

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
27 July 2006 (27.07.2006)

PCT

(10) International Publication Number
WO 2006/079077 A3

(51) International Patent Classification:

A61K 31/5513 (2006.01) A61P 25/28 (2006.01)
A61P 3/00 (2006.01) A61P 29/00 (2006.01)
A61P 9/00 (2006.01)

(21) International Application Number:

PCT/US2006/002475

(22) International Filing Date: 20 January 2006 (20.01.2006)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/645,669 20 January 2005 (20.01.2005) US

(71) Applicant (for all designated States except US): ACADIA
PHARMACEUTICALS INC. [US/US]; 3911 Sorrento
Valley Blvd., San Diego, California 92121-1402 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): OLSSON, Roger
[SE/SE]; Klagshamnsvagen 99a, S-23044 Bunkeflo Strand
(SE). BURSTEIN, Ethan [US/US]; 4168 Sturgeon Court,
San Diego, California 92130 (US). KNAPP, Anne Eeg
[DK/DK]; Bakkegaards Alle 2, 1.tv., DK-1804 Frederiks-
berg C (DK).(74) Agent: HART, Daniel; KNOBBE MARTENS OLSON
& BEAR LLP, 2040 Main Street, 14th Floor, Irvine, CA
92614 (US).(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US,
UZ, VC, VN, YU, ZA, ZM, ZW.(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT,
RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

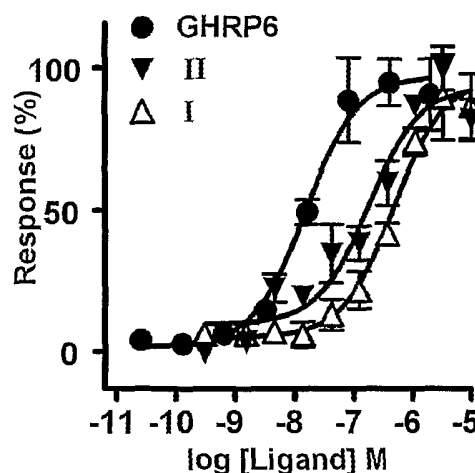
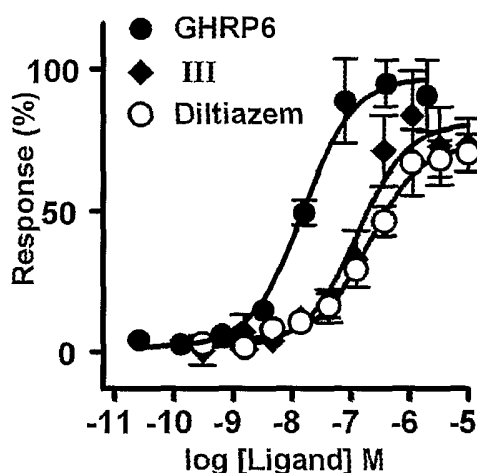
- with international search report
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the international search report:

21 September 2006

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: USE OF DILTIAZEM OR ANALOGS THEREOF AS MODULATORS OF GHRELIN RECEPTOR



(57) Abstract: Disclosed herein are compounds of Formula (I) as defined herein, or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof, that selectively activate the ghrelin receptor, and pharmaceutical compositions comprising the same. Disclosed herein are also methods of treatment of diseases and disorders comprising administering to a subject in need thereof a therapeutically effective amount of a compound of Formula (I).

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/002475

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/5513 A61P3/00

A61P9/00

A61P25/28

A61P29/00

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)

A61K A61P

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, BIOSIS, EMBASE, PAJ, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/073645 A (COMPELLIS PHARMACEUTICALS; ADAMS, CHRISTOPHER, P; FLYNN, JAMES) 2 September 2004 (2004-09-02) claims 1-22	1-5,7, 10-26, 28,31-39
X	US 5 571 807 A (SALIMBENI ET AL) 5 November 1996 (1996-11-05) the whole document	1,6,22, 27
X	EP 0 400 665 A (E.R. SQUIBB & SONS, INC) 5 December 1990 (1990-12-05) claims 1-23	1,22
X	EP 0 433 683 A (MARION MERRELL DOW INC) 26 June 1991 (1991-06-26) page 2, lines 31-50 page 4, lines 9-48	1,22
	-/--	

☒ 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
- *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.
- * & * document member of the same patent family

Date of the actual completion of the international search

31 May 2006

Date of mailing of the international search report

12/07/2006

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

Young, A

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/002475

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/093813 A (PHARMACIA CORPORATION; STEPHENSON, DIANE, T; TAYLOR, DUNCAN, P) 4 November 2004 (2004-11-04) claims 1-15 -----	1,5,10, 22,26,31
Y	ADEGHATE E ET AL: "Ghrelin stimulates insulin secretion from the pancreas of normal and diabetic rats" JOURNAL OF NEUROENDOCRINOLOGY, vol. 14, no. 7, July 2002 (2002-07), pages 555-560, XP002380843 ISSN: 0953-8194 page 559, right-hand column, paragraph 3 -----	1-39
Y	PEMBERTON CHRIS J ET AL: "Ghrelin induces vasoconstriction in the rat coronary vasculature without altering cardiac peptide secretion" AMERICAN JOURNAL OF PHYSIOLOGY - HEART AND CIRCULATORY PHYSIOLOGY, vol. 287, no. 4, October 2004 (2004-10), pages H1522-H1529, XP002380844 ISSN: 0363-6135 page H1528, right-hand column, paragraph 3 -----	1-39

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2006/002475

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 19-39 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:

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/002475

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2004073645	A	02-09-2004	US 2004167117 A1	26-08-2004
US 5571807	A	05-11-1996	NONE	
EP 0400665	A	05-12-1990	AU 633565 B2	04-02-1993
			AU 5494890 A	06-12-1990
			CA 2016465 A1	02-12-1990
			HU 54892 A2	29-04-1991
			JP 3034926 A	14-02-1991
			NZ 233904 A	24-02-1997
			ZA 9004230 A	27-03-1991
EP 0433683	A	26-06-1991	AU 637161 B2	20-05-1993
			AU 6670990 A	30-05-1991
			CA 2030159 A1	23-05-1991
			JP 3170434 A	24-07-1991
WO 2004093813	A	04-11-2004	NONE	