

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
26 September 2024 (26.09.2024)



(10) International Publication Number
WO 2024/197065 A3

(51) International Patent Classification:

C12N 15/113 (2010.01) A61K 9/51 (2006.01)
C12N 9/22 (2006.01) C07K 14/775 (2006.01)
A61K 9/127 (2025.01)

(21) International Application Number:

PCT/US2024/020769

(22) International Filing Date:

20 March 2024 (20.03.2024)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

63/453,207 20 March 2023 (20.03.2023) US
63/554,838 16 February 2024 (16.02.2024) US

(71) Applicant: **VERVE THERAPEUTICS, INC.** [US/US];
201 Brookline Avenue, Boston, Massachusetts 02215 (US).

(72) Inventors: **HALLOCK, Peter Thomas**; Boston, Massachusetts 02215 (US). **CORNELL, Liam**; Somerville, Massachusetts (US). **DE ALMEIDA PINTO GARCIA, Sara Cristina**; Brookline, Massachusetts (US). **SRIDHAR, Srinidhi**; Quincy, Massachusetts (US). **REISS, Caroline**; Concord, Massachusetts (US). **WANG, Kui**; Wellesley, Massachusetts (US). **CHENG, Christopher J.**; North Reading, Massachusetts (US).

(74) Agent: **CAMPBELL, Keith M.** et al.; 111 Washington Ave. S., Suite 700, Minneapolis, Minnesota 55401 (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, 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).

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))

(88) Date of publication of the international search report:

21 November 2024 (21.11.2024)

(54) Title: IN VIVO NICKASE-BASED EDITING OF THE *LPA* GENE FOR TREATMENT OF CARDIOVASCULAR DISEASE

(57) Abstract: Provided herein are gene editing systems and compositions directed to effectuate *in vivo* edits in the *LPA* gene. Treatment or prevention of cardiovascular disease through disruption of the production of apo(a) through genetic editing and the reduction of the blood lipoprotein(a) [Lp(a)] concentration is disclosed herein. Disclosed are nickase-based gene editing systems designed to effectuate the installation of insertions and/or deletions (indel variants) and/or non-synonymous variants in the coding sequence of *LPA*. The nickase-based gene editing systems generally comprise one or more mRNAs that encode one or more nickases and a plurality of guide oligonucleotides (e.g., gRNAs) and may be delivered *in vivo* to a mammalian subject in need thereof via a suitable delivery system, such as lipid nanoparticles (LNPs) (with or without GalNAc targeting moieties) intravenously, or otherwise, administered to a patient as potentially a once-and-done therapeutic. The manufacturing, use, and formulation of the gene editing systems and compositions are also disclosed.



WO 2024/197065 A3