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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
22 December 2016 (22.12.2016)

WIPO | PCT

(10) International Publication Number
WO 2016/205410 A2

(51) International Patent Classification:
A61K 48/00 (2006.01) *A61K 47/48* (2006.01)

(21) International Application Number:
PCT/US2016/037685

(22) International Filing Date:
15 June 2016 (15.06.2016)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

62/175,709	15 June 2015 (15.06.2015)	US
62/175,714	15 June 2015 (15.06.2015)	US
62/175,718	15 June 2015 (15.06.2015)	US
62/203,243	10 August 2015 (10.08.2015)	US
62/216,317	9 September 2015 (09.09.2015)	US
62/216,314	9 September 2015 (09.09.2015)	US
62/216,318	9 September 2015 (09.09.2015)	US

(71) Applicant: **MPEG LA, LLC** [US/US]; 5425 Wisconsin Avenue, Suite 801, Chevy Chase, MD 20815 (US).

(72) Inventors: **HADWIGER, Philipp**; Axolabs Gmbh, Frizhornschuch-strabe 9, D-95326 Kulmbach (DE). **VORNLOCHER, Hans-Peter**; Axolabs Gmbh, Fritzhornschuch-strabe 9, D-95326 Kulmbach (DE). **BROWN, Jonathan, Miles**; MPEG LA, LLC, 5425 Wisconsin Avenue; Suite 801, Chevy Chase, MD 20815 (US). **DAHLMAN, James, Everett**; 1295 E Rock Springs Road NE, Apartment 403, Atlanta, GA 30306 (US). **NEUMAN, Kristin, K.H.**; 10 Sackett Drive, Larchmont, NY 10538 (US).

(74) Agents: **HUBNER, Isaac, A.** et al.; Nutter McClennen & Fish LLP, Seaport West, 155 Seaport Boulevard, Boston, MA 02210-2604 (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, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, 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, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, 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))*

WO 2016/205410 A2

(54) Title: DEFINED MULTI-CONJUGATE OLIGONUCLEOTIDES

(57) Abstract: Defined multi-conjugate oligonucleotides can have predetermined sizes and compositions. For example, in various embodiment, defined multi-conjugate oligonucleotides can have advantageous properties, for example in the form of defined multi-conjugate siRNA (i.e., including two, three or more siRNA) having enhanced intracellular delivery and/or multi-gene silencing effects. In various embodiment, the defined multi-conjugate oligonucleotides can be synthesized via new synthetic intermediates and methods. The defined multi-conjugate oligonucleotides can be used, for example, in reducing gene expression, biological research, treating or preventing medical conditions, or to produce new or altered phenotypes in cells or organisms.