Title: HUMAN PLGF-2 FOR THE PREVENTION OR TREATMENT OF HEART FAILURE

Abstract: The present invention relates to treating and/or preventing heart failure or one or more individual heart failure phenotypes in mammals using placental growth factor 2 (P1GF-2).
INTERNATIONAL SEARCH REPORT

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 and necessary to the claimed invention, the international search was carried out on the basis of:
   a. (means)
      ☐ on paper
      ☑ in electronic form
   b. (time)
      ☐ in the international application as filed
      ☐ together with the international application in electronic form
      ☐ 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 application No.
PCT/EP201 4/061 259

Form PCT/ISA/21 0 (continuation of first sheet (1)) (July 2009)
INTERNATIONAL SEARCH REPORT

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.:

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.

Form PCT/ISA/21 0 (continuation of first sheet (2)) (April 2005)
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**

INV. A61K38/18 A61P9/04

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)

A61K A61P

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, EMBASE, BIOSIS, WPI Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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* 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 establishes 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

* Z: document member of the same patent family

Date of the actual completion of the international search

2 December 2014

Date of mailing of the international search report

11/12/2014

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

Hars, Jesko
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<td>A,P</td>
<td>M Wu ET AL: &quot;Systemic recombinant human placental growth factor-2 administered on and improves myocardial perfusion and contractile function at rest and during stress&quot;, EUROPEAN HEART JOURNAL, vol. 34, no. Suppl. 1, 1 August 2013 (2013-08-01), page 415, ISSN: 0195-668X, DOI: 10.1093/eurheartj/eht308. P2272 the whole document</td>
<td>1-5, 9, 11-18</td>
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<td>A</td>
<td>ARINA M. JABA ET AL: &quot;NO triiggers RGS4 degradation to coordinate angiogenesis and cardiomyocyte growth&quot;, JOURNAL OF CLINICAL INVESTIGATION, vol. 123, no. 4, 1 March 2013 (2013-03-01), pages 1718-1731, ISSN: 0021-9738, DOI: 10.1172/JCI65112 the whole document</td>
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<td>&amp; ARINA M. JABA ET AL: &quot;NO triiggers RGS4 degradation to coordinate angiogenesis and cardiomyocyte growth - Supplemental Data&quot;, JOURNAL OF CLINICAL INVESTIGATION, vol. 123, no. 4, 1 April 2013 (2013-04-01), pages 1-8, ISSN: 0021-9738, DOI: 10.1172/JCI65112 figure 1</td>
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Form PCT/ISA/210 (continuation of second sheet) (April 2005)
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<td>wo 2010/049538 AI (CT DE RECH PUBLIC DE LA SANTE [LU] ; DEVAUX YVAN [FR] ; WAGNER DANI EL R) 6 May 2010 (2010-05-06) claim 1; sequence 9</td>
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</table>
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-5, 9, 11-18 (al1 partly)

   A composition comprising placent al growth factor 2 protein (P1GF-2) for use in treating or preventing a heart failure phenotype in a mammal, where said heart failure phenotype is ventricular dysfunction defined by an increased end-systolic volume and/or a reduced ejection fraction.

2. Claims: 1, 6, 7, 9, 11-18 (al1 partly)

   A composition comprising placent al growth factor 2 protein (P1GF-2) for use in treating or preventing a heart failure phenotype in a mammal, where said heart failure phenotype is ventricular remodeling.

3. Claims: 1, 2, 8, 9, 11-18 (al1 partly)

   A composition comprising placent al growth factor 2 protein (P1GF-2) for use in treating or preventing a heart failure phenotype in a mammal, where said heart failure phenotype is ventricular dysfunction defined by an impaired relaxation, an increased ventricular filling pressure and a preserved ejection fraction.

4. Claims: 10 (completely); 1-9, 11-18 (partly)

   A composition comprising placent al growth factor 2 protein (P1GF-2) for use in treating or preventing a heart failure phenotype in a mammal, where a said mammal is atherosclerotic.