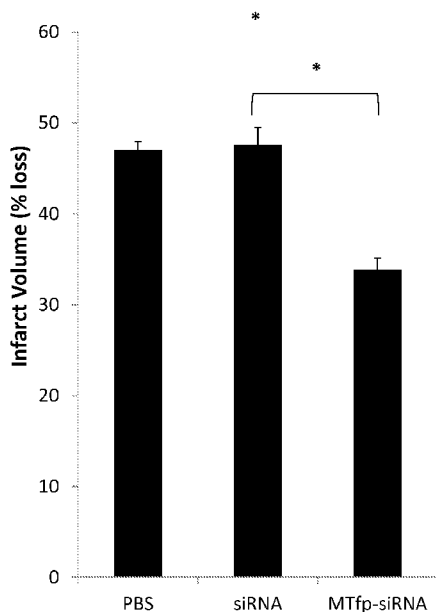




- (51) **International Patent Classification:**
C12N 15/113 (2010.01) A61K 31/713 (2006.01)
- (21) **International Application Number:** PCT/US2015/028743
- (22) **International Filing Date:** 1 May 2015 (01.05.2015)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
61/987,228 1 May 2014 (01.05.2014) US
62/033,903 6 August 2014 (06.08.2014) US
62/144,598 8 April 2015 (08.04.2015) US
- (71) **Applicant:** **BIOASIS TECHNOLOGIES, INC.** [CA/CA]; 10551 Shellbridge Way, Suite 125, Richmond, British Columbia V6X 2W9 (CA).
- (72) **Inventors:** **JEFFERIES, Wilfred**; 12682 Crescent Road, South Surrey, British Columbia V4A 2V5 (CA). **GABATHULER, Reinhard**; 201, Chemin du Golf, Suite 702, Montreal, Québec H3E 1Z4 (CA).
- (74) **Agents:** **ROGEL, Mark E.** et al.; Cooley LLP, 1299 Pennsylvania Avenue, NW, Suite 700, Washington, District of Columbia 20004 (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,

[Continued on next page]

(54) **Title:** P97-POLYNUCLEOTIDE CONJUGATES



Mean ± SEM
* P ≤ 0.05 (1 way Anova)

FIG. 10

(57) **Abstract:** Provided are conjugates between p97 (melanotransferrin) and polynucleotides such as small interfering RNA (siRNA) molecules, and related compositions and methods of use thereof, for instance, to facilitate delivery of polynucleotides such as siRNA molecules across the blood-brain barrier (BBB) and/or improve their tissue penetration in CNS and/or peripheral tissues, and thereby treat and/or diagnose various diseases, including those having a central nervous system (CNS) component.

WO 2015/168521 A3



SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

— 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))

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

— with sequence listing part of description (Rule 5.2(a))

(88) Date of publication of the international search report:
23 December 2015

Published:

- with international search report (Art. 21(3))

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2015/028743

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N15/113 A61K31/713
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2008/118013 A2 (TO BBB HOLDING B V [NL]; GAILLARD PIETER JAAP [NL]) 2 October 2008 (2008-10-02) pages 21,37,38; claims 1,4 -----	1-7, 12-18
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Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search 3 November 2015	Date of mailing of the international search report 11/11/2015
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Piret, Bernard
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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2015/028743

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>LUCA COSTANTINO ET AL: "Is there a clinical future for polymeric nanoparticles as brain-targeting drug delivery agents?", DRUG DISCOVERY TODAY, vol. 17, no. 7-8, 1 April 2012 (2012-04-01), pages 367-378, XP055202467, ISSN: 1359-6446, DOI: 10.1016/j.drudis.2011.10.028</p> <p>-----</p>	1-10, 12-18, 20,21
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X,P	<p>WO 2014/064258 A1 (NLIFE THERAPEUTICS S L [ES]) 1 May 2014 (2014-05-01)</p> <p>page 4 - lines 6-20 page 41 - page 42</p> <p>-----</p>	1-10, 12-18, 20,21
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A	<p>WO 03/057179 A2 (BIOMARIN PHARM INC [US]; STARR CHRISTOPHER M [US]; ZANKEL TODD [US]) 17 July 2003 (2003-07-17)</p> <p>-----</p>	13,14

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2015/028743

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

1-10, 12-15, 20, 21(completely); 16-18(partially)

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 8-10, 20, 21(completely); 1-7, 12, 15-18(partially)

p97 conjugated to a siRNA targeting a NOX gene

2. claims: 11(completely); 1-7, 12, 15-18(partially)

p97 conjugated to a CRISPR dsRNA oligonucleotide

3. claims: 13, 14(completely); 1-7, 12, 15-18(partially)

p97 oligopeptide (instead of full-length p97) conjugated to a dsNA

4. claims: 19, 22(completely); 1-7, 12, 15-18(partially)

use of a p97/nucleic acid conjugate for therapy, insofar as this subject-matter is not already encompassed by the previous inventions

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2015/028743

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