(19) World Intellectual Property Organization

International Bureau





(43) International Publication Date 24 July 2003 (24.07.2003)

PCT

(10) International Publication Number WO 2003/059387 A3

(51) International Patent Classification⁷: A61K 39/395, 38/21, 38/00 // (A61K 39/395, 38:21) (A61K 39/395, 38:00)

(21) International Application Number:

PCT/US2002/040851

(22) International Filing Date:

19 December 2002 (19.12.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/342,939 21 December 2001 (21.12.2001) US 60/387,795 11 June 2002 (11.06.2002) US 60/319,531 6 September 2002 (06.09.2002) US

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier applications:

US 60/342,939 (CON)
Filed on 21 December 2001 (21.12.2001)
US 60/387,795 (CON)
Filed on 11 June 2002 (11.06.2002)
US 60/319,531 (CON)
Filed on 6 September 2002 (06.09.2002)

(71) Applicant (for all designated States except US): ILEX ONCOLOGY, INC. [US/US]; 4545 Horizon Hill Boulevard, San Antonio, TX 78229-2263 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): SHAKED, Ze'ev

[US/US]; 20 Arnold Palmer Drive, San Antonio, TX 78257 (US). **BRYCE, Richard, P.** [GB/US]; 27565 Woodlawn Green, Borne, TX 78015 (US). **FONG, Sonny, B.** [CA/US]; 604 Pilon, Lasalle, Quebec H8P 3N3 (CA).

(74) Agent: HIGHLANDER, Steven, L.; Fulbright & Jaworski L.L.P., Suite 2400, 600 Congress Avenue, Austin, TX 78701 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

with international search report

(88) Date of publication of the international search report: 17 June 2004

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: COMBINATION COMPRISING ANTI-CD52 ANTIBODIES AND OTHER THERAPEUTIC AGENTS FOR TREATMENT FOR MULTIPLE SCLEROSIS

(57) Abstract: The present invention provides for the treatment of multiple sclerosis by combination therapies of CD52 specific antibodies, such as CAMPATH-1H, with either a Type 1 interferon or coploymer-1.



Interna Application No PCT/US 02/40851

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K39/395 A61K38/21 (A61K39/395,38:00)

A61K38/00

//(A61K39/395,38:21),

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

 $\begin{array}{ccc} \text{Minimum documentation searched} & \text{(classification system followed by classification symbols)} \\ \text{IPC} & 7 & \text{A61K} & \text{C07K} \end{array}$

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)

EMBASE, EPO-Internal, BIOSIS, WPI Data, PAJ

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
Y	WO 93 10817 A (HALE GEOFFREY ;WALDMANN HERMAN (GB)) 10 June 1993 (1993-06-10) claims	1–13	
Y	LEARY S M ET AL: "Current management of multiple sclerosis" INTERNATIONAL JOURNAL OF CLINICAL PRACTICE 2000 UNITED KINGDOM, vol. 54, no. 3, 2000, pages 161-169, XP008018314 ISSN: 1368-5031 page 162 page 163, right-hand column, paragraph 6 /	1–13	

Y 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	Daté of mailing of the international search report
18 June 2003	30/06/2003
Name and mailing address of the ISA	Authorized officer
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	COVONE-VAN HEES, M

Interna Application No
PCT/US 02/40851

=		PCT/us 02/40851			
C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT					
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.			
A	DHIB-JALBUT S ET AL: "Comparative effects of interferon - consensus 1, interferon - alpha 2a, and interferon -beta 1b on HLA expression and lymphoproliferation: a preclinical model for treatment of multiple sclerosis" JOURNAL OF INTERFERON AND CYTOKINE RESEARCH, MARY ANN LIEBERT, NEW YORK, NY, US, vol. 16, no. 3, 1 March 1996 (1996-03-01), pages 195-200, XP002081554 ISSN: 1079-9907 the whole document	1-13			
A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1 March 2000 (2000-03-01) NJENGA M KARIUKI ET AL: "Short-term treatment with interferon-alpha/beta promotes remyelination, whereas long-term treatment aggravates demyelination in a murine model of multiple sclerosis." Database accession no. PREV200000173279 XP002244684 abstract & JOURNAL OF NEUROSCIENCE RESEARCH., vol. 59, no. 5, 1 March 2000 (2000-03-01), pages 661-670, ISSN: 0360-4012	1-13			
A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1999 COLES ALASDAIR J ET AL: "Monoclonal antibody treatment exposes three mechanisms underlying the clinical course of multiple sclerosis." Database accession no. PREV199900491069 XP002244685 abstract & ANNALS OF NEUROLOGY, vol. 46, no. 3, 1999, pages 296-304, ISSN: 0364-5134	1–13			

tional application No. 1'CT/US 02/40851

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. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 113 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 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.

Interna upplication No
PCT/US 02/40851

Patent document cited in search report	Publication date		Patent family member(s)	Publication date
WO 9310817 A	10-06-1993	AT	177011 T	15-03-1999
		ΑU	3089692 A	28-06-1993
		CA	2124964 A1	10-06-1993
		DE	69228556 D1	08-04-1999
		DE	69228556 T2	08-07-1999
		DK	616537 T3	27-09-1999
		EP	0616537 A1	28-09-1994
		ES	2128363 T3	16-05-1999
		WO	9310817 A1	10-06-1993
		GR	3029683 T3	30-06-1999
		HK	1011618 A1	28-04-2000
		IL	103981 A	13-07-1997
		JP	3383303 B2	04-03-2003
		JP	7504888 T	01-06-1995
		KR	271333 B1	01-11-2000
		MX	9207032 A1	01-07-1993
		US	6120766 A	19-09-2000
		ZA	9209446 A	19-08-1993