C07D 239/28

(21) International Application Number: PCT/US03/03022

(22) International Filing Date: 31 January 2003 (31.01.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/353,333 1 February 2002 (01.02.2002) US
60/353,267 1 February 2002 (01.02.2002) US
60/399,673 27 July 2002 (29.07.2002) US

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier application:
US 60/353,333 (CIP)
Filed on 1 February 2002 (01.02.2002)

(71) Applicant (for all designated States except US): RIGEL PHARMACEUTICALS, INC. [US/US]; 240 East Grand Avenue, South San Francisco, CA 94080 (US).

(72) Inventors: and


Declaration under Rule 41.7:
— as to applicant’s entitlement to apply for and be granted a patent (Rule 41.7(ii)) for the following designations 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, LI, 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, SI, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, 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, HU, IE, IT, LI, LV, LT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BI, 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:
4 December 2003

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: 2,4-PYRIMIDINEDIAMINE COMPOUNDS AND THEIR USES

(57) Abstract: The present invention provides 2,4-pyrimidinediamine compounds that inhibit the IgE and/or IgG receptor signaling cascades that lead to the release of chemical mediators, intermediates and methods of synthesizing the compounds and methods of using the compounds in a variety of contexts, including in the treatment and prevention of diseases characterized by, caused by or associated with the release of chemical mediators via degranulation and other processes effected by activation of the IgE and/or IgG receptor signaling cascades.
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**
- IPC(7) : A61K 31/505; C07D 239/28.

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)
- U.S. : 514/275; 544/323, 325, 332

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 practicable, search terms used)
- CAS ON-LINE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

<table>
<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>JP 03-127790 A (MORISHITA PHARM., CO., LTD.) 30 May 1991 (30.05.1991), column 11, compound #4, and column 21, compound #80.</td>
<td>8, 37, 46 10-15, 38-42</td>
</tr>
<tr>
<td>X</td>
<td>WO 02/004429 A1 (ASTRAZENECA AB) 17 January 2002 (17.01.2002), page 38, compounds #5-10.</td>
<td>8, 37, 46 10-15, 38-42</td>
</tr>
<tr>
<td>A</td>
<td>GB 2,373,186 A (ASTRAZENECA AB) 18 September 2002 (18.09.2002), page 36, Examples 77-81</td>
<td>8, 37, 46 10-15, 38-42</td>
</tr>
</tbody>
</table>

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 application or patent published on or after the international filing date, and before the priority date claimed
  - "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 principles 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: 21 July 2003 (21.07.2003)

Date of mailing of the international search report: 25 AUG 2003

Authorized officer: [Signature]

Mukund Shah

Telephone No. 703-308-1235

Form PCT/ISA/210 (second sheet) (July 1998)
**INTERNATIONAL SEARCH REPORT**

**Box I** Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

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

1. □ Claim Nos.:
   because they relate to subject matter not required to be searched by this Authority, namely:

2. ✗ Claim Nos.: 1-7, 33, 36, 45 and 47-71
   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:
   Please See Continuation Sheet

3. ✗ Claim Nos.: 9, 16-34
   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.

Form PCT/ISA/210 (continuation of first sheet(1)) (July 1996)
Continuation of Box I Reason 2:
Claim 1 recites $L^1$ and $L^2$ as a "linker" which embraces a broad range of moieties, functional groups, and rings. Said claim also recites "electronegative group" for $R^5$ and $R^6$ which covers practically all moieties and functional groups in the field of organic chemistry. An on-line search for the claimed formula (I) would yield an incomplete search. Thus, no meaningful search can be carried out. Furthermore, claim 1 recites provisos that exclude quite a number of compounds. Thus, the metes and bounds of the claimed genus cannot be determined for a meaningful search. Claims 2-7, 35, 36, 45, and 47-71 are dependent on claim 1 for the definition of $L^1$ and $L^2$ as well as $R^5$ and $R^6$. Therefore, said claims are also unsearchable.