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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
03 September 2020 (03.09.2020)

WIPO | PCT

(10) International Publication Number
WO 2020/172720 A1

(51) International Patent Classification:
C12N 15/00 (2006.01) *A61K 48/00* (2006.01)
C12N 9/00 (2006.01)

(21) International Application Number:
PCT/AU2020/050182

(22) International Filing Date:
28 February 2020 (28.02.2020)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/812,187 28 February 2019 (28.02.2019) US

(71) Applicant: **BENITEC BIOPHARMA LIMITED** [AU/AU]; Level 14, 114 William Street, Melbourne, Victoria 3000 (AU).

(72) Inventors: **STRINGS-UFOMBAH, Vanessa**; 3940 Trust Way, Hayward, California 94545 (US). **SUHY, David**; 3940 Trust Way, Hayward, California 94545 (US). **KAO, Shih-Chu**; 3940 Trust Way, Hayward, California 94545 (US). **ROELVINK, Petrus W.**; 3940 Trust Way, Hayward, California 94545 (US).

(74) Agent: **FB RICE**; Level 23, 44 Market Street, Sydney, New South Wales 2000 (AU).

(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, 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).

(54) Title: COMPOSITIONS AND METHODS FOR TREATING OCULOPHARYNGEAL MUSCULAR DYSTROPHY (OPMD)

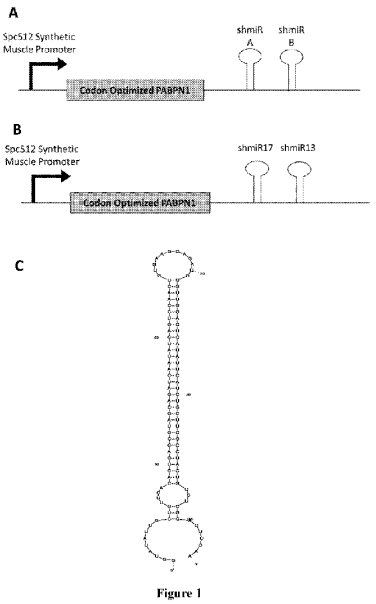


Figure 1

(57) Abstract: The present disclosure relates to modified adeno-associated virus (AAV) delivery vectors comprising 'silence and replace' DNA constructs, compositions comprising same, and the use of the modified AAV and compositions to treat oculopharyngeal muscular dystrophy (OPMD) in individuals suffering from OPMD or which are predisposed thereto. In particular, the disclosure relates to AAV having a capsid protein with a modified subunit 1 (VP1) and comprising a 'silence and replace' DNA construct, wherein the 'silence and replace' DNA construct comprises (i) a DNA-directed RNAi (ddRNAi) construct encoding short hairpin microRNA (shmiR) targeting PABPN1 causative of OPMD and (ii) a PABPN1 construct encoding functional PABPN1 protein having a mRNA transcript which is not targeted by the shmiRs at (i). The present disclosure also relates to the methods of treating OPMD comprising direct injection of an AAV of the disclosure to a subject's pharyngeal muscles.

WO 2020/172720 A1

[Continued on next page]

Published:
— *with international search report (Art. 21(3))*
— *with sequence listing part of description (Rule 5.2(a))*