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LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG,
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(54) Title: USE OF IL-18 INHIBITORS IN HYPERSENSITIVITY DISORDERS

(57) Abstract: The invention relates to the use of inhibitors of IL-18 in the preparation of a medicament for treatment and/or prevention of hypersensitivity disorders, and in particular of delayed-type hypersensitivity.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 02/08591

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/17 A61K38/21 A61K39/395 A61K48/00 A61P37/00
 //(A61K38/21, 38:17), (A61K39/395, 38:21), (A61K38/17, 31:00),
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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 C07K A61K

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 110 969 A (HAYASHIBARA BIOCHEM LAB) 27 June 2001 (2001-06-27) the whole document ---	1-5, 9-12, 15-27
X	EP 0 974 600 A (HAYASHIBARA BIOCHEM LAB) 26 January 2000 (2000-01-26) page 2 page 5, paragraph 1 page 7, paragraph 2 - paragraph 3 page 8, paragraph 3 - paragraph 5 claims; examples 1-6 ---	1,2,4-7, 15,21-27
X	EP 0 864 585 A (HAYASHIBARA BIOCHEM LAB) 16 September 1998 (1998-09-16) page 2, paragraph 2; claims 1,2,4,20-26 page 5, line 34 - line 48; claims 24,25 page 6, paragraph 2 - paragraph 3 --- -/--	1,2,4, 10,15-27

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 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

9 October 2002

Date of mailing of the international search report

17/10/2002

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 02/08591

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 71719 A (HYSEQ INC) 30 November 2000 (2000-11-30) page 4, paragraph 3 page 8, paragraph 1 page 40, paragraph 1 page 66, line 29 -page 67, line 3 page 76, paragraph 2 page 7, paragraph 4 page 55, paragraph 2 -page 56, paragraph 2 -----	1-5, 10-27
X	WO 99 46248 A (WANNAMAKER MARION W ; VERTEX PHARMA (US); CHARIFSON PAUL (US); LAUF) 16 September 1999 (1999-09-16) page 1, line 15 - line 17 page 7, line 34 -page 8, line 4 page 40, paragraph 3 page 42, line 33 -page 43, line 30 page 46, line 6 -page 47, line 10 claims 15-23 -----	1-3,5, 13,14, 17,18, 20-23,27

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 11

Present claims 1-5, 9-27 relate to a compounds defined by reference to a desirable characteristic or property, namely "inhibitor of IL-18", "caspase-1 (ICE) inhibitors", "inhibitors of the IL-18 pathway", "antagonist of IL-18 which compete with IL-18 and block the IL-18 receptor", "IL-18-binding proteins, isoforms, muteins, fused proteins, functional derivatives, active fractions or circularly permuted derivatives thereof", "fused protein comprising an immunoglobulin fusion wherein the fused protein binds to IL-18", "anti-inflammatory agent", and "anti-allergic agent", or "fuctional derivative comprises at least one moiety attached to one or more functional groups, which occur as one or more side chains on the amino acid residues".

The claims 1-5, 9-27 cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed in the examples, namely IL-18BP and the general concept of inhibition of IL-18 in the treatment of hypersensitivity disorders.

Moreover, claims 1-2, 24-26 relate to the use of a pharmaceutical preparation for prophylaxis or treatment of "hypersensitivity disorder" or "allergic disorders", which encompass a multitude of different diseases. The claims thus cover a rather large number of diseases, whereas the application provides support within the meaning of Article 84 EPC and disclosure within the meaning of Article 5 PCT for only a limited number of diseases. Consequently, the claims lack support and the application lacks disclosure. Independent of the above reasoning, the claims 1-3, 23-25 also lack clarity because it is not fully possible to determinethe diseases for which protection might legitimately be sought (Art. 6 PCT). Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed in the examples and claims 3 and 4, namely DTH and contact hypersensitivity.

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

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 02/08591

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. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 27 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.
2. Claims Nos.: 11
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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 02/08591

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