

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
23 September 2021 (23.09.2021)



(10) International Publication Number
WO 2021/189059 A2

(51) International Patent Classification:

C07K 14/725 (2006.01) C12N 15/85 (2006.01)
A61K 48/00 (2006.01) C12N 15/11 (2006.01)

(21) International Application Number:

PCT/US2021/023540

(22) International Filing Date:

22 March 2021 (22.03.2021)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/992,518 20 March 2020 (20.03.2020) US

(71) Applicant: ORNA THERAPEUTICS, INC. [US/US];
450 Kendall Street, Cambridge, MA 02142 (US).

(72) Inventors: WESSELHOEFT, Alex; c/o 450 Kendall
Street, Cambridge, MA 02142 (US). GOODMAN, Brian;
c/o 450 Kendall Street, Cambridge, MA 02142 (US).

(74) Agent: CAI, Yingying et al.; Goodwin Procter LLP, 100
Northern Avenue, IP Docketing Dept./7th Fl, Boston, MA
02210 (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,
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, 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))

(54) Title: CIRCULAR RNA COMPOSITIONS AND METHODS

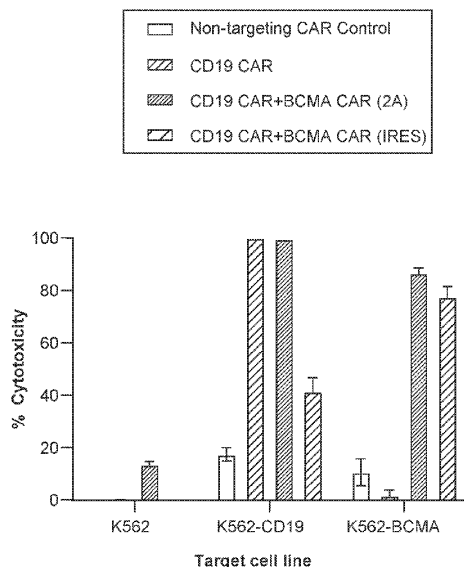


FIG. 44

(57) Abstract: Circular RNA, along with related compositions and methods are described herein. In some embodiments, the inventive circular RNA comprises post splicing group I in iron fragments, spacers, an IRES, optional duplex forming regions, and more than one expression sequence. In some embodiments, the expression sequences are separated by one or more polynucleotide sequences encoding a cleavage site. In some embodiments, circular RNA of the invention has improved expression, functional stability, immunogenicity, ease of manufacturing, and/or half-life when compared to linear RNA. In some embodiments, inventive methods and constructs result in improved circularization efficiency, splicing efficiency, and/or purity when compared to existing RNA circularization approaches.