(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)

WIPO | PCT

(10) International Publication Number
WO 2021/168405 A1

(51) International Patent Classification:
A61K 31/7088 (2006.01) *A61K 31/711* (2006.01)
A61K 31/7105 (2006.01)

(21) International Application Number:
PCT/US2021/019028

(22) International Filing Date:
22 February 2021 (22.02.2021)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/979,619 21 February 2020 (21.02.2020) US
63/059,458 31 July 2020 (31.07.2020) US

(71) Applicant: **COMBINED THERAPEUTICS, INC.** [US/US]; 650 E Kendall Street, Cambridge, MA 02142 (US).

(72) Inventors: **MICOL, Romain**; c/o Combined Therapeutics, Inc., 650 E Kendall Street, Cambridge, MA 02142 (US). **DUVAL, Valerie**; c/o Combined Therapeutics, Inc., 650 E Kendall Street, Cambridge, MA 02142 (US).

(74) Agent: **VALLABH, Rajesh** et al.; Patent Group, Foley Hoag LLP, 155 Seaport Boulevard, Boston, MA 02210-2600 (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).

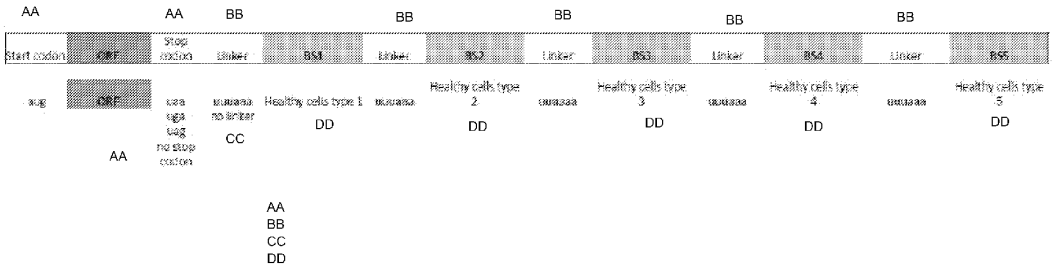
Declarations under Rule 4.17:
— *of inventorship (Rule 4.17(iv))*

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))*

WO 2021/168405 A1

(54) Title: COMPOSITIONS AND METHODS FOR ORGAN-PROTECTIVE EXPRESSION AND MODULATION OF CODING RIBONUCLEIC ACIDS

Figure 1



(57) Abstract: Compositions are provided comprising messenger RNA constructs having at least one open reading frame (ORF), wherein the ORF is operatively linked to at least one untranslated region (UTR), wherein the UTR comprises at least one organ protection sequence (OPS), wherein the OPS sequence comprises at least a first, a second and a third micro-RNA (miRNA) target sequence, and wherein each of the at least a first, second and third the miRNA target sequences are optimised to hybridise with a corresponding miRNA sequence. The compositions and molecules provided are useful in therapies such as for the treatment of cancer, in immunotherapies, and in vaccines.