



(51) International Patent Classification:

C12N 15/113 (2010.01) A61K 31/7088 (2006.01)
C12N 9/22 (2006.01) A61P 25/28 (2006.01)
A61K 9/127 (2006.01)

(21) International Application Number:

PCT/US2022/034454

(22) International Filing Date:

22 June 2022 (22.06.2022)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

63/202,744	22 June 2021 (22.06.2021)	US
63/202,812	25 June 2021 (25.06.2021)	US
63/263,466	03 November 2021 (03.11.2021)	US
63/264,435	22 November 2021 (22.11.2021)	US
63/314,878	28 February 2022 (28.02.2022)	US

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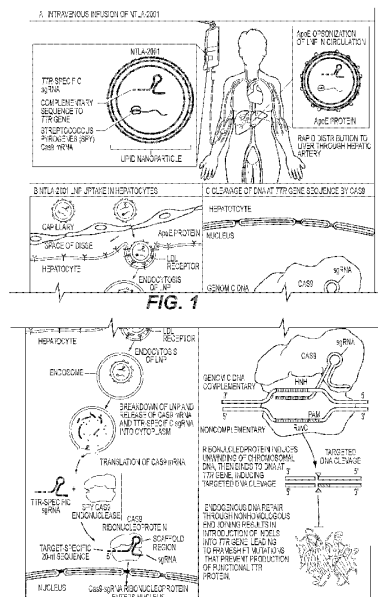
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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, 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,

(54) Title: METHODS FOR IN VIVO EDITING OF A LIVER GENE



(57) Abstract: The first systemic administration of a CRISPR/Cas9-based therapeutic for in vivo editing in a clinical trial is described. Described herein are methods for in vivo editing of a liver gene by systemically administering a lipid nanoparticle composition comprising an mRNA encoding a Cas nuclease and a guide RNA that targets the gene. For example, disclosed herein are methods for in vivo editing of a transthyretin gene by systemically administering a lipid nanoparticle composition comprising an mRNA encoding a Cas nuclease and a guide RNA that targets the TTR gene. Assessment of biosafety metrics and clinical efficacy metric, as well as methods of treatment, are also described herein.

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).

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))*