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Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

— *with international search report (Art. 21(3))*

(88) Date of publication of the international search report:
27 February 2014

(54) Title: ALIPHATIC SPIROLACTAM CGRP RECEPTOR ANTAGONISTS

(57) Abstract: The present invention is directed to aliphatic spirolactam derivatives which are antagonists of CGRP receptors and useful in the treatment or prevention of diseases in which CGRP is involved, such as migraine. The invention is also directed to pharmaceutical\compositions comprising these compounds and the use of these compounds and compositions in the prevention or treatment of such diseases in which CGRP is involved.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/039373

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 31/4523 (2013.01)
USPC - 514/422
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(8) - A61K 31/435, 31/4439, 31/4523; A61P 25/06 (2013.01)
USPC - 514/278, 422; 546/15

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC - C07D 401/12, 417/14, 471/10 (2013.01)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatBase, STN, Google Patents, Google Scholar, PubChem

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2011/0021516 A1 (SELNICK et al) 27 January 2011 (27.01.2011) entire document	1, 2, 4, 5, 8, 9, 13
A	US 2006/0189593 A1 (BELL et al) 24 August 2006 (24.08.2006) entire document	1, 2, 4, 5, 8, 9, 13
A	US 2011/0306626 A1 (SELNICK et al) 15 December 2011 (15.12.2011) entire document	1, 2, 4, 5, 8, 9, 13
A	US 2011/0190329 A1 (WOOD et al) 04 August 2011 (04.08.20011) entire document	1, 2, 4, 5, 8, 9, 13
A	US 2009/0247514 A1 (BELL et al) 01 October 2009 (01.10.2009) entire document	1, 2, 4, 5, 8, 9, 13
A	US 2010/0069359 A1 (BELL et al) 18 March 2010 (18.03.2010) entire document	1, 2, 4, 5, 8, 9, 13

☐ Further documents are listed in the continuation of Box C. ☐

* 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 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	Date of mailing of the international search report
19 November 2013	26 NOV 2013
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/039373

Box No. 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.: 14
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. 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 Extra 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 additional fees, this Authority did not invite payment of additional fees.

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, 2, 4, 5, 8, 9, and 13

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/039373

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees need to be paid.

Group I+: Claims 1-13 are drawn to a compound of Formula I.

The first invention of Group I+ is restricted to a compound of Formula I wherein B is C3-C10cycloalkyl, A1 is a bond, A2 is -CReRf-, A3 is -CReRf-, A5 and A7 are each independently -O-, A6 and A8 are each independently -O-, G1 is -C(R2a)=, G2 is -C(R2b)=, G3 is -C(R2c)=, R2a, R2b and R2c are each independently hydrogen, J is =C(R3a)-, Y is =C(R3b)-, R3a and R3b are each independently hydrogen, R4 and R5 are not present based on the selection of J and Y, Ra is not present, Rb and Rc are not present, Rd is not present, Re and Rf are hydrogen, Rg and Rh are not present, v is not present, or a pharmaceutically salt thereof. It is believed that claims 1, 2, 4, 5, 8, 9, and 13 read on this first named invention and thus these claims will be searched without fee to the extent that they read on the above embodiment.

Applicant is invited to elect additional formulas to be searched in a specific combination by paying additional fee for each set of election. An exemplary election would be a compound of Formula I wherein B is phenyl, A1 is a bond, A2 is -CReRf-, A3 is -CReRf-, A5 and A7 are each independently -O-, A6 and A8 are each independently -O-, G1 is -C(R2a)=, G2 is -C(R2b)=, G3 is -C(R2c)=, R2a, R2b and R2c are each independently hydrogen, J is =C(R3a)-, Y is =C(R3b)-, R3a and R3b are each independently hydrogen, R4 and R5 are not present based on the selection of J and Y, Ra is not present, Rb and Rc are not present, Rd is not present, Re and Rf are hydrogen, Rg and Rh are not present, v is not present, or a pharmaceutically salt thereof. Additional formulas will be searched upon the payment of additional fees. Applicants must specify the claims that read on any additional elected inventions. Applicants must further indicate, if applicable, the claims which read on the first named invention if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined.

The inventions listed in Groups I+ do not relate to a single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2 they lack the same or corresponding special technical features for the following reasons:

The Groups I+ formulas do not share a significant structural element that is responsible for the represented drug effects, requiring the selection of alternatives where B, A1, A2, A3, A5, A6, A7, A8, G1, G2, G3, R2a, R2b, R2c,J, Y, R3a, R3b, R4, R5, Ra, Rb, Rb, Rd, Re, Rf, Rg, Rh, and v are each selected from a group of bonds, elements, or compounds.

The Group I+ claims share the technical features of a compound having a core structure of Formula I or a pharmaceutically acceptable salt thereof and a pharmaceutical acceptable carrier. However, these technical features do not represent a contribution over the prior art. Specifically, US 2011/0021516 A1 to Selnick et al. teaches a compound having a core structure of Formula I: wherein: B is 2-oxopiperidinyl, wherein B is optionally substituted with 1-7 substituents each independently selected from the group consisting of: –C1-6alkyl and phenyl, wherein the phenyl is optionally substituted with 1-5 substituents each independently selected from the group consisting of: halo; A1 is selected from: a bond, or -CReRf-; A2 is selected from –CReRf-, or a bond, wherein A2 cannot be a bond unless A3 is –C(Rg)=C(Rh)- or -C≡C-; A3 is -C≡C-; A5 and A7 are each a bond; A6 and A8 are each -CReRf-; G1 is -C(R2a)=; G2 is -C(R2b)=; G3 is –C(R2c)=; R2a, R2b and R2c are each hydrogen; J is =C(R3a)-; Y is =C(R3b)-; R3a and R3b and the carbon atoms to which they are attached join to form a ring selected as pyridyl; Re and Rf are each hydrogen; or a pharmaceutically acceptable salt thereof (Pg. 51, Table 2-continued, Example 31) and a pharmaceutically acceptable carrier (Para. [0768], ...Accordingly, the pharmaceutical compositions of the present invention encompass any composition made by admixing a compound of the present invention and a pharmaceutically acceptable carrier...).

Further, US 2006/0189593 A1 to Bell et al. teaches a compound having a core structure of Formula I: wherein B is naphthyl; A1 is a bond; A2 is -S(O)v-; A3 is -(NRb)-; A5 and A7 are each a bond; A6 and A8 are each -CReRf-; G1 is -C(R2a)=; G2 is -C(R2b)=; G3 is –C(R2c)=; R2a, R2b and R2c are each hydrogen; J is -N(Rb)-; Y is -C(=O)-; Rb is hydrogen; Re and Rf are each hydrogen; and v is 2 (Para. [0342], Example 28) and a pharmaceutically acceptable carrier (Para. [0264], ...combining a compound of the present invention with a pharmaceutical carrier...).

The inventions listed in Groups I+ therefore lack unity under Rule 13 because they do not share a same or corresponding special technical feature.