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(72) Inventors; and

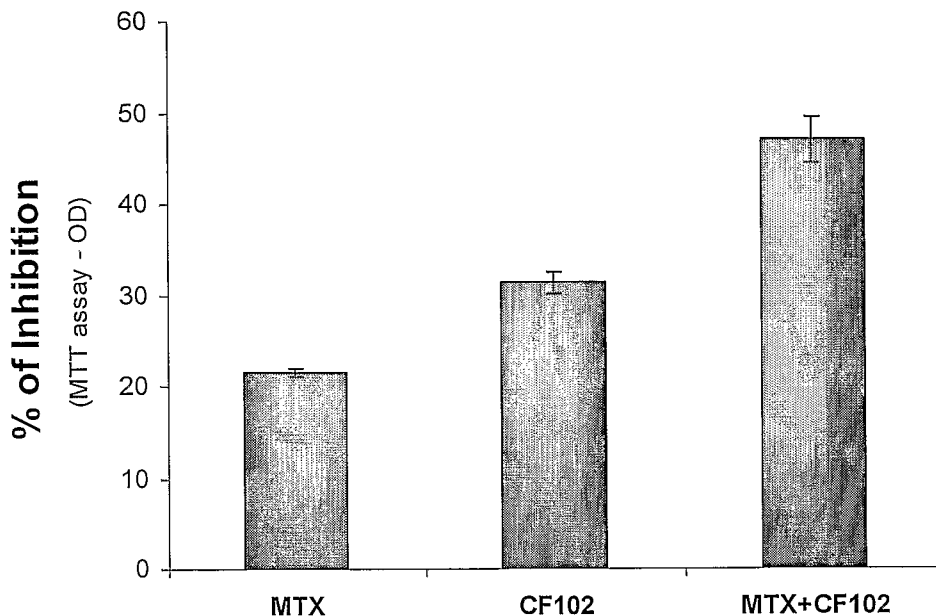
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[Continued on next page]

(54) Title: USE OF A COMBINATION OF METHOTREXATE AND AN A3AR AGONIST FOR THE TREATMENT OF CANCER



(57) Abstract: The therapeutic treatment of cancer by a combined administration of methotrexate and an agonist of the A3 adenosine receptor. Provided are pharmaceutical compositions comprising such a combined administration useful in the therapeutic treatment of cancer as well as the use of any of these active agents for preparing such a pharmaceutical composition.

WO 2008/023362 A3



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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/519 A61K31/52 A61K45/06 A61P35/00

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)
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, BIOSIS, EMBASE, SCISEARCH, 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.
X	WO 2006/059328 A (CAN FITE BIOPHARMA LTD [IL]; FISHMAN PNINA [IL]; BAR-YEHUDA SARA [IL]) 8 June 2006 (2006-06-08) page 3, paragraph 7 page 4, paragraph 3 page 5, paragraph 1 page 6, paragraphs 1,2 page 15, paragraph 2 claims 1-8,11-19,22,23,26-33 ----- -/--	1-44

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
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- *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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Cielen, Elsie

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.
Y	<p>WO 01/19360 A (CAN FITE TECHNOLOGIES LTD [IL]; FISHMAN PNINA [IL] CAN FITE BIOPHARMA) 22 March 2001 (2001-03-22) page 3, line 26 - page 4, line 6 page 6, lines 3-11,17-20,26-29 page 7, lines 13-20 page 9, line 19 - page 10, line 2 page 13, line 13 - page 14, line 3 page 22, lines 10-24 page 23, lines 13-17 page 23, line 26 - page 24, line 22 page 30, lines 11-24 examples 2,5-8 claims 7,27-29,31,33,34,56-61,68-71</p>	1-44
Y	<p>US 2004/229246 A1 (FISHMAN PNINA [IL] ET AL) 18 November 2004 (2004-11-18) page 1, paragraph 10 page 3, paragraphs 32,33,41 examples 3,4,8,9 claims 1,2,8-10</p>	1-44
Y	<p>JOSHI BHALCHANDRA V ET AL: "Purine derivatives as ligands for A(3) adenosine receptors" CURRENT TOPICS IN MEDICINAL CHEMISTRY, vol. 5, no. 13, 2005, pages 1275-1295, XP008089968 ISSN: 1568-0266 abstract page 1276, column 2, paragraph 2 figure 3; compounds 10-11 page 1282, column 2, paragraph 2 figure scheme13; compound 88 figures 4,scheme15; compound 91 page 2190, column 1, last paragraph - column 2, paragraph 1 table 1; compounds 10,11,88,91</p>	1-10, 16-23, 30-32, 34-42
Y	<p>WO 2004/038006 A (US GOVERNMENT [US]; EWHA WOMANS UNIVERSITY [KR]; JEONG LAK SHIN [KR];) 6 May 2004 (2004-05-06)</p> <p>pages 3-4, paragraph 7-9 page 5, paragraph 17 - page 6, paragraph 18 page 21, paragraph 47 page 22, paragraph 54-57 page 42, paragraphs 127,128 pages 45-46, paragraph 133 table 4; compound 36 claims 6,7,11-14</p>	1-6, 10-12, 16-20, 24-26, 30-36, 40-44

INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2007/001009

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>WO 2006/031505 A (UMAN SERVICES ENDED BY THE SEC [US]; JACOBSON KENNETH A; JOSHI BHALCHA) 23 March 2006 (2006-03-23)</p> <p>page 2, paragraph 7 page 17, paragraph 68 pages 23-24, paragraph 93 page 25, paragraph 99 table 1; compounds 16,5 claims 1,7,19,20,55</p>	1-6, 16-20, 30,31, 34-36,40
Y	<p>PARFITT, K.: "Martindale, The complete drug reference, Thrity-second edition" 1999. PHARMACEUTICAL PRESS, LONDON, UK, XP002478059</p> <p>page 547, column 1 - page 551, column 3, paragraph 1</p>	1-17, 24-34, 40-44
A	<p>WO 2006/034190 A (INOTEK PHARMACEUTICALS CORP [US]; JAGTAP PRAKASH [US]; SALZMAN ANDREW) 30 March 2006 (2006-03-30)</p> <p>page 62, lines 9-34 page 69, lines 11-29 page 71, line 19 - page 75; line 11 page 77, line 26 - page 78, last line example 10 claims 1,31,49</p>	1-5, 10-19, 24-35, 40-43
P,Y	<p>FISHMAN P ET AL: "The anti-cancer effect of A3 adenosine receptor agonists: A novel, targeted therapy" IMMUNOLOGY, ENDOCRINE AND METABOLIC AGENTS IN MEDICINAL CHEMISTRY 200708 NL, vol. 7, no. 4, August 2007 (2007-08), pages 298-303; XP008089962 ISSN: 1871-5222 abstract page 300, column 1, paragraph 1 - column 2, last paragraph figure 1 page 301, column 1, paragraph 2 table 1 page 301, column 2, paragraph 5 - page 302, column 1, paragraph 2</p>	1-44

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL2007/001009

Box No. 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 1-29 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 No. 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 fees, this Authority did not invite payment of additional fees.
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 and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IL2007/001009

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