

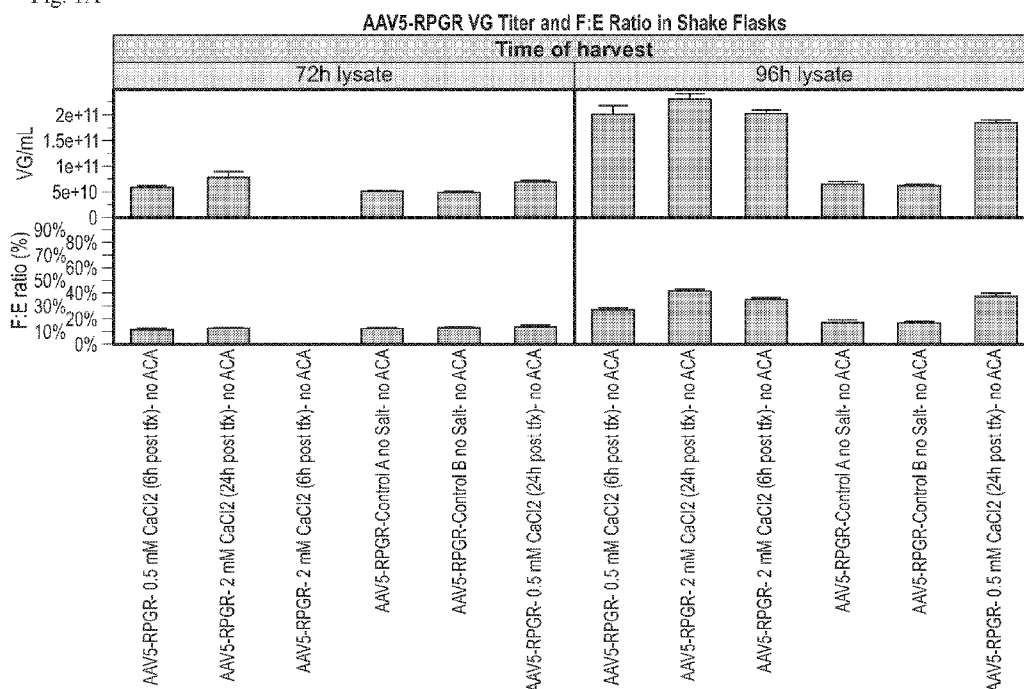


- (51) International Patent Classification:
C12N 15/86 (2006.01)
- (21) International Application Number:
PCT/IB2022/000347
- (22) International Filing Date:
17 June 2022 (17.06.2022)
- (25) Filing Language:
English
- (26) Publication Language:
English
- (30) Priority Data:
63/211,877 17 June 2021 (17.06.2021) US
- (71) Applicant: **MEIRAGTX UK II LIMITED** [GB/GB]; 92 Britiana Walk, London N1 7NQ (GB).
- (72) Inventors: **DZIOPA, Florian**; 22 Indigo Mews, Carysfort Road, London N16 9AE (GB). **VALINHAS, Ana**; 4 Grafton Yard, Flat 27, London NW5 2NF (GB). **LEEWIS, Bastiaan**; 55 Howitt Road, London NW3 4LU (GB).

- (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, IQ, IR, IS, IT, JM, 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,

(54) Title: AAV MANUFACTURING METHODS

Fig. 1A



(57) Abstract: Methods for producing recombinant adeno-associated virus (rAAV) particles include: an expansion phase including increasing the number of cells in at least one culture vessel containing culture medium; introducing into the cells a first polynucleotide sequence including a transgene flanked by AAV inverted terminal repeats, and optionally a second polynucleotide sequence including AAV rep and cap genes, and/or a third polynucleotide sequence including one or more helper genes; a production phase including culturing the cells into which the one or more polynucleotide sequences were introduced and adding calcium (Ca) ions (i.e., salts of Ca²⁺) to the production phase culture medium; and isolating the rAAV particles.



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

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))*

(88) Date of publication of the international search report:

26 January 2023 (26.01.2023)

INTERNATIONAL SEARCH REPORT

International application No PCT/IB2022/000347
--

A. CLASSIFICATION OF SUBJECT MATTER INV. C12N15/86 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 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		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2021/097157 A1 (BIOMARIN PHARM INC [US]) 20 May 2021 (2021-05-20) paragraph [0184]; claims 26,27 -----	31, 32
X	RIESER RUTH ET AL: "Comparison of Different Liquid Chromatography-Based Purification Strategies for Adeno-Associated Virus Vectors", PHARMACEUTICS, vol. 13, no. 5, 18 May 2021 (2021-05-18), page 748, XP093001911, DOI: 10.3390/pharmaceutics13050748 abstract -----	31, 32
X	WO 2020/061581 A1 (NIGHTSTARX LTD [GB]) 26 March 2020 (2020-03-26)	31, 32
A	paragraphs [0821], [0834], [0835] paragraphs [10695], [0033], [0036] -----	1-30
-/--		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.	<input checked="" type="checkbox"/> 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	"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	
"E" earlier application or patent but published on or after the international filing date	"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	
"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)	"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	
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	
"P" document published prior to the international filing date but later than the priority date claimed		
Date of the actual completion of the international search	Date of mailing of the international search report	
25 November 2022	12/12/2022	
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 Mauhin, Viviane	

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2022/000347

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2017/112948 A1 (UNIV FLORIDA [US]) 29 June 2017 (2017-06-29) page 2, lines 17, 27 figures 4D, 4E; example 2 -----	1-30

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/IB2022/000347
--

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2021097157 A1	20-05-2021	AU 2020384294 A1	02-06-2022
		BR 112022009279 A2	06-09-2022
		CA 3161154 A1	20-05-2021
		CN 114829391 A	29-07-2022
		CO 2022005641 A2	20-05-2022
		EP 4058475 A1	21-09-2022
		IL 292717 A	01-07-2022
		KR 20220098210 A	11-07-2022
		TW 202128733 A	01-08-2021
		WO 2021097157 A1	20-05-2021

WO 2020061581 A1	26-03-2020	AU 2019344073 A1	06-05-2021
		BR 112021005110 A2	15-06-2021
		CA 3112824 A1	26-03-2020
		CN 113227362 A	06-08-2021
		EA 202190512 A1	17-11-2021
		EP 3853357 A1	28-07-2021
		IL 281586 A	31-05-2021
		JP 2022501037 A	06-01-2022
		KR 20210093862 A	28-07-2021
		US 2021355503 A1	18-11-2021
		WO 2020061581 A1	26-03-2020

WO 2017112948 A1	29-06-2017	US 2020224173 A1	16-07-2020
		US 2022204945 A1	30-06-2022
		WO 2017112948 A1	29-06-2017
