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7 September 2007

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: USE OF TYROSINE KINASE INHIBITORS IN THE TREATMENT OF METABOLIC DISORDERS

(57) Abstract: The present invention relates to the use of c-Abl-, PDGF-R-, c-kit-, or ARG-tyrosine kinase inhibitors, or pharmaceutically acceptable salts thereof, for the treatment, amelioration, and diagnosis of disorders associated with aberrant expression of adipocyte-specific peptide hormone in a patient, e.g., metabolic disorders, e.g., type I diabetes or type II diabetes, and for the manufacture of pharmaceutical compositions for the treatment, amelioration, and diagnosis of disorders associated with aberrant expression of adipocyte-specific peptide hormone in a patient. Examples of c-Abl-, PDGF-R-, c-kit-, or ARG-tyrosine kinase inhibitors include Compound I and Compound II, and pharmaceutically acceptable salts thereof. The ability of the c-Abl-, PDGF-R-, c-kit-, or ARG-tyrosine kinase inhibitors, or pharmaceutically acceptable salts thereof, to treat metabolic disorders is based at least in part on their ability to bind adipocyte-specific peptide hormones such as adiponectin.

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/018342

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61P3/00 A61P3/10 A61K31/506

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, CHEM ABS Data, EMBASE, MEDLINE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LASSILA M ET AL: "IMATINIB ATTENUATES DIABETES-ASSOCIATED ATHEROSCLEROSIS" ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY, vol. 24, no. 5, May 2004 (2004-05), pages 935-942, XP008037837 ISSN: 1079-5642 abstract page 935, column 1, line 1 - line 2	1-6
X	WO 2005/009367 A (AMBIT BIOSCIENCES CORP [US]; BIGGS III WILLIAM H [US]; CARTER TODD [US] 3 February 2005 (2005-02-03) claims 17,21	1-6



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

"I" 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.

"&" document member of the same patent family

Date of the actual completion of the international search

16 May 2007

Date of mailing of the international search report

03/07/2007

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INTERNATIONAL SEARCH REPORT

International application No.
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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:

Although claims 1-6 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 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.:

1-5 (partially), 6

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: 1-5 (partially), 6 (completely)

A method of treating or preventing a disorder associated with aberrant expression of adipocyte-specific peptide hormone in a patient, comprising administering to the patient a cAbI-, PDGF-R-, c-kit-, or ARG-tyrosine kinase inhibitor or a pharmaceutically acceptable salt thereof, said compound being imatinib mesylate (compound I)

2. claims: 1-5 (partially), 7 (completely)

A method of treating or preventing a disorder associated with aberrant expression of adipocyte-specific peptide hormone in a patient, comprising administering to the patient a cAbI-, PDGF-R-, c-kit-, or ARG-tyrosine kinase inhibitor or a pharmaceutically acceptable salt thereof, said compound being "compound II"

3. claims: 8-12 (completely)

A method of determining whether a patient is suffering from or at risk for a disorder associated with aberrant expression of adipocyte-specific peptide hormone, the method comprising:

- a) providing a test biological sample obtained from the patient; and
- b) determining whether the level of expression of an adiponectin polypeptide in the biological sample is higher than that in a comparable biological sample obtained from normal tissue, wherein a higher level of expression in the test biological sample is an indication that the patient is suffering from or is at risk for a disorder associated with aberrant expression of adipocyte-specific peptide hormone.

4. claims: 13-17 (completely)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A method for identifying a candidate agent for treating disorders associated with aberrant expression of adipocyte-specific peptide hormone, the method comprising:

- a) providing a polypeptide comprising an adipocyte-specific peptide hormone;
- b) providing a c-Abl-, PDGF-R-, c-kit-, or ARG-tyrosine kinase inhibitor or a pharmaceutically acceptable salt thereof;
- c) contacting the polypeptide with a test compound;
- d) detecting if the binding between the polypeptide and c-Abl-, PDGF-R-, c-kit-, or ARG-tyrosine kinase inhibitor or a pharmaceutically acceptable salt thereof is inhibited by the test compound; and
- e) selecting the test compound if it inhibits said binding, wherein said test compound is a candidate agent for treating disorders associated with aberrant expression of adipocyte specific peptide hormone.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/018342

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005009367 A	03-02-2005	NONE	