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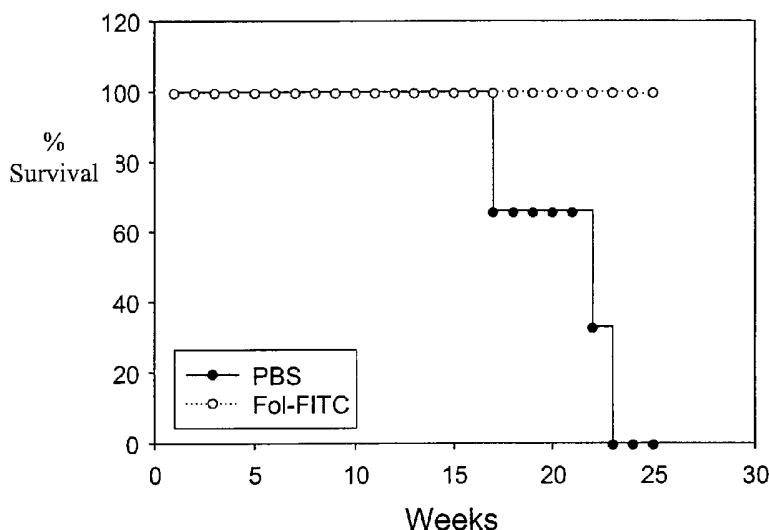
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60/468,330 6 May 2003 (06.05.2003) US
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- (72) Inventors; and
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- (74) Agent: **ADDISON, Bradford, G.**; Barnes & Thornburg, 11 South Meridian Street, Indianapolis, IN 46204 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, 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, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,

[Continued on next page]

(54) Title: TREATMENT OF LUPUS TARGETING THE MACROPHAGES OR THE FOLATE RECEPTOR



(57) Abstract: The invention relates to a method of treating lupus erythematosus. In one embodiment, the method comprises the step of administering to a patient suffering from lupus erythematosus an effective amount of a composition comprising a conjugate or complex of the general formula L-X where the group L comprises a ligand capable of binding to activated macrophages or other stimulated immune cells, and the group X comprises an immunogen, a cytotoxin, or another compound capable of altering macrophage function. In another embodiment, the method comprises the step of administering to a patient suffering from lupus erythematosus an effective amount of a composition comprising a conjugate of the general formula L-X where the group L comprises a vitamin, or a vitamin-receptor binding analog or derivative thereof, and the group X comprises an immunogen, a cytotoxin, or another compound capable of altering macrophage function.

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CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, 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, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, 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, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, 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, NA, NI, NO, NZ,

OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, 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, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/014097

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K47/48 A61P37/00 A61K51/04

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

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)

EP0-Internal, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/087424 A (TURK MARY JO ; LOW PHILIP STEWART (US)) 7 November 2002 (2002-11-07) page 1 figure 4; examples 1-8,11 -----	1-8
X	WO 99/41285 A (MEDAREX INC) 19 August 1999 (1999-08-19) page 48, line 3 - line 23 examples iI,II,IV,VI -----	1,4
X	WO 96/36367 A (PURDUE RESEARCH FOUNDATION) 21 November 1996 (1996-11-21) examples claims ----- -/--	1-3,5-8

☒ 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

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Date of mailing of the international search report

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Name and mailing address of the ISA

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Dullaart, A

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/014097

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	REDDY J A ET AL: "FOLATE-MEDIATED TARGETING OF THERAPEUTIC AND IMAGING AGENTS TO CANCERS" CRITICAL REVIEWS IN THERAPEUTIC DRUG CARRIER SYSTEMS, vol. 15, no. 6, 1998, pages 587-627, XP000901554 ISSN: 0743-4863 abstract page 594, paragraph V - page 602; table 4 -----	1-3,5-8
X	WO 01/74382 A (PURDUE RESEARCH FOUNDATION) 11 October 2001 (2001-10-11) examples -----	1-8
X	NAKASHIMA-MATSUSHITA N ET AL: "Selective expression of folate receptor beta and its possible role in methotrexate transport in synovial macrophages from patients with rheumatoid arthritis" ARTHRITIS AND RHEUMATISM, LIPPINCOTT, PHILADELPHIA, US, vol. 42, no. 8, August 1999 (1999-08), pages 1609-1616, XP002284073 ISSN: 0004-3591 abstract -----	1-3,5-8
X	TURK M J ET AL: "Folate-targeted imaging of activated macrophages in rats with adjuvant-induced arthritis" ARTHRITIS AND RHEUMATISM, LIPPINCOTT, PHILADELPHIA, US, vol. 46, no. 7, July 2002 (2002-07), pages 1947-1955, XP004536129 ISSN: 0004-3591 the whole document -----	1-3,5-8
X	WO 98/58678 A (DEN HARTOG MARCEL THEODORUS ; BOER MARK DE (NL); PANGENETICS B V (NL)) 30 December 1998 (1998-12-30) page 3 examples claims 14-16 -----	1,4
P,X	WO 03/092742 A (LEAMON CHRISTOPHER PAUL ; ENDOCYTE INC (US); PARKER MATTHEW A (US)) 13 November 2003 (2003-11-13) cited in the application example 3 -----	1-3,5-8

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/014097

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.:
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: 1-3 in part, and 5

Use of a conjugate as claimed in the manufacture of a medicament for treating lupus erythematosus, wherein the group L is a folate, and group X is an immunogen.

2. claims: 1-3 in part, and 6-7

Use of a conjugate as claimed in the manufacture of a medicament for treating lupus erythematosus, wherein the group L is a folate, and group X is a cytotoxin.

3. claims: 1-3 in part, and 8

Use of a conjugate as claimed in the manufacture of a medicament for treating lupus erythematosus, wherein the group L is a folate, and group X is a cytokine.

4. claims: 1 in part, and 4

Use of a conjugate as claimed in the manufacture of a medicament for treating lupus erythematosus, wherein the group L is an antibody or an antibody fragment.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/014097

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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