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(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ,
CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG,
KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY,
MA, MD, MG, MK, MN, MU, MW, MX, MY, MZ, NA,
NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO,
RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH,
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RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ,
DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT,
LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE,
SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— of inventorship (Rule 4.17(iv))

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05 December 2024 (05.12.2024)

(54) Title: MICROTUBULE-ASSOCIATED PROTEIN TAU TARGETING SIRNAS AND USES THEREOF

(57) Abstract: The present disclosure relates to siRNA, which target MAPT transcript in a cell, leading to reduced expression of MAPT protein. Reduction of MAPT protein expression is beneficial for the treatment of certain medical disorders, e.g., a tauopathy.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2024/053120

A. CLASSIFICATION OF SUBJECT MATTER C12N 15/113(2010.01)i; A61K 31/7088(2006.01)i; A61P 25/28(2006.01)i 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 15/113(2010.01); A61K 31/713(2006.01); C12N 15/11(2006.01) Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Korean utility models and applications for utility models Japanese utility models and applications for utility models Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) eKOMPASS(KIPO internal) & Keywords: Microtubule-associated protein tau, MAPT, targeting siRNA, sense strand, antisense strand, modulation		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	US 2021-0363523 A1 (UNIVERSITY OF MASSACHUSETTS) 25 November 2021 (2021-11-25) table 10; and SEQ ID NO: 74	1-3,46 22,23
A	WO 2021-202511 A2 (ALNYLAM PHARMACEUTICALS, INC.) 07 October 2021 (2021-10-07) the whole document	1-3,22,23,46
A	WO 2016-151523 A1 (UNIVERSITÀ DEGLI STUDI DI TRENTO) 29 September 2016 (2016-09-29) the whole document	1-3,22,23,46
A	NCBI Reference Sequence: XM_045182190.2 (2023.03.03) the whole document	1-3,22,23,46
A	NCBI Reference Sequence: XM_047547097.1 (2023.03.04) the whole document	1-3,22,23,46
☐ 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 “D” document cited by the applicant in the international application “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 18 October 2024		Date of mailing of the international search report 18 October 2024
Name and mailing address of the ISA/KR Korean Intellectual Property Office 189 Cheongsa-ro, Seo-gu, Daejeon 35208, Republic of Korea Facsimile No. +82-42-481-8578		Authorized officer HEO, Joo Hyung Telephone No. +82-42-481-5373

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.
 - b. ☐ furnished subsequent to the international filing date for the purposes of international search (Rule 13ter.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:

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.: **126-136**
because they relate to subject matter not required to be searched by this Authority, namely:

Claims 126-136 pertain to methods for treatment of human body by therapy, and thus relate to a subject matter which this International Searching Authority is not required, under PCT Article 17(2)(a)(i) and Rule 39.1(iv), to search.
2. ☒ Claims Nos.: **49,50,52-54,57,59,66,101,102,121-123,127-129,134**
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:

Claims 49, 50, 52-54, 57, 59, 66, 101, 102, 121-123, 127-129, 134 are unclear since they are referring to the multiple dependent claims which do not comply with PCT Rule 6.4(a).
3. ☒ Claims Nos.: **42-45,47,48,51,55,56,58,60-65,70,71,74,75,77-79,81-83,85-87,89-91,93-95,97-100,120,124-126,130-133,135,136**
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:

- Group 1 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 3, 23]: Inventions relating to SEQ ID No:1 (sense strand) and SEQ ID No:2 (antisense strand)
- Group 2 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 4, 24]: Inventions relating to SEQ ID No:3 (sense strand) and SEQ ID No:4 (antisense strand)
- Group 3 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 5, 25]: Inventions relating to SEQ ID No:5 (sense strand) and SEQ ID No:6 (antisense strand)
- Group 4 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 6, 26]: Inventions relating to SEQ ID No:7 (sense strand) and SEQ ID No:8 (antisense strand)
- Group 5 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 7, 27, 80-102, 107-110]: Inventions relating to SEQ ID No:9 (sense strand) and SEQ ID No:10 (antisense strand)
- Group 6 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 8, 28]: Inventions relating to SEQ ID No:11 (sense strand) and SEQ ID No:12 (antisense strand)
- Group 7 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 9, 29]: Inventions relating to SEQ ID No:13 (sense strand) and SEQ ID No:14 (antisense strand)
- Group 8 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 10, 30]: Inventions relating to SEQ ID No:15 (sense strand) and SEQ ID No:16 (antisense strand)
- Group 9 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 11, 31]: Inventions relating to SEQ ID No:17 (sense strand) and SEQ ID No:18 (antisense strand)
- Group 10 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 12, 32]: Inventions relating to SEQ ID No:19 (sense strand) and SEQ ID No:20 (antisense strand)
- Group 11 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 13, 33]: Inventions relating to SEQ ID No:21 (sense strand) and SEQ ID No:22 (antisense strand)
- Group 12 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 14, 34, 111-114]: Inventions relating to SEQ ID No:23 (sense strand) and SEQ ID No:24 (antisense strand)
- Group 13 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 15, 35]: Inventions relating to SEQ ID No:25 (sense strand) and SEQ ID No:26 (antisense strand)
- Group 14 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 16, 36, 115-119]: Inventions relating to SEQ ID No:27 (sense strand) and SEQ ID No:28 (antisense strand)
- Group 15 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 17, 37]: Inventions relating to SEQ ID No:29 (sense strand) and SEQ ID No:30 (antisense strand)
- Group 16 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 18, 38]: Inventions relating to SEQ ID No:31 (sense strand) and SEQ ID No:32 (antisense strand)
- Group 17 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 19, 39]: Inventions relating to SEQ ID No:33 (sense strand) and SEQ ID No:34 (antisense strand)

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International application No.

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

Group 18 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 20, 40]: Inventions relating to SEQ ID No:35 (sense strand) and SEQ ID No:36 (antisense strand)

Group 19 [claims 1, 2, 22, 42-66, 120-125 (all partial); and claims 21, 41, 67-79, 103-106]: Inventions relating to SEQ ID No:64 (sense strand) and SEQ ID No:65 (antisense strand)

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 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.: **1-3,22,23,42-66,120-125**

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.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

PCT/IB2024/053120

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INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

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