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GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
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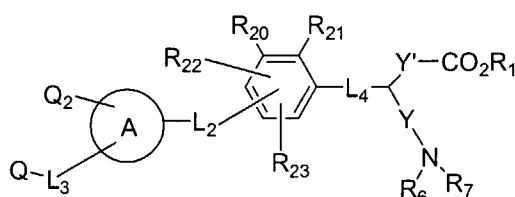
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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: SUBSTITUTED AMINO CARBOXYLIC ACIDS AS INHIBITORS OF PROTEIN TYROSINE PHOSPHATASE-1B



(57) Abstract: Disclosed are compounds and pharmaceutically acceptable salts of formula (I): which are useful in the treatment of metabolic disorders related to insulin resistance, leptin resistance, or hyperglycemia. Compounds of the invention include inhibitors of Protein tyrosine phosphatases, in particular Protein tyrosine phosphatase-1B (PTP-1B), that are useful in the treatment of diabetes and other PTP mediated diseases, such as cancer, neurodegenerative diseases and the like. Also disclosed are pharmaceutical compositions comprising compounds of the

invention and methods of treating the aforementioned conditions using such compounds.



WO 2004/099171 A3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/013700

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D307/91 C07D209/08 C07D405/12 C07D307/79 C07D239/26
 C07D317/56 C07C323/59 C07D333/76 C07D307/81 C07D417/04
 C07D405/04 A61K31/343 A61P3/10

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 C07D C07C

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, CHEM ABS Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 232 322 B1 (MALAMAS MICHAEL S ET AL) 15 May 2001 (2001-05-15) column 7, lines 54-60 columns 18-22; claim 1; examples 44,45 -----	1-20
X	MALAMAS M S ET AL: "Novel Benzofuran and Benzothiophene Biphenyls as Inhibitors of Protein Tyrosine Phosphatase 1B with Antihyperglycemic Properties" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 43, 2000, pages 1293-1310, XP002216395 ISSN: 0022-2623 page 1300; compounds 109,110 ----- -/--	1-20



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
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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
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- *G* document member of the same patent family

Date of the actual completion of the international search

15 October 2004

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/013700

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 5 968 980 A (FUJIMURA KEN-ICHI ET AL) 19 October 1999 (1999-10-19) column 16, lines 7-15; claim 1 -----	1-20
X	WO 99/36393 A (TANABE SEIYAKU CO ; MARTIN RICHARD (US); SIRCAR ILA (US); GUDMUNDSSON) 22 July 1999 (1999-07-22) page 78; compounds 38-42 page 121; example 216 page 122; example 220 page 155; examples 348-350 -----	1-20
X	WO 01/12183 A (HAGMANN WILLIAM K ; CHANG LINDA L (US); YANG GINGER X (US); DOHERTY GE) 22 February 2001 (2001-02-22) page 17; compound 20 page 20; compound 6 claim 1; example 85 -----	1-20
X	DATABASE CAPLUS CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; XP002300704 Database accession no. 1997:440050 compounds 191426-69-4, 191426-73-0, 191426-77-4 & JP 09 118662 A (FUJISAWA PHARMACEUT CO LTD) 6 May 1997 (1997-05-06) -----	1-20

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/013700

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.:

1-14, 18-20 (all part)

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: 1-14,18-20(all part)

Compounds according to claim 1 in which L4 is
-(C1-C6)alkyl-.

2. claims: 1-20(all part)

Compounds according to claim 1 in which L4 is
-S(O)u-(C1-C4)alkyl- or -(C1-C4)alkyl-S(O)u-(C1-C4)alkyl-.

3. claims: 1-6,18,19(all part)

Compounds according to claim 1 in which L4 is -C2-C6
alkenyl-.

4. claims: 1-6,18-20(all part)

Compounds according to claim 1 in which -C1-C6 alkyl-O-C1-C6
alkyl-, -O-C1-C6 alkyl-, or -C1-C6 alkyl-O-.
