
2. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.
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.:
1-45 (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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INV. C12N15/113 A61K31/713
ADD. A61P25/28

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)

C12N 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, BIOSIS, Sequence Search, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2021/188626 A1 (UNIV MASSACHUSETTS [US]) 23 September 2021 (2021-09-23)	1, 4-8, 19-24, 31-45
Y	the whole document -----	1-45
Y	HU BO ET AL: "Therapeutic siRNA: state of the art", SIGNAL TRANSDUCTION AND TARGETED THERAPY, vol. 5, no. 1, 101, 1 December 2020 (2020-12-01), pages 1-25, XP055801687, DOI: 10.1038/s41392-020-0207-x Retrieved from the Internet: URL: https://www.nature.com/articles/s41392-020-0207-x.pdf cited in the application the whole document ----- -/--	1-45

X Further documents are listed in the continuation of Box C.	X 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 16 March 2023	Date of mailing of the international search report 25/05/2023
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 Andres, Serge

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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	WO 2004/058940 A2 (UNIV IOWA RES FOUND [US]; PAULSON HENRY [US]; MILLER VICTOR [US]) 15 July 2004 (2004-07-15) page 92; claims -----	1, 31-45
A	WO 2021/202511 A2 (ALNYLAM PHARMACEUTICALS INC [US]) 7 October 2021 (2021-10-07) the whole document -----	1-45
A	WO 2016/151523 A1 (UNIVERSITÀ DEGLI STUDI DI TRENTO [IT]) 29 September 2016 (2016-09-29) the whole document -----	1-45
A	LEVEILLE ETIENNE ET AL: "Tau and MAPT genetics in tauopathies and synucleinopathies", PARKINSONISM AND RELATED DISORDERS, vol. 90, 1 September 2021 (2021-09-01), pages 142-154, XP086813021, ISSN: 1353-8020, DOI: 10.1016/J.PARKRELDIS.2021.09.008 [retrieved on 2021-09-14] the whole document -----	1-45

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Information on patent family members

International application No

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2021188626 A1	23-09-2021	AU 2021238319 A1	06-10-2022
		CA 3171246 A1	23-09-2021
		CN 115552006 A	30-12-2022
		EP 4121537 A1	25-01-2023
		JP 2023518439 A	01-05-2023
		KR 20230004448 A	06-01-2023
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		BR 112022019606 A2	16-11-2022
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		EP 4126230 A2	08-02-2023
		IL 296851 A	01-11-2022
		KR 20230005194 A	09-01-2023
		TW 202143984 A	01-12-2021
		WO 2021202511 A2	07-10-2021
WO 2016151523 A1	29-09-2016	EP 3274456 A1	31-01-2018
		ES 2820713 T3	22-04-2021
		US 2018066254 A1	08-03-2018
		WO 2016151523 A1	29-09-2016

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-45 (partially)

An RNAi agent targeting MAPT in a region defined by compounds 6-9, 12, 25, 26, 77 and 78 in Table 1. Modified forms thereof, compositions comprising it and their uses in therapy of tauopathies.

2. claims: 1-45 (partially)

An RNAi agent targeting MAPT in a region defined by compounds 1-5 in Table 1. Modified forms thereof, compositions comprising it and their uses in therapy of tauopathies.

3. claims: 1-45 (partially)

An RNAi agent targeting MAPT in a region defined by compound 10 in Table 1. Modified forms thereof, compositions comprising it and their uses in therapy of tauopathies.

4. claims: 1-45 (partially)

An RNAi agent targeting MAPT in a region defined by compound 11 in Table 1. Modified forms thereof, compositions comprising it and their uses in therapy of tauopathies.

5. claims: 1-45 (partially)

An RNAi agent targeting MAPT in a region defined by compounds 27 and 28 in Table 1. Modified forms thereof, compositions comprising it and their uses in therapy of tauopathies.

6. claims: 1-45 (partially)

An RNAi agent targeting MAPT in a region defined by compounds 29 and 30 in Table 1. Modified forms thereof, compositions comprising it and their uses in therapy of tauopathies.
