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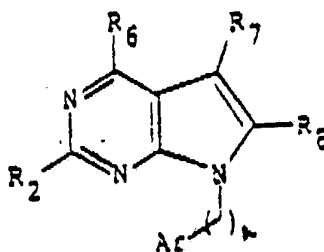
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International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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| <p>(51) International Patent Classification<sup>4</sup> :<br/>C07D 487/04, A61K 31/505<br/>C07D 239/42 // (C07D 487/04<br/>C07D 239:00, 209:00)</p>  | <p>A3</p>  | <p>(11) International Publication Number: <b>WO 88/ 03142</b><br/>(43) International Publication Date: 5 May 1988 (05.05.88)</p> |
| <p>(21) International Application Number: PCT/US87/02727<br/>(22) International Filing Date: 19 October 1987 (19.10.87)<br/>(31) Priority Application Numbers: 923,521<br/>086,231<br/>(32) Priority Dates: 24 October 1986 (24.10.86)<br/>20 August 1987 (20.08.87)<br/>(33) Priority Country: US<br/>(60) Parent Applications or Grants<br/>(63) Related by Continuation<br/>US 923,521 (CON)<br/>Filed on 24 October 1986 (24.10.86)<br/>US 086,231 (CON)<br/>Filed on 20 August 1987 (20.08.87)<br/>(71) Applicant (for all designated States except US): WARNER-LAMBERT COMPANY [US/US]; 2800 Plymouth Road, Ann Arbor, MI 48105 (US).<br/>(72) Inventors; and<br/>(75) Inventors/Applicants (for US only) : MALONE, Thomas, C. [US/US]; 42337 Carriage Cove Circle, Canton, MI 48187 (US). SIRCAR, Jagadish, C. [US/US]; 3615 Charter Place, Ann Arbor, MI 48105 (US).</p> | <p>(74) Agents: THIERSTEIN, Joan; Warner-Lambert Company, 2800 Plymouth Road, Ann Arbor, MI 48105 (US) et al.<br/>(81) Designated States: AT (European patent), AU, BB, BE (European patent), BG, BJ (OAPI patent), BR, CF (OAPI patent), CG (OAPI patent), CH (European patent), CM (OAPI patent), DE (European patent), DK, FI, FR (European patent), GA (OAPI patent), GB (European patent), HU, IT (European patent), JP, KP, KR, LK, LU (European patent), MC, MG, ML (OAPI patent), MR (OAPI patent), MW, NL (European patent), NO, RO, SD, SE (European patent), SN (OAPI patent), SU, TD (OAPI patent), TG (OAPI patent), TS, TT<br/><b>Published</b><br/><i>With international search report.</i><br/><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><br/>(88) Date of publication of the international search report: 19 May 1988 (19.05.88)</p> |  |

(54) Title: 7-DEAZAGUANINES AS IMMUNOMODULATORS



(I)

(57) Abstract

Various 7-deazaguanines of formula (I), wherein R<sub>6</sub> is OH or SH, R<sub>2</sub> is hydrogen or NH<sub>2</sub>, R<sub>7</sub> and R<sub>8</sub> are hydrogen or NH<sub>2</sub>, n is an integer of from one through four, Ar is (i) phenyl unsubstituted or substituted by halogen, trifluoromethyl, alkyl, hydroxy or alkoxy, (ii) 2- or 3-thienyl, or (iii) 2- or 3-furanyl; having activity as immunomodulators. Also included are pharmaceutical compositions and methods of use thereof.

**FOR THE PURPOSES OF INFORMATION ONLY**

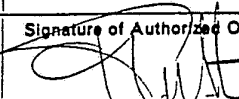
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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 87/02727

|  |   |                                     |
|--|---|-------------------------------------|
| <b>I. CLASSIFICATION OF SUBJECT MATTER</b> (if several classification symbols apply, indicate all) <sup>6</sup>  |   |                                     |
| According to International Patent Classification (IPC) or to both National Classification and IPC<br><sup>4</sup> C 07 D 487/04; A 61 K 31/505; C 07 D 239/42; //(C 07 D 487/04, IPC : 239:00,209:00)  |   |                                     |
| <b>II. FIELDS SEARCHED</b>   |   |                                     |
| Minimum Documentation Searched <sup>7</sup>  |   |                                     |
| Classification System  | Classification Symbols  |                                     |
| IPC <sup>4</sup>   | C 07 D 487/00; A 61 K 31/00; C 07 D 239/00  |                                     |
| Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched <sup>8</sup>   |   |                                     |
|  |   |                                     |
| <b>III. DOCUMENTS CONSIDERED TO BE RELEVANT <sup>9</sup></b>   |   |                                     |
| Category <sup>9</sup>  | Citation of Document, <sup>11</sup> with indication, where appropriate, of the relevant passages <sup>12</sup>  | Relevant to Claim No. <sup>13</sup> |
| X  | Tetrahedron Letters, volume 26, no. 16, 1985, Pergamon Press Ltd (GB)<br>M. Legraverend et al.: "A new route to 7-deazaguanine derivatives", pages 2001-2002, see compound 10a cited in the application<br>-- | 1                                   |
| A  | EP, A, 0156559 (WARNER-LAMBERT) 2 October 1985, see claim 1; page 7, lines 11,12; page 8<br>--  | 1,7                                 |
| A  | FR, A, 2574407 (RHONE-POULENC) 13 June 1986, see claim 1; page 5, lines 26-31<br>-----  | 1,7                                 |
| <p><sup>10</sup> * Special categories of cited documents:</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> <p>"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</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"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.</p> <p>"&amp;" document member of the same patent family</p> |   |                                     |
| <b>IV. CERTIFICATION</b>   |   |                                     |
| Date of the Actual Completion of the International Search  | Date of Mailing of this International Search Report   |                                     |
| 16th February 1988   | 26 APR 1988   |                                     |
| International Searching Authority  | Signature of Authorized Officer   |                                     |
| EUROPEAN PATENT OFFICE   | <br><b>P.C.G. VAN DER PUTTEN</b>  |                                     |

## FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

V.  OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE <sup>1</sup>

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1.  Claim numbers 8, 9, because they relate to subject matter not required to be searched by this Authority, namely:  
See PCT-Rule 39.1 (iv): methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.
2.  Claim numbers ....., 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.  Claim numbers ....., because they are dependent claims and are not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).

VI.  OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING <sup>2</sup>

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 of the international application.
2.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:
3.  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 claim numbers:
4.  As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

## Remark on Protest

- The additional search fees were accompanied by applicant's protest.
- No protest accompanied the payment of additional search fees.

ANNEX TO THE INTERNATIONAL SEARCH REPORT  
ON INTERNATIONAL PATENT APPLICATION NO.

US 8702727

SA 19649

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 18/04/88. The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

| Patent document cited in search report | Publication date | Patent family member(s)         | Publication date     |
|--|------------------|---------------------------------|----------------------|
| EP-A- 0156559                          | 02-10-85         | AU-A- 4021985<br>JP-A- 60248690 | 03-10-85<br>09-12-85 |
| FR-A- 2574407                          | 13-06-86         | None                            |                      |