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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
30 November 2023 (30.11.2023)

WIPO | PCT

(10) International Publication Number
WO 2023/230587 A2

(51) International Patent Classification:
A61K 39/00 (2006.01) *A61K 47/69* (2017.01)

(21) International Application Number:
PCT/US2023/067517

(22) International Filing Date:
25 May 2023 (25.05.2023)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

63/345,823	25 May 2022 (25.05.2022)	US
63/346,197	26 May 2022 (26.05.2022)	US
18/324,097	25 May 2023 (25.05.2023)	US

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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, 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:
— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*
— *with sequence listing part of description (Rule 5.2(a))*

WO 2023/230587 A2

(54) Title: LIPID NANOPARTICLES FOR DELIVERY OF NUCLEIC ACIDS AND METHODS OF USE THEREOF

(57) Abstract: The present disclosure provides for improved compositions of ionizable lipid nanoparticles for the delivery of therapeutic nucleic acids to cells. Anionic phospholipids, including phosphatidyl serine and phosphatidylglycerol are included in the lipid nanoparticles to increase the transfection efficiency in human dendritic cells. The further incorporation of mono-unsaturated alkyl chain analogs in dimethylaminopropyl-di oxolane or heterocyclic ketal ionizable lipids in the formulation demonstrated high levels of transfection in human dendritic cells, compared to other ionizable lipids in the same family, and demonstrated good stability to oxidative damage. Finally, the use of an ammonium salt of phosphatidylserine allows for the efficient production of PS-targeted LNPs.