Figure 1. Inhibition of IL-8 (a), Gro-a (b) and IL-6/II-7 (c) induced calcium flux by ZVFL5A-G8 Antibody.

(54) Title: ANTI-CXC CHEMOKINE RECEPTOR-2 BINDING MOLECULES AND USES THEREOF

(57) Abstract: This disclosure relates to an anti-CXCR2 binding molecules and uses thereof, in particular in treatment of cancers and inflammatory diseases. Furthermore, the disclosure provides compositions and methods for treating cancers and inflammatory diseases.
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))
<table>
<thead>
<tr>
<th>Box No.</th>
<th>Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>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:</td>
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<tr>
<td>a.</td>
<td>forming part of the international application as filed:</td>
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<td></td>
<td>in the form of an Annex C/ST.25 text file.</td>
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<td>on paper or in the form of an image file.</td>
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<td>b.</td>
<td>furnished together with the international application under PCT Rule 13fer1 (a) for the purposes of international search only in the form of an Annex C/ST.25 text file.</td>
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<tr>
<td>c.</td>
<td>furnished subsequent to the international filing date for the purposes of international search only:</td>
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<td></td>
<td>in the form of an Annex C/ST.25 text file (Rule 13fer1 (a)).</td>
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<td>on paper or in the form of an image file (Rule 13fer1 (b) and Administrative Instructions, Section 7:3).</td>
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<td>2.</td>
<td>In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.</td>
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<tr>
<td>3.</td>
<td>Additional comments:</td>
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</table>
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.:
   l-66(partially)

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.
A. CLASSIFICATION OF SUBJECT MATTER

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

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, BIOSIS, EMBASE

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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</table>

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 application or patent but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which may affect the patentability of the invention
- "O" document referring to an oral disclosure, use, exhibition or other special reason (as specified)
- "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 novel or cannot be considered to involve an inventive step when the document is taken together 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: 14 July 2015

Date of mailing of the international search report: 15/12/2015

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

Chapman, Rob
<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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<tbody>
<tr>
<td>X</td>
<td>AIHUA LI ET AL: &quot;Autocrine Role of Interleukin-8 in Induction of Endothelial Cell Proliferation, Survival, Migration and MMP-2 Production and Angiogenesis&quot;, ANGIOGENESIS, KLUWER ACADEMIC PUBLISHERS, DOI: 10.1007/S10456-005-5208-4</td>
<td>1-66</td>
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<tr>
<td>Category</td>
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<tr>
<td>Y</td>
<td>THOMAS JAMIESON ET AL: &quot;Inhibition of CXCR2 profoundly suppresses inflammation on-ddevelopment and spontaneous tumori genesis&quot;. JOURNAL OF CLINICAL INVESTIGATION, vol. 122, no. 9, 4 September 2012 (2012-09-04), pages 3127-3144, ISSN: 0021-9738, DOI: 10.1172/JCI61067. The whole document, in particular, p. 3141, col. 3</td>
<td>64-66</td>
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<tr>
<td>T</td>
<td>ROSSANT CHRISTINE ET AL: &quot;Phage display and hybrid generation of antibodies to human CXCR2 yields antibodies with distinct mechanisms and epitopes&quot;. MABS, vol. 6, no. 6, December 2014 (2014-12), pages 1425-1438, XP009185346, the whole document</td>
<td>------</td>
</tr>
</tbody>
</table>
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. **Claims:** l-66(partially)

   An isolated binding molecule or anti-binding fragment thereof which specifically binds to CXC chemokine receptor-2 (CXCR2), wherein the binding molecule can inhibit binding to interleukin 8 (IL-8), and related subject-matter

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2. **Claims:** l-66(partially)

   An isolated binding molecule or anti-binding fragment thereof which specifically binds to CXC chemokine receptor-2 (CXCR2), wherein the binding molecule can inhibit binding to growth-related protein alpha (Gro-alpha), and related subject-matter

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3. **Claims:** l-66(partially)

   An isolated binding molecule or anti-binding fragment thereof which specifically binds to CXC chemokine receptor-2 (CXCR2), wherein the binding molecule can inhibit the IL-8 or Gro-a induced calcium responses, and related subject-matter

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4. **Claims:** l-66(partially)

   An isolated binding molecule or anti-binding fragment thereof which specifically binds to CXC chemokine receptor-2 (CXCR2), wherein the binding molecule can inhibit IL-8, Gro-y, Gro-P, Gro-y, ENA-78, GCP-2 and NAP-2 induced beta-arrestin recruitment in a mammalian cell, and related subject-matter

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