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17 April 2008

(54) Title: RYANODINE RECEPTOR INHIBITORS AND METHODS RELATING THERETO

(57) Abstract: The present invention provides novel ryanodine receptor type 2 (RyR2) inhibitors and methods of their use in the treatment of cardiac conditions. In general, the RyR2 inhibitors of the present invention assist in the normalization of intracellular calcium homeostasis. In certain embodiments, the RyR2 inhibitors are store-overload-induced Ca^{2+} release (SOICR) inhibitors that minimally inhibit or do not inhibit Ca^{2+} -induced Ca^{2+} release (CICR), thereby providing beneficial effects in cardiac therapy.



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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2007/003006

A. CLASSIFICATION OF SUBJECT MATTER

IPC: *C07D 209/88* (2006.01) , *A61K 31/403* (2006.01) , *A61K 31/5377* (2006.01) , *A61P 9/06* (2006.01) , *A61P 9/10* (2006.01) , *C07D 413/12* (2006.01)

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: *C07D 209/88* (2006.01) , *A61K 31/403* (2006.01) , *A61K 31/5377* (2006.01) , *A61P 9/06* (2006.01) , *A61P 9/10* (2006.01) , *C07D 413/12* (2006.01)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
STN, Canadian Patent Database, Delphion, Espacenet, West (search terms: carvedilol derivatives, carbazole derivatives, ryanodine, aminoalkoxy carbazole derivatives, carbazoly1-(4)-oxypropanolamine derivatives)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CA 2,392,085 (Franchini, M. et al.) 25 May 2001 (25-05-2001) Abstract, claims 1-9	1, 4, 7, 10, 11, 21-28
X	CA 1,129,416 (Wiedeman, F. et al.) 10 August 1982 (10-08-1982) Abstract	24, 26-28
X	CA 2,447,005 (Shanghvi, D. S. et al.) 21 November 2002 (21-11-2002) Claims 1-9	24, 26-28
X	CA 2,462,275 (Oh, C.K.) 10 April 2003 (10-04-2003) Abstract and claims	24, 26-28

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"&" document member of the same patent family
"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	

Date of the actual completion of the international search

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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 2003/0105138 (Lukas-Laskey, M. A. et al.) 05 June 2003 (05-05-2003) Abstract and claims	24, 26-28

INTERNATIONAL SEARCH REPORTInternational application No.
PCT/IB2007/003006**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the 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. ☒ Claim Nos. : 24-28

because they relate to subject matter not required to be searched by this Authority, namely :

Claims 24-28 are directed to a method for the treatment of the human or animal body by surgery or therapy which the International Search Authority is not required to search. Regardless, this Authority has carried out a search based on the alleged effects or purposes/uses of the product defined in claims 1-23.

2. ☒ Claim Nos. : 24, 26-28 (all in part)

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 :

See Extra Sheet

3. ☐ Claim Nos. :

because they are dependant 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 :

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 claim 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 claim Nos. :

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.

Continuation of Box II:

Claims 24, 26-28 are directed to a method of medical treatment which uses a compound defined by its function: "RyR2 inhibitor", without further defining the structure of the compound(s) of interest. Therefore, it is impossible to determine the nature of all compounds encompassed by the above definition. As a result, a limited search has been carried out and was directed to the use of compounds of Formula I, as defined by the applicant in claim 1, without regard to provisos found in said claim.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2007/003006

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