TREATMENT OF TH2 DOMINATED IMMUNOLOGICAL DISEASE STATES WITH PROGESTERONE RECEPTOR ANTAGONISTS

The novel use of antagonists for the human progesterone receptor in the treatment and/or prophylaxis of immunological disease states which are associated with a Th2 dominated reaction pattern of the pathological immune response is described.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/00  A61K31/277  A61K31/567  A61K31/569  A61K31/57
A61K31/573  A61K31/575  A61K31/58  A61P9/00  A61P11/02
A61P11/06  A61P17/02  A61P19/04  A61P31/04  A61P31/08

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 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)

WPI Data, PAJ, EPO-Internal, MEDLINE, BIOSIS, EMBASE, BEILSTEIN Data, CHEMABS Data, PASCAL, SCISEARCH, CANCERLIT

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
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<th>Category</th>
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<td>WO 94 22451 A (OKLAHOMA MED RES FOUND)</td>
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<td>13 October 1994 (1994-10-13) page 10, line 13 - line 16</td>
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<td>page 11 - page 12, chapter &quot;Autoimmune Disorders&quot; claims 4,6,9,11</td>
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<td>EP 1 148 054 A (PFIZER PROD INC)</td>
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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 doubt 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

6 March 2003

Name and mailing address of the ISA
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Fax: (+31-70) 540-3016

Authorized officer

Albrecht, S

Form PCT/ISA/210 (second sheet) (July 1992)
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

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Date of the actual completion of the international search

6 March 2003

Date of mailing of the international search report

Authorized officer

Albrecht, S

Form PCT/2/SA/210 (second sheet) (July 1992)
### 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:

2. ☑ Claims Nos.: 1-6,11-15 (1-6,11,12 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 dependant 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:

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 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.:

   1-6, 11-15 (1,2,11-15 partially)

**Remark on Protest**

☑ The additional search fees were accompanied by the applicant’s protest.

☐ No protest accompanied the payment of additional search fees.
Continuation of Box 1.2

Claims Nos.: 1-6,11-15 (1-6,11,12 partially)

a) Present claims 1, 2, 11-12 are directed to a method of treatment, as they encompass the administration of active agents to patients. However, the intended purpose is defined by reference to a desirable characteristic or property, namely "for the treatment and/or prophylaxis of an immunological disease state associated with a Th2 dominated reaction pattern of the pathological immune response". Such is not a method of therapy according to R.67.1(iv) PCT as the intended disease(s), disorder(s) or dysfunction(s) to be treated is/are not defined. Claims 1, 2, 11-12 cover all methods having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT only for a limited number of such methods. Accordingly, since a meaningful search over the whole of the claimed scope is impossible, the search has thus been restricted to autoimmune diseases, including systemic lupus erythematosus, systemic scleroderma, Sjogren's syndrome and immune myocarditis (listed in claims 3-6).

b) Present claims 1-6 and 12 relate to compounds defined by reference to desirable characteristics or properties, namely progesterone receptor antagonists (claims 1-6) and mesoprostogens (claim 12) respectively. These claims cover all compounds having these characteristics or properties, and thus relate to an extremely large number of possible compounds, rendering a complete search impossible. Consequently, the search has been limited to the mesoprostogen J1042, mentioned on p.3, paragraph 3 of the description and the compounds which are listed in claim 11.

In addition, the applicant's attention is drawn to the fact that some compounds may be already known to treat the diseases/disorders claimed by the applicant but are as yet not identified as antagonists of the progesterone receptor or mesoprostogens.

c) Concerning claims 13-15, since they do not indicate the nature of the substance to be used for the claimed treatment, they contain so many options, variables, possible permutations and provisos that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has not been carried out for these claims.

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.
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-6,11-15 (1,2,11-15 partially)
   Use of progesterone receptor antagonists for the manufacture of a medicament for the treatment and/or prophylaxis of autoimmune diseases

2. Claims: 1,2,7,8,11-15 (1,2,11-15 partially)
   Use of progesterone receptor antagonists for the manufacture of a medicament for the treatment and/or prophylaxis of chronic rejection reaction after transplantation

3. Claims: 1,2,9,11-15 (1,2,11-15 partially)
   Use of progesterone receptor antagonists for the manufacture of a medicament for the treatment and/or prophylaxis of allergic diseases

4. Claims: 1,2,10-15 (1,2,11-15 partially)
   Use of progesterone receptor antagonists for the manufacture of a medicament for the treatment and/or prophylaxis of infectious diseases
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