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Declaration under Rule 4.17:

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

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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: PHARMACEUTICAL PREPARATIONS CONTAINING THIAZOLIDINEDIONES FOR THE TREATMENT OR PREVENTION OF IP-10 MEDIATED DISEASES

(57) Abstract: The present invention refers to new therapeutic applications of pharmaceutical formulations containing, as active principles, thiazolidinediones, for the treatment or prevention of diseases characterised by an increase in the levels of IP-10, such as Primary Biliary Cirrhosis, acute and chronic rejection of kidney and pancreatic islet transplantation and endocrine autoimmune diseases. The invention also refers to a diagnostic method for the prevision of kidney transplantation rejection using the pre-transplantation levels of IP-10 as a serum marker.

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INTERNATIONAL SEARCH REPORT

International Application No
 T/EP2004/002069

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A61K31/4439 G01N33/68 A61P1/16 A61P37/00 A61P37/06

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 G01N

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, CHEM ABS Data, EMBASE, BIOSIS, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 953 355 A (SANKYO CO) 3 November 1999 (1999-11-03) page 2, paragraph 1 page 3, paragraph 10 - page 9, paragraph 18 page 27, line 45 - line 54 page 28, line 33 - line 50 claims 1-7 ----- -/--	1,5

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
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Date of the actual completion of the international search 30 September 2004	Date of mailing of the international search report 07/10/2004
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Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Cielen, E
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INTERNATIONAL SEARCH REPORT

International Application No.

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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 01/62238 A (SAN DIEGO STATE UNIVERSITY) 30 August 2001 (2001-08-30) page 1, line 9 - line 13 page 3, line 10 - line 23 page 4, line 7 - line 18 page 10, line 14 - line 21 page 11, line 10 - line 22 page 14, line 3 - line 18 page 14, line 28 - page 15, line 13 page 16, line 31 - page 17, line 32 page 18, line 26 - page 19, line 2 claims 1,5-7,18-21,26-29,31	1,2,5
X	OKAI TAKASHI ET AL: "Beneficial hepatic effect of troglitazone in a patient with antimitochondrial antibody-negative primary biliary cirrhosis." THE AMERICAN JOURNAL OF GASTROENTEROLOGY. JAN 2002, vol. 97, no. 1, January 2002 (2002-01), pages 209-210, XP001193329 ISSN: 0002-9270 the whole document	1
X	WO 02/080956 A (DESREUMAUX PIERRE ; AUWERX YOHAN (FR); DHARANCY SEBASTIEN (FR)) 17 October 2002 (2002-10-17) page 1, line 12 - line 28 page 13, line 15 - page 14, line 5 page 20, line 19 - line 25 claims 1,8-10,13,17	1,5
A	GOSSET PHILIPPE ET AL: "Peroxisome proliferator-activated receptor gamma activators affect the maturation of human monocyte-derived dendritic cells" EUROPEAN JOURNAL OF IMMUNOLOGY, vol. 31, no. 10, October 2001 (2001-10), pages 2857-2865, XP001193843 ISSN: 0014-2980 abstract page 2861, column 1, paragraph 1 figure 5 page 2862, column 2, paragraph 3	1,5
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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>NISHIOJI K ET AL: "Increase of chemokine interferon - inducible protein - 10 (IP - 10) in the serum of patients with autoimmune liver diseases and increase of its mRNA expression in hepatocytes." CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (2001 FEB) 123 (2) 271-9. JOURNAL CODE: 0057202. ISSN: 0009-9104., February 2001 (2001-02), XP001193770 abstract figure 2 page 277, column 1, paragraph 3 page 278, column 1, paragraph 2</p>	1
A	<p>KRAFT MATTHIAS ET AL: "PPAR-gamma ligands potently inhibit CXC-chemokine secretion in colonic epithelial cell lines" GASTROENTEROLOGY, vol. 120, no. 5 Supplement 1, April 2001 (2001-04), page A.319, XP008032020 & 102ND ANNUAL MEETING OF THE AMERICAN GASTROENTEROLOGICAL ASSOCIATION AND DIGESTIVE DISEASE WEEK; ATLANTA, GEORGIA, USA; MAY 20-23, 2001 ISSN: 0016-5085 the whole document</p>	1
P,X	<p>TRAUNER M. ET AL: "Cholestatic syndromes." CURRENT OPINION IN GASTROENTEROLOGY, 19/3 (216-231). REFS: 273 ISSN: 0267-1379 CODEN: COGAEK, 2003, XP008031758 abstract page 223, column 2, paragraph 1</p>	1
X	<p>US 2002/019344 A1 (PERSHADSINGH HARRIHAR A) 14 February 2002 (2002-02-14) page 1, paragraph 2 page 2, paragraphs 11,12 page 2, paragraph 14 - page 3 examples 4,5 claims 1,4,7,8,10,11,20,21</p>	2,5
X	<p>US 6 369 098 B1 (PERSHADSINGH HARRIHAR A ET AL) 9 April 2002 (2002-04-09) column 20, line 54 - column 21, line 11 column 26, line 31 - line 49 examples 8,9 table IV</p>	2,5
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>BERTONI E ET AL: "High Pre-Transplant Serum Levels of CXCL10 Predict Early Renal Allograft Failure"</p> <p>TRANSPLANTATIONSMEDIZIN: ORGAN DER DEUTSCHEN TRANSPLANTATIONSGESELLSCHAFT 2003 GERMANY, vol. 15, no. 2, 2003, pages 91-96, XP008031756 ISSN: 0946-9648 abstract page 95, column 3, paragraph 2 - page 96, column 1, paragraph 5</p> <p>-----</p>	6
A	<p>ROMAGNANI P ET AL: "High expression of chemokines Interferon-gamma Inducible Protein of 10 kDa (IP-10), Monokine induced by Interferon-gamma (Mig) and of their receptor (CXCR3) in different renal diseases"</p> <p>JN JOURNAL OF NEPHROLOGY, vol. 13, no. 6, November 2000 (2000-11), page 453, XP001193776 & 41ST CONGRESS OF THE ITALIAN SOCIETY OF NEPHROLOGY; TAORMINA, ITALY; JUNE 14-JULY 17, 2000 ISSN: 1121-8428 the whole document</p> <p>-----</p>	6
A	<p>US 2002/018776 A1 (HANCOCK WAYNE W) 14 February 2002 (2002-02-14) page 1, paragraph 8 page 3, paragraph 23 page 6, paragraph 41-43 page 7, paragraph 55 - page 8, paragraph 57 page 8, paragraph 60 page 8, paragraph 68 - page 9 page 9, paragraph 77 - page 10, paragraph 80 claims 1,3,25,26,64,66</p> <p>-----</p>	2,6
A	<p>US 2001/036631 A1 (MEUER STEFAN ET AL) 1 November 2001 (2001-11-01) page 1, paragraphs 3,5,6 page 3, paragraph 34 claims 1,6,7,25</p> <p>-----</p>	6
P,X	<p>WO 03/098185 A (RENOVAR INC ; HU HUAIZHONG (US); PUCHALSKI ALICE (US); AIZENSTEIN BRIA) 27 November 2003 (2003-11-27) page 2, line 16 - page 3, line 5 page 8, line 28 - page 9, line 5 page 23, line 28 - page 24, line 3 example 1 claims 1,2,4-6</p> <p>-----</p>	6

INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	<p>ROTONDI MARIO ET AL: "High pretransplant serum levels of CXCL10 / IP 10 are related to increased risk of renal allograft failure ."</p> <p>AMERICAN JOURNAL OF TRANSPLANTATION : OFFICIAL JOURNAL OF THE AMERICAN SOCIETY OF TRANSPLANTATION AND THE AMERICAN SOCIETY OF TRANSPLANT SURGEONS, (2004 SEP) 4 (9) 1466-74. JOURNAL CODE: 100968638. ISSN: 1600-6135., September 2004 (2004-09), XP001199657 abstract</p> <p>page 1466, column 2, paragraph 3 - page 1467, column 1, paragraph 1</p> <p>page 1468, column 1, paragraph 1 - column 2, paragraph 2</p> <p>page 1469, column 2, paragraph 2</p> <p>figures 4,6</p> <p>page 1472, column 1, paragraph 3 - page 1473, column 1, paragraph 2</p> <p style="text-align: center;">-----</p>	6

INTERNATIONAL SEARCH REPORT

International application No.
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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:

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:

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.:

1-2 (entirely), 5 (partially), 6 (entirely)

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1 (entirely), 5 (partially)

Use of thiazolidinediones in the preparation of pharmaceutical preparations for the treatment of Primary Biliary Cirrhosis.

2. claims: 2 (entirely), 5 (partially), 6 (entirely)

Use of thiazolidinediones in the preparation of pharmaceutical preparations to be used in the prevention of acute and chronic rejection of kidney and pancreatic islet transplantation.

Diagnostic method for prevision of kidney transplantation rejection in which the blood levels of IP-10 of patients before transplantation are compared to the mean levels of healthy subjects.

3. claims: 3-4 (entirely), 5 (partially)

Use of thiazolidinediones in the preparation of pharmaceutical preparations for the treatment of endocrine autoimmune diseases other than Primary Biliary Cirrhosis.

INTERNATIONAL SEARCH REPORT

Information on patent family members

national Application No

T/EP2004/002069

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