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(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, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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9 July 2009

(54) Title: ION CHANNEL MODULATORS AND METHODS OF USE

(57) Abstract: In general, the invention relates to compounds useful as ion channel modulators. It has now been found that compounds of this invention, and pharmaceutically acceptable compositions thereof, are useful as inhibitors of voltage-gated sodium channels.



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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/064314

A. CLASSIFICATION OF SUBJECT MATTER
 INV. C07C311/58 C07C311/59 C07C311/60 C07C311/51 C07C311/53
 A61K31/18 C07D215/18

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)
 C07C C07D

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, BEILSTEIN Data

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X	WO 2006/008109 A2 (BAYER CROPSCIENCE AG [DE]; FISCHER REINER [DE]; ANDERSCH WOLFRAM [DE];) 26 January 2006 (2006-01-26) pages 39-42, Claim 1 (compounds of formulae IID and IIE)	1,2,4-7, 25,26, 33,37, 38,41-43
X	EP 0 602 878 A1 (LILLY CO ELI [US]) 22 June 1994 (1994-06-22) examples 1-12, claims 1-6	1,2,4-7, 20,25, 26,36, 38-43

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.

Z document member of the same patent family

Date of the actual completion of the international search 16 April 2009	Date of mailing of the international search report 27/05/2009
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Bueno Torres, Pilar
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X	<p>DATABASE WPI Week 200062 Thomson Scientific, London, GB; AN 2000-640875 XP002502981 -& JP 2000 198272 A (OJI PAPER CO) 18 July 2000 (2000-07-18) Claim 1, Formulae II and II, Compounds 1-19,23-38, abstract</p>	1,2,4-7, 25,26, 33,37, 38,41-43
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X	<p>EP 0 116 518 A1 (CIBA GEIGY AG [CH]) 22 August 1984 (1984-08-22)</p> <p>claims 1-22, Tables 3 and 6</p>	1,2,4-7, 20-23, 25,26, 36, 38-40, 42,43
X	<p>EP 0 365 484 A1 (CIBA GEIGY AG [CH]) 25 April 1990 (1990-04-25)</p> <p>claims 1-37, Tabelle 1 (compounds 1001-1156), ex. H1 and H4</p>	1-10,25, 26,33, 35,37, 38,41-43
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International application No

PCT/US2008/064314

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X	US 2 907 692 A (ERICH HAACK ET AL) 6 October 1959 (1959-10-06) the whole document	1, 2, 4, 7, 25, 26, 36-38, 40, 42, 43
X	EP 0 562 512 A1 (HOECHST AG [DE]) 29 September 1993 (1993-09-29) ex 509-529, claims 1-13,	1-9, 19, 25, 26, 35, 38, 41-43
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X	US 3 409 644 A (GERHARD MULLER ET AL) 5 November 1968 (1968-11-05) claims 1, 5-7, example 3	1, 2, 4-7, 25, 26, 30, 38, 43
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International application No

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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.
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X	DE 12 72 299 B (GEVAERT PHOTO PROD NV) 11 July 1968 (1968-07-11) claim 1, ex 8, 27	1, 20-22, 26, 36, 37, 39, 43
X	DATABASE CA CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; XP002522587 Database accession no. 1980:146783 abstract & RO 62 697 A (INTREPRINDEREA "SINTOFARM", ROM) 25 November 1977 (1977-11-25)	1-3, 8, 9, 20-23, 25, 26, 36, 37, 39, 40, 42, 43, 45-48
X	WQ 96/38144 A1 (WARNER LAMBERT CO [US]) 5 December 1996 (1996-12-05) claim 1, 8, 13, eg page 52, line 10; page 54, line 10	1, 20-22, 25, 26, 29, 39, 41-43, 45-48

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INTERNATIONAL SEARCH REPORT

International application No

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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 4 461 773 A (GREGORY WALTER A [US]) 24 July 1984 (1984-07-24) claim 1, compounds 34-36	1, 20-22, 25, 26, 29, 42, 43
X	HASSAN M FAID-ALLAH & HASSAN M MOKHTAR: "Pyrazole derivatives with possible hypoglycemic activity" INDIAN JOURNAL OF CHEMISTRY. SECTION B: ORGANIC AND MEDICINAL CHEMISTRY, SCIENTIFIC PUBLISHERS, JODHPUR, IN, vol. 27, no. 1-12, 1 January 1988 (1988-01-01), pages 245-249, XP009114586 ISSN: 0376-4699 Table 2, compounds 6a1-6a4, 6b1-6b3, 6c1-6c2, 6e1-6e3	1, 20, 25, 26, 36, 37, 39, 40, 42, 43
X	HASSAN M FAID ALLAH AND RAAFAT: "Cyclization of diketones to pyridazine and furan derivatives" JOURNAL OF HETEROCYCLIC CHEMISTRY, HETEROCORPORATION. PROVO, US, vol. 24, 1 January 1987 (1987-01-01), pages 1745-1748, XP009114579 ISSN: 0022-152X Compounds 8a-8f	1, 20, 25, 26, 36, 37, 39, 40, 42, 43
X	SOLIMAN R: "Synthesis of Substituted 4(3H)-Quinazolinone Sulfonylurea Derivatives with Possible Antimicrobial or Hypoglycemic Effect" PHARMAZIE, DIE, GOVI VERLAG, ESCHBORN, DE, vol. 34, no. 7, 1 January 1979 (1979-01-01), pages 441-442, XP009114610 ISSN: 0031-7144 Experimental 2 (page 442), Table 2, compounds 4a-j	1, 20, 25-27, 36, 37, 39, 40, 42, 43
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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2008/064314

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	SHERIF A. F. ROSTOM: "Synthesis and in vitro antitumor evaluation of some indeno[1,2-c]-pyrazol(in)es substituted with sulfonamide, sulfonylurea(-thiourea)pharmacophores, and some derived thiazole ring systems" BIOORGANIC & MEDICINAL CHEMISTRY, vol. 14, 2006, pages 6475-6485, XP002523841 Compounds 4-6, page 6477	1,20-22, 25,26, 36,37, 39,41-43
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/064314

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:

Although claims 44-48 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 compounds.
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 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 additional sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. As all searchable claims could be searched without effort justifying an 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.:

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: Claim 1 (part), 2-19, 25-37 (part), 38, 40-48 (part)

Compounds of formula I wherein R¹ and R₁ are independently -Z-R₄, compounds of Formula Ia, pharmaceutical composition thereof and use of said compounds in therapeutic methods

2. claims: Claim 1 (part), 20-24, 25-37 (part), 39, 40-48 (part)

Compounds of formula I wherein R¹ and R₁ together with the nitrogen atom to which they are attached for an optionally substituted heterocycloaliphatic, Compounds of formula Ib, pharmaceutical compositions thereof and use of said compounds in therapeutic methods.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2008/064314

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