



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁵ : A61K 37/02	A3	(11) International Publication Number: WO 94/17773 (43) International Publication Date: 18 August 1994 (18.08.94)
(21) International Application Number: PCT/EP94/00283 (22) International Filing Date: 1 February 1994 (01.02.94) (30) Priority Data: 93400242.9 1 February 1993 (01.02.93) EP (34) Countries for which the regional or international application was filed: GB et al. (71)(72) Applicants and Inventors: GOLDMAN, Michel [BE/BE]; Hôpital Erasme, Service d'Immunologie, Route de Lennik 808, B-1070 Brussels (BE). VELU, Thierry [BE/BE]; IRIBHN, Campus Erasme, Route de Lennik 808, B-1070 Brussels (BE). (72) Inventors; and (75) Inventors/Applicants (for US only): ABRAMOWICZ, Daniel [BE/BE]; Hôpital Erasme, Service d'Immunologie, Route de Lennik 808, B-1070 Brussels (BE). BRUYNS, Catherine [BE/BE]; IRIBHN, Campus Erasme, Route de Lennik 808, B-1070 Brussels (BE). CAPEL, Paul [BE/BE]; Hôpital Erasme, Service d'Immunologie, Route de Lennik 808, B-1070 Brussels (BE). DELVAUX, Anne [BE/BE]; IRIBHN, Campus Erasme, Route de Lennik 808, B-1070 Brussels (BE). DONCKIER, Vincent [BE/BE]; Hôpital Erasme, Service d'Immunologie, Route de Lennik 808, B-1070		Brussels (BE). GERARD, Catherine [BE/BE]; IRIBHN, Campus Erasme, Route de Lennik 808, B-1070 Brussels (BE). MARCHANT, Arnaud [BE/BE]; Hôpital Erasme, Service d'Immunologie, Route de Lennik 808, B-1070 Brussels (BE). PRADIER, Olivier [BE/BE]; Hôpital Erasme, Service d'Immunologie, Route de Lennik 808, B-1070 Brussels (BE). SCHANDENÉ, Liliane [BE/BE]; Hôpital Erasme, Service d'Immunologie, Route de Lennik 808, B-1070 Brussels (BE). WILLEMS, Fabienne [BE/BE]; Hôpital Erasme, Service d'Immunologie, Route de Lennik 808, B-1070 Brussels (BE). (74) Agents: GUTMANN, Ernest et al.; Ernest Gutmann-Yves Plasseraud S.A., 3, rue Chauveau-Lagarde, F-75008 Paris (FR). (81) Designated States: AU, BB, BG, BR, CA, CN, CZ, FI, GE, HU, JP, KP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 22 December 1994 (22.12.94)
(54) Title: USE OF PHARMACEUTICAL COMPOSITIONS COMPRISING INTERLEUKIN 10 (57) Abstract The invention relates to a use of Interleukin-10 (IL-10) or analogs or agonists thereof, for the manufacture of a medicament for the treatment or prevention of diseases involving: i) Interleukin-5 production by T-lymphocytes, or; ii) activation of T-lymphocytes through the B7/CD28 or ICAM-1/LFA-1 pathway, or; iii) activation of the procoagulant activity of monocytes; iv) severe infectious diseases involving Tumour Necrosis Factor (TNF).		

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 94/00283

A. CLASSIFICATION OF SUBJECT MATTER

IPC 5 A61K37/02

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)

IPC 5 A61K C07K

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JOURNAL OF IMMUNOLOGY., vol.150, no.2, 15 January 1993, BALTIMORE US pages 353 - 360 DEL PETRE, G. ET AL 'Human IL-10 is produced by both type 1 helper (Th1) and type 2 helper (Th2) T cell clones and inhibits their antigen-specific proliferation and cytokine production' see the whole document, especially page 358, figure 4	1, 14, 15
Y	---	2-5
Y	EP,A,0 367 596 (SCHERING CORPORATION) 9 May 1990 see the whole document ---	2-5
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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 :

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- *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

28 September 1994

Date of mailing of the international search report

16. 11. 94

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Fernandez y Branas, F

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 94/00283

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ROBERT BERKOW 'THE MERCK MANUAL OF DIAGNOSIS AND THERAPY' 1992, MERCK RESEARCH LABORATORIES, RAHWAY, N.J. see page 1229 - page 1232 ---	2-5
E	WO,A,94 04180 (SCHERING CORPORATION) 3 March 1994 see page 8, line 21 - page 9, line 22 see page 15, line 28 - page 16, line 8 see page 29, line 14 - page 30, line 8 ---	1-8,14, 15
X	IMMUNOLOGY TODAY, vol.13, no.6, 1992, CAMBRIDGE, U.K. pages 198 - 200 HOWARD, M. ET AL 'Biological properties of Interleukin 10' see page 199, right column, "potential clinical applications of IL-10" ---	1,6-8, 10-15
X	INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, vol.99, 1992, NEW YORK pages 8 - 15 H. SPITS ET AL 'Functional characterization of human IL-10' see the whole document ---	1,6-15
X	INTERNATIONAL IMMUNOLOGY, vol.4, no.12, 1992, OXFORD pages 1389 - 1397 MARIA-TERESA BEJARANO ET AL 'Interleukin 10 inhibits allogenic proliferative and cytotoxic T cell responses generated in primary mixed lymphocyte cultures' see the whole document ---	1,6-9, 14,15
X,P	WO,A,93 17698 (SCHERING CORPORATION) 16 September 1993 see page 6, line 23 - page 8, line 5 see claims 1-15 ---	1,6-8, 14,15
X,P	WO,A,93 18783 (SCHERING CORPORATION) 30 September 1993 see claim 3 see page 1, line 1 - line 26 ---	1,10-15
X,P	EUROPEAN JOURNAL OF IMMUNOLOGY, vol.23, 1993, WEINHEIM pages 2700 - 2703 PRADIER O. ET AL 'Interleukin-10 inhibits the induction of monocyte procoagulant activity by bacterial lipopolysaccharide' see the whole document ---	1,10,11, 14,15
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INTERNATIONAL SEARCH REPORT

Intern al Application No

PCT/EP 94/00283

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	JOURNAL OF EXPERIMENTAL MEDICINE, vol.177, February 1993, NEW YORK pages 547 - 550 CATHERINE GERARD ET AL 'interleukin 10 reduces the release of tumor necrosis factor and prevents lethality in experimental endotoxemia' see the whole document ---	1,10-15
X,P	EP,A,0 541 214 (SCHERING CORPORATION) 12 May 1993 see claims 1-24 see page 42, line 40 - page 44, line 50 ---	1,10-15
X	JOURNAL OF IMMUNOLOGY, vol.147, no.11, 1991, BALTIMORE pages 3815 - 3822 DAVID F. FIORENTINO ET AL 'IL-10 inhibits cytokine production by activated macrophages' see the whole document ---	1,10-15
A	WO,A,91 00349 (SCHERING CORPORATION) 10 January 1991 see the whole document ---	1-15
A	WO,A,93 00920 (SCHERING AKTIENGESELLSCHAFT) 21 January 1993 see the whole document -----	1-15

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP 94/ 00283

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.:
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 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 annex

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/210

1.- Claims 1,14,15 (partially); claims 2-5 (completely): concerning the use of Interleukin-10 (IL-10) or analogs or agonists thereof for the manufacture of a medicament for the treatment or prevention of diseases involving Interleukin-5 production by T-lymphocytes.

2.- Claims 1,14,15 (partially); claims 6-9 (completely): concerning the use of IL-10 or analogs or agonists thereof for the manufacture of a medicament for the treatment or prevention of diseases involving activation of T-lymphocytes through the B7/CD28 or ICAM/LFA-1 pathway.

3.- Claims 1,14,15 (partially); claims 10,11 (completely): concerning the use of IL-10 or analogs or agonists thereof for the manufacture of a medicament for the treatment or prevention of disease involving activation of the procoagulant activity of monocytes.

4.- Claims 1,14,15 (partially); claims 12,13 (completely): concerning the use of IL-10 or analogs or agonists thereof for the manufacture of a medicament for the treatment or prevention of diseases involving severe infectious diseases involving Tumor Necrosis Factor production.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 94/00283

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A-0367596	09-05-90	AU-B- 633034	21-01-93
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