



## (51) International Patent Classification:

A61P 25/28 (2006.01) A61P 25/16 (2006.01)  
C12N 15/113 (2010.01)

## (21) International Application Number:

PCT/US2021/024858

## (22) International Filing Date:

30 March 2021 (30.03.2021)

## (25) Filing Language:

English

## (26) Publication Language:

English

## (30) Priority Data:

63/002,030 30 March 2020 (30.03.2020) US  
63/164,467 22 March 2021 (22.03.2021) US

## (71) Applicant: ALNYLAM PHARMACEUTICALS, INC.

[US/US]; 675 West Kendall Street, Henri A. Termeer Square, Cambridge, Massachusetts 02142 (US).

## (72) Inventors: SOUNDARAPANDIAN, Mangala

Meenakshi; 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). FISHILEVICH, Elane; c/o Alnylam Pharmaceu-

ticals, Inc., 675 West Kendall Street, Henri A. Termeer Square, Cambridge, Massachusetts 02142 (US). CAS-TORENO, Adam; c/o Alnylam Pharmaceuticals, Inc., 675 West Kendall Street, Henri A. Termeer Square, Cambridge, Massachusetts 02142 (US). KAITTANIS, Charalambos; 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). FARLEY, Jonathan Edward; 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).

(74) Agent: MEIGS, Julie Broadus et al.; Womble Bond Dickinson (US) LLP, P.O. Box 7037, 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, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN,

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

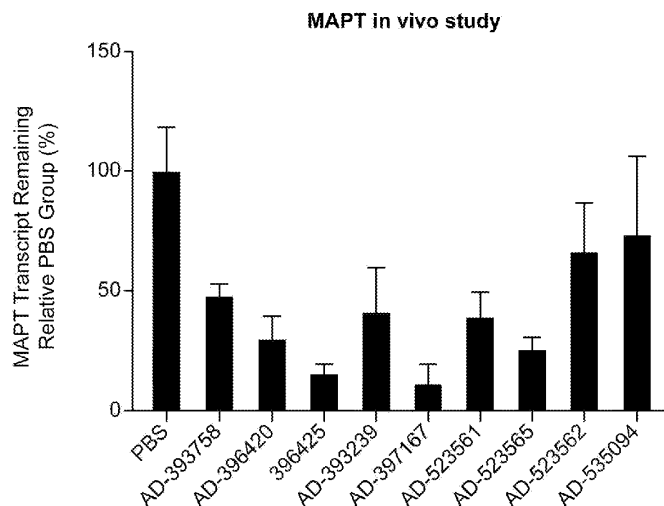


FIG. 1

(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.

[Continued on next page]

HR, HU, ID, IL, IN, IR, IS, IT, 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:**

- *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:**

25 November 2021 (25.11.2021)