

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

(19) World Intellectual Property
Organization
International Bureau



(10) International Publication Number
WO 2023/003922 A1

(43) International Publication Date
26 January 2023 (26.01.2023)

(51) International Patent Classification:

C12N 15/113 (2010.01) A61K 31/7125 (2000.01)
A61K 31/713 (2000.01) A61K 31/712 (2000.01)

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).

(21) International Application Number:

PCT/US2022/037658

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))

(22) International Filing Date:

20 July 2022 (20.07.2022)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

63/223,995	21 July 2021 (21.07.2021)	US
63/278,126	11 November 2021 (11.11.2021)	US
63/285,143	02 December 2021 (02.12.2021)	US
63/287,578	09 December 2021 (09.12.2021)	US
63/321,799	21 March 2022 (21.03.2022)	US
63/323,543	25 March 2022 (25.03.2022)	US

(71) Applicant: **ALNYLAM PHARMACEUTICALS, INC.**

[US/US]; 675 West Kendall Street, Henri A. Termeer Square, Cambridge, MA 02142 (US).

(72) Inventors: **DEATON, Aimee, M.**; 675 West Kendall

Street, Henri A. Termeer Square, Cambridge, MA 02142 (US). **ZUBER, Jeffrey**; 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, 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, 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: METABOLIC DISORDER-ASSOCIATED TARGET GENE IRNA COMPOSITIONS AND METHODS OF USE THERE-OF

(57) Abstract: The present invention relates to RNAi agents, e.g., double stranded RNA (dsRNA) agents, targeting a metabolic disorder-associated target gene, e.g., inhibin subunit beta E (INHBE), activin A receptor type 1C (ACVR1C), perilipin-1 (PLIN1), phosphodiesterase 3B (PDE3B), or inhibin subunit beta C (INHBC) gene. The invention also relates to methods of using such RNAi agents to inhibit expression of a metabolic disorder-associated target gene and to methods of preventing and beating a metabolic disorder, e.g., metabolic syndrome.

WO 2023/003922 A1