

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
16 December 2004 (16.12.2004)

PCT

(10) International Publication Number  
**WO 2004/108761 A3**

- (51) International Patent Classification<sup>7</sup>: C12N 15/12, (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, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (21) International Application Number: PCT/US2004/013550
- (22) International Filing Date: 3 May 2004 (03.05.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/467,405 1 May 2003 (01.05.2003) US
- (71) Applicant (for all designated States except US): **MERIAL LIMITED** [US/US]; 3239 Satellite Blvd., Duluth, GA 30096 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **FISHER, Laurent, Bernard** [FR/FR]; 17, Chemin Vert, F-69110, Sainte Foy Les Lyon (FR). **CACHET, Nathalie, Michele** [FR/FR]; 152, Chemin des Fontanières, F-69100, Sainte Foy Les Lyon (FR). **BARZU-LE-ROUX, Simona** [FR/FR]; 461 route de Saint Bel, F-69210 Lentilly (FR).
- (74) Agent: **JARECKI-BLACK, Judy, C., Ph. D., J.D.**; 3239 Satellite Blvd., Duluth, GA 30096 (US).
- (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, IT, LU, 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
- (88) Date of publication of the international search report: 17 March 2005
- 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.*



WO 2004/108761 A3

(54) Title: CANINE GHRH GENE, POLYPEPTIDES AND METHODS OF USE

(57) Abstract: The present invention relates to a canine pre-proGHRH polypeptide, a canine mature GHRH peptide, an isolated polynucleotide which encodes the canine pre-proGHRH or the canine mature GHRH. The invention also encompasses vectors encoding and expressing the canine pre-proGHRH or the canine GHRH which can be used to treat disease and growth hormone deficiencies by gene therapy in vertebrates, in particular in dogs.

# INTERNATIONAL SEARCH REPORT

ational Application No  
/US2004/013550

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7 C12N15/12 C07K14/60 A61K48/00 C12N15/86

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)  
 IPC 7 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, WPI Data, PAJ, BIOSIS, EMBASE, Sequence Search

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 052 286 A (PFIZER PROD INC) 15 November 2000 (2000-11-15) the whole document -----	1-18
A	EP 0 459 747 A (LILLY CO ELI) 4 December 1991 (1991-12-04) the whole document -----	
A	EP 0 137 689 A (SALK INST FOR BIOLOGICAL STUDI) 17 April 1985 (1985-04-17) the whole document -----	
	-/--	

Further documents are listed in the continuation of box C.       Patent family members are listed in annex.

° Special categories of cited documents :

<p>*A* document defining the general state of the art which is not considered to be of particular relevance</p> <p>*E* earlier document but published on or after the international filing date</p> <p>*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)</p> <p>*O* document referring to an oral disclosure, use, exhibition or other means</p> <p>*P* document published prior to the international filing date but later than the priority date claimed</p>	<p>*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</p> <p>*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</p> <p>*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.</p> <p>*&amp;* document member of the same patent family</p>
--	--

Date of the actual completion of the international search  <b>25 November 2004</b>	Date of mailing of the international search report  <b>10/12/2004</b>
--	---

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  <b>Roscoe, R</b>
--	--

## INTERNATIONAL SEARCH REPORT

International Application No  
.../US2004/013550

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>DRAGHIA-AKLI R ET AL: "Effects of plasmid-mediated growth hormone-releasing hormone in severely debilitated dogs with cancer" MOLECULAR THERAPY 01 DEC 2002 UNITED STATES, vol. 6, no. 6, 1 December 2002 (2002-12-01), pages 830-836, XP002307437 ISSN: 1525-0016 the whole document</p>	1-18
Y	<p>GONZÁLEZ-CRESPO S ET AL: "Expression of the rat growth hormone-releasing hormone gene in placenta is directed by an alternative promoter." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA. 1 OCT 1991, vol. 88, no. 19, 1 October 1991 (1991-10-01), pages 8749-8753, XP002307438 ISSN: 0027-8424 the whole document</p>	1-18
A	<p>GOMBERG-MAITLAND M ET AL: "Recombinant growth hormone: A new cardiovascular drug therapy" AMERICAN HEART JOURNAL, MOSBY- YEAR BOOK INC., ST. LOUIS, MO, US, vol. 132, no. 6, December 1996 (1996-12), pages 1244-1262, XP004530854 ISSN: 0002-8703 the whole document</p>	

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2004/013550

## 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

- in written format  
 in computer readable form

c. time of filing/furnishing

- contained in the international application as filed  
 filed together with the international application in computer readable 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

national application No.  
PCT/US2004/013550

## 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:  
  
Although claims 13-18 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.: 1-6 (all partially)  
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:  
  
see FURTHER INFORMATION sheet PCT/ISA/210
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:

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.:

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

## Continuation of Box II.1

Although claims 13-18 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

-----

## Continuation of Box II.2

Claims Nos.: 1-6 (all partially)

Applicant defines the proteins or DNAs of claims 1-6 as "consisting essentially" of defined sequences. This terminology is considered unclear. The lack of clarity is enhanced by applicants definition on p.4 of the application which explains that "consisting essentially of" has the meaning to specifically exclude non-canine GHRH sequences. This is (i) a complex disclaimer since not all GHRH sequences are known so the scope of the non-canine sequences is unclear, and more significantly (ii) although what is not in the scope is kind of defined, the actual extent of applicants canine sequences is not defined (what level of variation ?), neither is the extent of the non-canine sequences (e.g. although the porcine sequence could be considered to be disclaimed - what about variants thereof ?).

Hence, claims 1-6 have only been examined insofar as they relate to the exact sequences of Seq.ID Nos. 1-4.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

/US2004/013550

Patent document cited in search report	A	Publication date	Patent family member(s)	Publication date
EP 1052286	A	15-11-2000	BR 0001606 A	24-04-2001
			CA 2303702 A1	12-10-2000
			EP 1052286 A2	15-11-2000
			JP 2000350590 A	19-12-2000
			JP 2002302449 A	18-10-2002
			JP 2003052390 A	25-02-2003
			US 6759393 B1	06-07-2004
			US 2004171574 A1	02-09-2004
			<hr/>	
EP 0459747	A	04-12-1991	AU 639107 B2	15-07-1993
			AU 7800391 A	05-12-1991
			CA 2043049 A1	30-11-1991
			CS 9101583 A3	15-01-1992
			EP 0459747 A1	04-12-1991
			HU 58799 A2	30-03-1992
			IE 911816 A1	04-12-1991
			JP 5068559 A	23-03-1993
			NZ 238233 A	23-12-1992
			ZA 9103876 A	27-01-1993
			<hr/>	
EP 0137689	A	17-04-1985	US 4610976 A	09-09-1986
			US 4585756 A	29-04-1986
			US 4605643 A	12-08-1986
			AR 248284 A1	12-07-1995
			AT 24184 T	15-12-1986
			AU 577542 B2	29-09-1988
			AU 3244984 A	07-03-1985
			CA 1271899 A1	17-07-1990
			CS 251085 B2	11-06-1987
			DD 228266 A5	09-10-1985
			DE 3461641 D1	22-01-1987
			DK 413084 A ,B,	01-03-1985
			EG 17263 A	30-08-1991
			EP 0137689 A1	17-04-1985
			ES 8606401 A1	01-10-1986
			FI 843355 A ,B,	01-03-1985
			GR 80227 A1	02-01-1985
			HU 35000 A2	28-05-1985
			IE 57730 B1	24-03-1993
			IL 72717 A	31-01-1988
			JP 1945390 C	23-06-1995
			JP 6076437 B	28-09-1994
			JP 60072900 A	24-04-1985
			KR 9006560 B1	13-09-1990
			MX 7460 E	19-12-1988
			NO 843381 A ,B,	01-03-1985
			NZ 209357 A	29-04-1988
			PH 21316 A	28-09-1987
			PT 79094 A ,B	01-09-1984
			SU 1423000 A3	07-09-1988
			YU 148884 A1	30-04-1988
ZA 8406352 A	27-03-1985			
CA 1247604 A1	27-12-1988			
NZ 210924 A	30-08-1988			
PH 21475 A	28-10-1987			