METHOD FOR DETECTING INHIBITORS OF TUMOUR GROWTH

Compounds that block HH signalling through modifications of PTC and SMO vesicular sorting are of use in the preparation of medicaments for the treatment of a mammalian cancer.
INTERNATIONAL SEARCH REPORT

INTERNATIONAL APPLICATION No.
PCT/GB 01/04891

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68

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 C12Q

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)
MEDLINE, BIOSIS, EPO-Internal, 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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<tr>
<td>X</td>
<td>TAIPALE JUSSI ET AL: &quot;Effects of oncogenic mutations in Smoothened and Patched can be reversed by cyclopamine.&quot; NATURE (LONDON), vol. 406, no. 6799, 2000, pages 1005-1009, XP002239780 ISSN: 0028-0836 cited in the application the whole document</td>
<td>1-9</td>
</tr>
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</table>

Further documents are listed in the continuation of box C.

Patent family members are listed in 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 relating 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
29 April 2003

Date of mailing of the international search report
15/05/2003

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tc. 31 851 epo nl
Fac. (+31-70) 340-3018

Authorized officer
Luzzatto, E
<table>
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<td>X</td>
<td>HOPYAN SEVAN ET AL: &quot;Indian Hedgehog and Parathyroid hormone related protein signaling in cartilage tumors of bone.&quot;</td>
<td>PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL, no. 41, March 2000 (2000-03), page 206 XP002239782</td>
<td>1,4,7-9</td>
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<td>91st Annual Meeting of the American Association for Cancer Research.;San Francisco, California, USA; April 01-05, 2000, March, 2000</td>
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<td>A</td>
<td>SASAKI HIROSHI ET AL: &quot;A binding site for Gli proteins is essential for HNF-3-beta floor plate enhancer activity in transgenics and can respond to Shh in vitro.&quot;</td>
<td>DEVELOPMENT (CAMBRIDGE), vol. 124, no. 7, 1997, pages 1313-1322, XP002239784</td>
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<td>P,X</td>
<td>WO 01 19800 A (CURIS INC)</td>
<td>22 March 2001 (2001-03-22), page 87, line 15 –page 88, line 12</td>
<td>5,6</td>
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INTERNATIONAL SEARCH REPORT

Box I  Observations where certain claims were found unsearchable (Continuation of item 1 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. [X] Claims Nos.: 
   because they relate to subject matter not required to be searched by this Authority, namely:
   see FURTHER INFORMATION sheet PCT/ISA/210

2. [X] Claims Nos.: 1-4, 7-9 (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 II  Observations where unity of invention is lacking (Continuation of item 2 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.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1998)
Continuation of Box I.1

Although claim 8 is 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, i.e. cyclopamine (see further remarks on incomplete search).

Continuation of Box I.1

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Continuation of Box I.2

Claims Nos.: 1-4, 7-9 (all partially)

1) Claim 7 relates to compounds solely characterised in that they are obtainable by the method of claims 5 or 6. However, this only feature does not allow the skilled person to understand the actual scope of the claims; a meaningful search over their whole scope is therefore not possible. Claim 7 has thus been searched only insofar as related to the only compound disclosed in the application, namely cyclopamine.

2) Claims 1-4 relate to the use of a compound only characterised in that it blocks hedgehog signalling through modifications of PTC and SMO vesicular sorting. Again, this sole feature does not allow the skilled person to understand the actual scope of these claims, which therefore cannot be the object of a complete search. The search with respect to these claims has thus been limited to cyclopamine, for the reasons indicated with respect to claim 7. The same applies to claims 8 and 9.

The applicant's attention is drawn to the fact that claims, or parts of 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.
<table>
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<th>Publication date</th>
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