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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))

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))

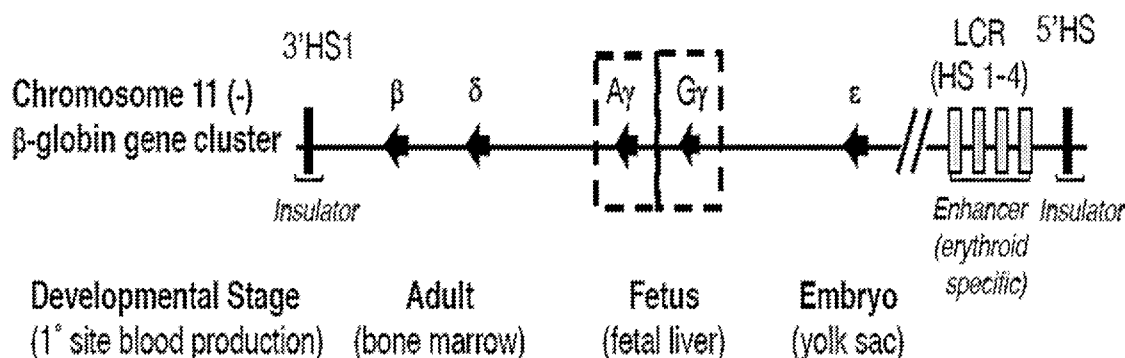
— with sequence listing part of description (Rule 5.2(a))

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

09 January 2025 (09.01.2025)

(54) Title: SYSTEMS AND METHODS FOR THE TREATMENT OF HEMOGLOBINOPATHIES

FIG. 1



(57) Abstract: Genome editing systems, guide RNAs, and CRISPR-mediated methods are provided for altering portions of the HBG1 and HBG2 loci in cells and increasing expression of fetal hemoglobin.



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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2024/033161

A. CLASSIFICATION OF SUBJECT MATTER
 INV. C12N5/0789 A61K35/28 C07K14/805 C12N15/113
 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 C07K 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 2018/142364 A1 (NOVARTIS AG [CH]; INTELLIA THERAPEUTICS INC [US]) 9 August 2018 (2018-08-09) abstract page 1, line 22 - page 2, line 9 page 17, line 1 - line 11 page 27, line 32 - page 28, line 8 -----	1 - 67
X	WO 2021/119040 A1 (EDITAS MEDICINE INC [US]) 17 June 2021 (2021-06-17) abstract page 4, paragraph 18 page 9, paragraph 34 page 10, paragraph 36 page 207; claim 40 page 206; claim 33 ----- - / - -	1 - 67

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	"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 13 November 2024	Date of mailing of the international search report 05/12/2024
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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 Grötzingler, Thilo
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International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>HAN YUANYUAN ET AL: "CRISPR/Cas9-based multiplex genome editing of BCL11A and HBG efficiently induces fetal hemoglobin expression", EUROPEAN JOURNAL OF PHARMACOLOGY, ELSEVIER SCIENCE, NL, vol. 918, 28 January 2022 (2022-01-28), XP086961090, ISSN: 0014-2999, DOI: 10.1016/J.EJPHAR.2022.174788 [retrieved on 2022-01-28] abstract page 2, left-hand column, paragraph 3 page 6, left-hand column - right-hand column, paragraph 1; figure 3 -----</p>	1-67
X	<p>CHRISTOPHER T. LUX ET AL: "TALEN-Mediated Gene Editing of HBG in Human Hematopoietic Stem Cells Leads to Therapeutic Fetal Hemoglobin Induction", MOLECULAR THERAPY- METHODS & CLINICAL DEVELOPMENT, vol. 12, 1 March 2019 (2019-03-01), pages 175-183, XP055737046, GB ISSN: 2329-0501, DOI: 10.1016/j.omtm.2018.12.008 abstract page 178; figure 3 page 180, right-hand column, paragraph 2 -----</p>	1-67

INTERNATIONAL SEARCH REPORT

International application No.

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
 - a. forming part of the international application as filed.
 - b. furnished subsequent to the international filing date for the purposes of international search (Rule 13^{ter}.1(a)).
 - accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2024/033161

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