

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
17 July 2025 (17.07.2025)



(10) International Publication Number
WO 2025/151408 A1

(51) International Patent Classification:

A61K 47/68 (2017.01) *A61P 25/28* (2006.01)
C12N 15/113 (2010.01) *C07K 16/28* (2006.01)
C07K 19/00 (2006.01)

(21) International Application Number:

PCT/US2025/010553

(22) International Filing Date:

07 January 2025 (07.01.2025)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

63/618,798 08 January 2024 (08.01.2024) US

(71) Applicant: **DENALI THERAPEUTICS INC.** [US/US];
161 Oyster Point Blvd., South San Francisco, California
94080 (US).

(72) Inventors: **DEVOS, Sarah L.**; c/o Denali Therapeu-
tics Inc., 161 Oyster Point Blvd., South San Francis-
co, California 94080 (US). **BARKER, Scarlett**; c/o De-
nali Therapeutics Inc., 161 Oyster Point Blvd., South
San Francisco, California 94080 (US). **THAYER, Mai
B.**; c/o Denali Therapeutics Inc., 161 Oyster Point Blvd.,
South San Francisco, California 94080 (US). **NILEWSKI,
Lizanne G.**; c/o Denali Therapeutics Inc., 161 Oys-
ter Point Blvd., South San Francisco, California 94080
(US). **OSIPOV, Maksim**; c/o Denali Therapeutics Inc.,
161 Oyster Point Blvd., South San Francisco, California
94080 (US). **KLAR, Richard**; c/o Secarna Pharmaceuticals
GmbH & Co. KG, Rudolf-Bultmann-Str. 4H, 35039 Mar-
burg (DE). **MICHEL, Sven**; c/o Secarna Pharmaceuticals
GmbH & Co. KG, Rudolf-Bultmann-Str. 4H, 35039 Mar-
burg (DE). **JASCHINSKI, Frank**; c/o Secarna Pharmaceu-
ticals GmbH & Co. KG, Rudolf-Bultmann-Str. 4H, 35039
Marburg (DE). **ROTHKIRCH, Larissa**; c/o Secarna Phar-
maceuticals GmbH & Co. KG, Rudolf-Bultmann-Str. 4H,
35039 Marburg (DE).

(74) Agent: **EKENA, Kirk** et al.; Alston & Bird LLP, Vantage
South End, 1120 South Tryon Street, Suite 300, Charlotte,
North Carolina 28203-6818 (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, 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,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UY, UZ, VC, VN,
WS, ZA, ZM, ZW.

(84) Designated States (*unless otherwise indicated, for every
kind of regional protection available*): ARIPO (BW, CV,
GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, 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, 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:

- *as to the identity of the inventor (Rule 4.17(i))*
- *as to applicant's entitlement to apply for and be granted a
patent (Rule 4.17(ii))*

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))*

(54) Title: COMPOSITIONS AND METHODS FOR MODULATING TAU EXPRESSION

(57) Abstract: Described are Microtubule-associated protein tau (MAPT) antisense oligonucleotides (ASOs) and MAPT ASO conju-
gates, and methods of using the MAPT ASOs and MAPT ASO conjugates to treat neurodegenerative disorders, such as Alzheimer's
disease.

WO 2025/151408 A1