

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
3 August 2006 (03.08.2006)

PCT

(10) International Publication Number
WO 2006/081430 A3

(51) International Patent Classification:
C12N 15/62 (2006.01)

(21) International Application Number:
PCT/US2006/002951

(22) International Filing Date: 27 January 2006 (27.01.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/647,013 27 January 2005 (27.01.2005) US

(71) Applicant (for all designated States except US): **FIVE PRIME THERAPEUTICS, INC.** [US/US]; 1650 Owens Street., Suite 200, San Francisco, CA 94158-2261 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **HALENBECK, Robert, Forgan** [US/US]; 59 Golden Hinde Boulevard, San Rafael, CA 94903 (US). **BOSCH, Elizabeth** [US/US]; 23047 Cricket Hill Road, Cupertino, CA 95014 (US). **LIN-NEMANN, Thomas** [DE/US]; 1338 Baker Street #7, San Francisco, CA 94115 (US). **LEE, Ernestine** [US/US]; 226 Arlington Avenue, Kensington, CA 94707 (US).

(74) Agent: **GARRETT, Arthur, S.**; Finnegan, Henderson, Farabow, Garrett & Dunner LLP, 901 New York Avenue, NW, Washington, DC 20001-4413 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
5 April 2007

(15) Information about Correction:

Previous Correction:

see PCT Gazette No. 48/2006 of 30 November 2006

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: LEADER SEQUENCES FOR DIRECTING SECRETION OF POLYPEPTIDES AND METHODS FOR PRODUCTION THEREOF

(57) Abstract: The present invention provides leader sequences that are useful for the production of heterologous secretable polypeptides; heterologous secreted polypeptides; nucleic acid constructs that encode such leader sequences and heterologous secreted polynucleotides; vectors that contain such nucleic acid constructs; recombinant host cells that contain such nucleic acid constructs; vectors, polypeptides, and methods of making and using such secreted polypeptides with such heterologous leader sequences.

WO 2006/081430 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2006/002951

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

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
- a. type of material
- ☒ a sequence listing
- ☐ table(s) related to the sequence listing
- b. format of material
- ☒ on paper
- ☒ in electronic form
- c. time of filing/furnishing
- ☐ contained in the international application as filed
- ☐ filed together with the international application in electronic form
- ☒ furnished subsequently to this Authority for the purpose of search
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2006/002951

Box 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 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 fee, this Authority did not invite payment of any additional fee.
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.:
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.:

1-5, 8-32 all partially

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ 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:

Invention 1:1-5,8-32 all partially

A heterologous polypeptide comprising a secretory leader and a second polypeptide, wherein the secretory leader has the SEQ ID No:20

Invention 2: 1-5,8-32 all partially

A heterologous polypeptide comprising a secretory leader and a second polypeptide, wherein the secretory leader has the SEQ ID No:21

Invention 3-97: claims 1-5,8-32 all partially

A heterologous polypeptide comprising a secretory leader and a second polypeptide, wherein the secretory leader has the SEQ ID

No:23-25,27,32-36,38-40,48-53,76-78,80,81,83-85,87,95,96,103,108-110,112-115,117-119,121-126,128-130,132-136,138,139,141-144,154-158,160-166,178-180,186-188,197-199,210-214,223-226,233,234,240,246 or 247

4. claims: Group of invention number 98: claims 6,7

A secretory leader peptide

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/002951

A. CLASSIFICATION OF SUBJECT MATTER

INV. C12N15/62

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 practical, search terms used)

EPO-Internal, BIOSIS, MEDLINE, EMBASE, FSTA, Sequence Search, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LO K-M ET AL: "High level expression and secretion of Fc-X fusion proteins in mammalian cells" PROTEIN ENGINEERING, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 11, no. 6, June 1998 (1998-06), pages 495-500, XP002125745 ISSN: 0269-2139 abstract page 495, right-hand column, paragraph 2 - page 497, left-hand column, paragraph 1; figure 1; table 1 page 499, left-hand column, paragraph 2 ----- -/--	1,2,4,5, 8,9,11, 12, 21-23, 25-31

☒ 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 document 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

11 October 2006

Date of mailing of the international search report

14. 02. 2007

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Strobel, Andreas

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/002951

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHOI J H ET AL: "Secretory and extracellular production of recombinant proteins using Escherichia coli" APPLIED MICROBIOLOGY AND BIOTECHNOLOGY, vol. 64, no. 5, June 2004 (2004-06), pages 625-635, XP002402621 ISSN: 0175-7598 abstract table 2	1,2,4,5, 8,11,21, 25,28,29