

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
30 March 2023 (30.03.2023)



(10) International Publication Number
WO 2023/049871 A2

- (51) **International Patent Classification:**
C12N 15/85 (2006.01) A61K 48/00 (2006.01)
- (21) **International Application Number:**
PCT/US2022/076979
- (22) **International Filing Date:**
23 September 2022 (23.09.2022)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
63/248,119 24 September 2021 (24.09.2021) US
63/321,573 18 March 2022 (18.03.2022) US
63/403,327 02 September 2022 (02.09.2022) US

(71) **Applicant:** ALNYLAM PHARMACEUTICALS, INC.
[US/US]; 675 West Kendall Street, Henri A. Termeer
Square, Cambridge, Massachusetts 02142 (US).

(72) **Inventors:** FARLEY, Jonathan Edward; c/o Alnylam
Pharmaceuticals, Inc., 675 West Kendall Street, Henri A.
Termeer Square, Cambridge, Massachusetts 02142 (US).
SCHLEGEL, Mark K.; c/o Alnylam Pharmaceuticals,
Inc., 675 West Kendall Street, Henri A. Termeer Square,
Cambridge, Massachusetts 02142 (US). MCININCH,
James D.; c/o Alnylam Pharmaceuticals, Inc., 675 West
Kendall Street, Henri A. Termeer Square, Cambridge,
Massachusetts 02142 (US). ZUBER, Jeffrey; c/o Alnylam
Pharmaceuticals, Inc., 675 West Kendall Street, Henri A.
Termeer Square, Cambridge, Massachusetts 02142 (US).
CASTORENO, Adam; c/o Alnylam Pharmaceuticals, Inc.,
675 West Kendall Street, Henri A. Termeer Square, Cam-
bridge, Massachusetts 02142 (US). ABBOTT, Stephen; c/
o Alnylam Pharmaceuticals, Inc., 675 West Kendall Street,
Henri A. Termeer Square, Cambridge, Massachusetts 02142
(US). BARRY, Joseph; c/o Alnylam Pharmaceuticals, Inc.,
675 West Kendall Street, Henri A. Termeer Square, Cam-
bridge, Massachusetts 02142 (US).

(74) **Agent:** MEIGS, Julie Broadus et al.; Womble Bond
Dickinson (US) LLP, PO Box 570489, Atlanta, Georgia
30357-0037 (US).

(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, ME, MG, MK, MN, 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,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS,
ZA, ZM, ZW.

(84) **Designated States** (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ,
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, 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, 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:

- as to applicant's entitlement to apply for and be granted a
patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the
earlier application (Rule 4.17(iii))

Published:

- without international search report and to be republished
upon receipt of that report (Rule 48.2(g))
- with sequence listing part of description (Rule 5.2(a))

(54) **Title:** MICROTUBULE ASSOCIATED PROTEIN TAU (MAPT) IRNA AGENT COMPOSITIONS AND METHODS OF USE
THEREOF

(57) **Abstract:** The disclosure relates to double stranded ribonucleic acid interference (dsRNAi) agents and compositions targeting a
microtubule-associated protein tau (MAPT) gene, as well as methods of inhibiting expression of a MAPT gene and methods of treating
subjects having a MAPT-associated disease or disorder, e.g., Alzheimer's disease, frontotemporal dementia, progressive supranuclear
palsy, or other tauopathies, using such dsRNAi agents and compositions.

WO 2023/049871 A2