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(71) Applicant (*for all designated States except US*): INSTITUTE OF EXPERIMENTAL BOTANY ASCR [CZ/CZ]; Slechtitelu 11, 783 71 Olomouc (CZ).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): FUKSOVA, Kveta [CZ/CZ]; Navigátoru 605, 161 00 Praha 6 (CZ). HAVLICEK, Libor [CZ/CZ]; Vrutecka 2766, 141 04 Praha 4 (CZ). KRYSTOF, Vladimir [CZ/CZ]; Krizikova 10, 702 00 Ostrava (CZ). LENOBEL, Rene [CZ/CZ]; Ostravska 695, 738 02 Frydek Mistek (CZ). STRNAD, Miroslav [CZ/CZ]; Zapadni 25, 779 00 Olomouc (CZ).

(74) Agent: CLYDE-WATSON, Zöe; D Young & Co, 21 New Fetter Lane, London EC4A 1DA (GB).

Declaration under Rule 4.17:

— of inventorship (Rule 4.17(iv)) for US only

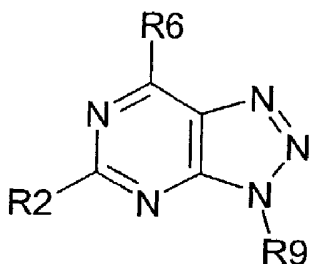
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: AZAPURINE DERIVATIVES



(I)

(57) Abstract: The present invention relates to a compound of formula (I), or a pharmaceutically acceptable acid salt thereof. The invention further relates to the use of said compounds in the treatment of hyperproliferative skin disorders, viral infections, cancer, rheumatoid arthritis, lupus, type I diabetes, multiple sclerosis, restenosis, polycystic kidney disease, graft rejection, graft versus host disease and gout, or for psoriasis, parasitoses such as those caused by fungi or protists, or Alzheimer's disease. Further aspects of the invention relate to the use of such compounds in the inhibition of cell proliferation, in the induction of apoptosis, to modulate the activity of adrenergic and/or purinergic receptors or to suppress immunostimulation. The invention also relates to the use of 2,6,9-trisubstituted 8-azapurines in maintaining mammalian oocytes at the germinal vesicle stage.

INTERNATIONAL SEARCH REPORT

International Application No.
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A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K31/505 C07D487/04 A61P3/10 A61P9/00 A61P25/00 A61P31/12 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) IPC 7 A61K A61P C07D														
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, PAJ, WPI Data, CHEM ABS Data, BEILSTEIN Data														
C. DOCUMENTS CONSIDERED TO BE RELEVANT <table border="1"> <thead> <tr> <th>Category *</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X</td> <td>WO 97/20842 A (CENTRE NAT RECH SCIENT ; MEIJER LAURENT (FR); BISAGNI EMILE (FR); LEGR) 12 June 1997 (1997-06-12) olomoucine; claims and examples -----</td> <td>1-47</td> </tr> <tr> <td>X</td> <td>US 5 866 702 A (LUM ROBERT T ET AL) 2 February 1999 (1999-02-02) claims and examples; table 3 (see certificate of correction) -----</td> <td>1-47</td> </tr> <tr> <td>X</td> <td>EP 1 142 893 A (PENN STATE RES FOUNDATION INC ; ARCH DEV CORP (US); US OF AMERICA (US)) 10 October 2001 (2001-10-10) cpds. 8a-b claims 4-6 ----- -/--</td> <td>1-12</td> </tr> </tbody> </table>			Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X	WO 97/20842 A (CENTRE NAT RECH SCIENT ; MEIJER LAURENT (FR); BISAGNI EMILE (FR); LEGR) 12 June 1997 (1997-06-12) olomoucine; claims and examples -----	1-47	X	US 5 866 702 A (LUM ROBERT T ET AL) 2 February 1999 (1999-02-02) claims and examples; table 3 (see certificate of correction) -----	1-47	X	EP 1 142 893 A (PENN STATE RES FOUNDATION INC ; ARCH DEV CORP (US); US OF AMERICA (US)) 10 October 2001 (2001-10-10) cpds. 8a-b claims 4-6 ----- -/--	1-12
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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 : *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. *Z* document member of the same patent family														
Date of the actual completion of the international search 1 March 2004		Date of mailing of the international search report 12/03/2004												
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 Stroeter, T												

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International Publication 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	US 6 107 301 A (ALDRICH PAUL EDWARD ET AL) 22 August 2000 (2000-08-22) tables 16, 19 and 21, e.g. cpds. 592, 637, 638, 640, 1120 claims 4-7 -----	1-12
X	WO 99/41254 A (ASTRA PHARMA PROD ; BROWN ROGER (GB); WILLIS PAUL (GB); THOM STEPHEN ()) 19 August 1999 (1999-08-19) examples, e.g. ex. 90, 91; claims -----	1-12
X	WO 99/05143 A (ASTRA PHARMA PROD ; GUILLE SIMON (GB); WILLIS PAUL (GB); INGALL ANTHONY) 4 February 1999 (1999-02-04) claims, various examples, e.g. ex. 82 or 102ff (page 113) -----	1-12
X	PATENT ABSTRACTS OF JAPAN vol. 0081, no. 62 (C-235), 26 July 1984 (1984-07-26) & JP 59 062595 A (ESUESU SEIYAKU KK), 10 April 1984 (1984-04-10) formulae (I), (I-3), (I-4), (I-5), (II) and (VII) abstract -----	1-12
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X	WO 97/35846 A (DU PONT MERCK PHARMA) 2 October 1997 (1997-10-02) citations on: page 11, line 15 - page 12, line 15 -----	1-12
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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	SHEALY Y. F. ET AL: "v-Triazolo'4,5-d!pyrimidines. I." JOURNAL OF ORGANIC CHEMISTRY, vol. 26, 1961, pages 4433-4440, XP002271921 cpds. of tab. 1, e.g. VIa - XII, XV - XVII -----	1-12
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X	CHORVAT R J ET AL: "SYNTHESIS, CORTICOTROPIN-RELEASING FACTOR RECEPTOR BINDING AFFINITY AND PHARMACOKINETIC PROPERTIES OF TRIAZOLO-, IMIDAZO- AND PYRROLOPYRIMIDINES AND -PYRIDINES" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 42, no. 5, 11 March 1999 (1999-03-11), pages 833-848, XP001093941 ISSN: 0022-2623 cpds. 3, 4s, 4an (tab. 3) -----	1-12
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 03/04188

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.: 1,2
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 14-24 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.: 1,2
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:
see FURTHER INFORMATION sheet PCT/ISA/210
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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 14-24 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.

Continuation of Box I.2

Claims Nos.: 1,2

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty for claims 1 and 2. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claim(s) is impossible. Consequently, the search has been restricted to those compounds of claims 1 (or 2) wherein R6 is as defined in claim 3 (R6 = X-R6' = N(substituted arylalkyl)-R6') or in claim 4 (R6 = X-R6' = X-aryl). All further claims are consequently based on the compounds of formula I so defined.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

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