

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
26 August 2021 (26.08.2021)



(10) International Publication Number
WO 2021/167841 A1

- (51) **International Patent Classification:**
C12N 15/113 (2010.01) A61K 31/713 (2006.01)
- (21) **International Application Number:**
PCT/US2021/017826
- (22) **International Filing Date:**
12 February 2021 (12.02.2021)

- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
62/977,875 18 February 2020 (18.02.2020) US
63/144,516 02 February 2021 (02.02.2021) US

- (71) **Applicant: ALNYLAM PHARMACEUTICALS, INC.**
[US/US]; 675 West Kendall Street, Henri A. Termeer
Square, Cambridge, MA 02142 (US).

- (72) **Inventors: TREMBLAY, Frederic**; 675 West Kendall
Street, Henri A. Termeer Square, Cambridge, MA 02142
(US). **BONDURANT, Lucas, D.**; 675 West Kendall Street,
Henri A. Termeer Square, Cambridge, MA 02142 (US).
MCININCH, James, D.; 675 West Kendall Street, Hen-
ri A. Termeer Square, Cambridge, MA 02142 (US). **CAS-
TORENO, Adam**; 675 West Kendall Street, Henri A. Ter-
meer Square, Cambridge, MA 02142 (US). **SCHLEGEL,
Mark, K.**; 675 West Kendall Street, Henri A. Termeer
Square, Cambridge, MA 02142 (US). **KAITTANIS, Char-
alambos**; 675 West Kendall Street, Henri A. Termeer
Square, Cambridge, MA 02142 (US).

- (74) **Agent: ZACHARAKIS, Maria, Laccotripe et al.**; Mc-
Carter & English, LLP, 265 Franklin Street, Boston, MA
02110 (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, IR, IS, IT, 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,

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))

WO 2021/167841 A1

- (54) **Title:** APOLIPOPROTEIN C3 (APOC3) IRNA COMPOSITIONS AND METHODS OF USE THEREOF

(57) **Abstract:** The present invention relates to RNAi agents, e.g., double stranded RNA (dsRNA) agents, targeting the apolipoprotein C3 gene (APOC3). The invention also relates to methods of using such RNAi agents to inhibit expression of an APOC3 gene and to methods of preventing and treating an APOC3-associated disorder, e.g., hypertriglyceridemia, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, polycystic ovary syndrome, kidney disease, obesity, type 2 diabetes mellitus (insulin resistance), hypertension, atherosclerosis and pancreatitis.