

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
10 August 2023 (10.08.2023)



(10) International Publication Number
WO 2023/150623 A3

(51) International Patent Classification:

C12N 9/26 (2006.01) C12N 15/86 (2006.01)
C07K 16/00 (2006.01) C12N 15/90 (2006.01)
C07K 19/00 (2006.01) A61K 48/00 (2006.01)
C12N 9/22 (2006.01) A61P 3/00 (2006.01)
C12N 15/11 (2006.01) A61P 43/00 (2006.01)
C12N 15/861 (2006.01)

(21) International Application Number:

PCT/US2023/061858

(22) International Filing Date:

02 February 2023 (02.02.2023)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

63/306,040 02 February 2022 (02.02.2022) US
63/369,902 29 July 2022 (29.07.2022) US

(71) Applicant: **REGENERON PHARMACEUTICALS, INC.** [US/US]; 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US).

(72) Inventors: **BAIK, Andrew**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **PRAGGASTIS, Maria**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **CYGNAR, Katherine**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **SABIN, Leah**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **SAMAI, Poulami**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **PEFANIS, Evangelos**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **CALAFATI, Philip**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **KEATING, Nicole**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **AIMÉ-WILSON, Pascaline**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **DUGAN, John**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **GAO, Min**; c/o Regen-

eron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **BABB, Robert**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **FORGET, Anthony**; c/o Intellia Therapeutics, Inc., 40 Erie Street, Cambridge, MA 02139 (US).

(74) Agent: **SCHILLING, Stephen H.** et al.; Alston & Bird LLP, One South at The Plaza, Suite 4000, 101 South Tryon Street, 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, 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, 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, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, 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))
- 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))

(54) Title: ANTI-TFR:GAA AND ANTI-CD63:GAA INSERTIONS FOR TREATMENT OF POMPE DISEASE

(57) Abstract: Nucleic acid constructs and compositions that allow insertion of a multidomain therapeutic protein (e.g., GAA fusion protein) coding sequence into a target genomic locus such as an endogenous *ALB* locus and/or expression of the multidomain therapeutic protein (e.g., GAA fusion protein) coding sequence are also provided. The nucleic acid constructs and compositions can be used in methods of integration of a multidomain therapeutic protein (e.g., GAA fusion protein) nucleic acid into a target genomic locus, methods of expression of a multidomain therapeutic protein (e.g., GAA fusion protein) in a cell, methods of reducing glycogen accumulation, methods of treating Pompe disease or GAA deficiency in a subject, and method of preventing or reducing the onset of a sign or symptom of Pompe disease in a subject, including neonatal cells and subjects.

WO 2023/150623 A3

[Continued on next page]

(88) Date of publication of the international search report:
28 September 2023 (28.09.2023)