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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))
- of inventorship (Rule 4.17(iv))

Published:

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- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:

12 April 2007

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: PYRROLOPYRIDINEDERIVATIVES AS MODULATORS OF THE CANNABINOID RECEPTOR FOR THE TREATMENT OF IMMUNE AND INFLAMMATORY DISORDERS

(57) Abstract: The present invention relates to novel pyrrolopyridine derivatives of formula (I), pharmaceutical compositions containing these compounds and their use in the treatment of diseases, particularly pain, which diseases are caused directly or indirectly by an increase or decrease-in activity of the cannabinoid receptor, wherein: X<sub>1</sub> is NH and X<sub>2</sub> and X<sub>3</sub> together form a -CR<sup>13</sup>=CR<sup>11</sup>-group or X<sub>3</sub> is NR<sup>12</sup> and X<sub>2</sub> and X<sub>1</sub> together form a -CR<sup>13</sup>=CR<sup>11</sup>-group; X<sub>4</sub> is O, SO<sub>2</sub>, S, or a bond, or X<sub>4</sub> is -NHCO or -NHCH<sub>2</sub> such that R<sup>6</sup>X<sub>4</sub> is R<sup>6</sup>CONH or R<sup>6</sup>CH<sub>2</sub>NH; R<sup>1</sup> is selected from hydrogen, C<sub>1-6</sub> alkyl, C<sub>3-6</sub> cycloalkyl and halosubstituted C<sub>1-6</sub> alkyl; R<sup>2</sup> is hydrogen or (CH<sub>2</sub>)mR<sup>3</sup> where m is 0 or 1; or R<sup>1</sup> and R<sup>2</sup> together with N to which they are attached form an optionally substituted 4- to 8- membered non-aromatic heterocyclyl ring; R<sup>3</sup> is a 4- to 8- membered non-aromatic heterocyclyl group, a C<sub>3-8</sub> cycloalkyl group, a straight or branched C<sub>1-10</sub> alkyl, a C<sub>2-10</sub> alkenyl, a C<sub>3-8</sub> cycloalkenyl, a C<sub>2-10</sub> alkynyl, a C<sub>3-8</sub> cycloalkynyl or phenyl group, any of which can be unsubstituted or substituted, or R<sup>5</sup>; wherein p is 0, 1 or 2, and X is CH<sub>2</sub>, O, S, or SO<sub>2</sub>; R<sup>6</sup> is phenyl, C<sub>3-6</sub> cycloalkyl, a straight or branched C<sub>1-6</sub> alkyl group, -CH<sub>2</sub>-C<sub>3-6</sub> cycloalkyl, -CH<sub>2</sub>-phenyl, 4- to 8- membered non-aromatic heterocyclyl group, or a bicyclic group any of which can be unsubstituted or substituted, however when X<sub>4</sub> is a bond R<sup>6</sup> is substituted phenyl; R<sup>7</sup> is OH, C<sub>1-6</sub> alkoxy, NR<sup>8a</sup>R<sup>8b</sup>, NHCOR<sup>9</sup>, NHSO<sub>2</sub>R<sup>9</sup> or SOqR<sup>9</sup>; R<sup>8a</sup> is H or C<sub>1-6</sub> alkyl; R<sup>8b</sup> is H or C<sub>1-6</sub> alkyl; R<sup>9</sup> is C<sub>1-6</sub> alkyl; R<sup>10</sup> is hydrogen, substituted or unsubstituted (C<sub>1-6</sub>)alkyl or chloro; R<sup>11</sup> is hydrogen or C<sub>1-6</sub> alkyl; R<sup>12</sup> is hydrogen or C<sub>1-6</sub> alkyl; R<sup>13</sup> is hydrogen or C<sub>1-6</sub> alkyl; q is 0, 1 or 2.

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# INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2006/007875

## A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D471/04 A61K31/437 A61P37/02 A61P29/00 A61P19/02

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)

C07D 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, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2005/066126 A (LILLY CO ELI [US]) 21 July 2005 (2005-07-21) preparations 11, 88 examples 1,5 claims 27,28,32,36,38	1-19
A	US 2002/022624 A1 (DINNELL KEVIN [GB] ET AL) 21 February 2002 (2002-02-21) examples 2-4 claim 28, formulae a2, a3 claim 36	1-19
A	WO 01/58869 A2 (SQUIBB BRISTOL MYERS CO [US]) 16 August 2001 (2001-08-16) example 14 claim 5	1-19
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☒ 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 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.

\*Z\* document member of the same patent family

Date of the actual completion of the international search

30 January 2007

Date of mailing of the international search report

12/02/2007

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## INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2006/007875

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	WO 2005/121140 A (GLAXO GROUP LTD [GB]) 22 December 2005 (2005-12-22) the whole document -----	1-19

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP2006/007875

### Box 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:  
  
Although claims 17 and 18 are 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.:  
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 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:

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/EP2006/007875

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2005066126	A	21-07-2005	AR 047160 A1	11-01-2006
			AU 2004312311 A1	21-07-2005
			CA 2549396 A1	21-07-2005
			EP 1699761 A1	13-09-2006
US 2002022624	A1	21-02-2002	NONE	
WO 0158869	A2	16-08-2001	AR 027406 A1	26-03-2003
			AU 3495801 A	20-08-2001
			CA 2399791 A1	16-08-2001
			EP 1254115 A2	06-11-2002
			JP 2004502642 T	29-01-2004
WO 2005121140	A	22-12-2005	AR 050158 A1	04-10-2006
			AU 2005251913 A1	22-12-2005