

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

(19) World Intellectual Property  
Organization  
International Bureau

(43) International Publication Date  
05 January 2023 (05.01.2023)



(10) International Publication Number  
**WO 2023/279099 A1**

(51) International Patent Classification:

*A61K 47/68* (2017.01) *C07K 16/40* (2006.01)  
*A61P 25/28* (2006.01) *C12N 15/00* (2006.01)  
*C07K 16/28* (2006.01)

(21) International Application Number:

PCT/US2022/073377

(22) International Filing Date:

01 July 2022 (01.07.2022)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

|            |                              |    |
|------------|------------------------------|----|
| 63/217,743 | 01 July 2021 (01.07.2021)    | US |
| 63/298,193 | 10 January 2022 (10.01.2022) | US |
| 63/333,449 | 21 April 2022 (21.04.2022)   | US |

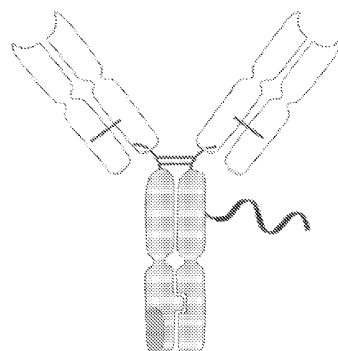
(71) Applicant: **DENALI THERAPEUTICS INC.** [US/US];  
161 Oyster Point Blvd., South San Francisco, California  
94080 (US).

(72) Inventors: **BARKER, Scarlett**; c/o Denali Therapeutics  
Inc., 161 Oyster Point Blvd., South San Francisco, Cali-  
fornia 94080 (US). **DENNIS, Mark S.**; c/o Denali Ther-  
apeutics Inc., 161 Oyster Point Blvd., South San Francis-  
co, California 94080 (US). **DEVOS, Sarah L.**; c/o Denali

Therapeutics Inc., 161 Oyster Point Blvd., South San Fran-  
cisco, California 94080 (US). **ESTRADA, Anthony A.**; c/  
o Denali Therapeutics Inc., 161 Oyster Point Blvd., South  
San Francisco, California 94080 (US). **KARIOLIS, Mi-  
halis S.**; c/o Denali Therapeutics Inc., 161 Oyster Point  
Blvd., South San Francisco, Alaska 94080 (US). **MA-  
HON, Cathal S.**; c/o Denali Therapeutics Inc., 161 Oyster  
Point Blvd., South San Francisco, California 94080 (US).  
**NILEWSKI, Lizanne G.**; c/o Denali Therapeutics Inc.,  
161 Oyster Point Blvd., South San Francisco, California  
94080 (US). **PARK, Joshua I.**; c/o Denali Therapeutics  
Inc., 161 Oyster Point Blvd., South San Francisco, Califor-  
nia 94080 (US). **SHAN, Lu**; c/o Denali 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, Califor-  
nia 94080 (US). **TONG, Raymond Ka Hang**; c/o Denali  
Therapeutics Inc., 161 Oyster Point Blvd., South San Fran-  
cisco, California 94080 (US). **TRAN, Hai L.**; c/o Denali  
Therapeutics Inc., 161 Oyster Point Blvd., South San Fran-  
cisco, California 94080 (US). **WELLS, Robert C.**; c/o De-  
nali Therapeutics Inc., 161 Oyster Point Blvd, South San  
Francisco, California 94080 (US). **ZUCHERO, Joy Yu**; c/  
o Denali Therapeutics Inc., 161 Oyster Point Blvd., South  
San Francisco, California 94080 (US).

(54) Title: OLIGONUCLEOTIDE CONJUGATES TARGETED TO THE TRANSFERRIN RECEPTOR

FIGURE 1



Oligonucleotide  
Transport Vehicle (OTV)

(57) Abstract: Provided herein are conjugates comprising proteins that bind to a transferrin receptor and oligonucleotides that are capable of modulating the expression of a target gene or sequence, as well as methods of use thereof.

WO 2023/279099 A1

[Continued on next page]

(74) **Agent: EKENA, Kirk et al.;** Alston & Bird LLP, 101 South Tryon Street, One South at The Plaza, Suite 4000, Charlotte, North Carolina 28280-4000 (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, 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 the identity of the inventor (Rule 4.17(i))*

**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))*