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(71) Applicant (*for all designated States except US*): **PHAR-**
MACIA CORPORATION [US/US]; 700 Chesterfield
Parkway West, Chesterfield, MO 63017-1732 (US).

(72) Inventor; and

(75) Inventor/Applicant (*for US only*): **ROBERDS, Steven,**
L. [US/US]; 48444 Hickory Lane, Mattawan, MI 49071
(US).

(74) Agents: **BAUER, S., Christopher** et al.; Pharmacia Cor-
poration, Corporate Patent Department, P.O. Box 1027, St
Louis, MO 63006 (US).

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ning of each regular issue of the PCT Gazette.*

(54) Title: ANTISENSE MODULATION OF Nav1.3 EXPRESSION

(57) Abstract: Antisense compounds, compositions, and methods are provided for modulating the expression of Type III sodium channel Nav1.3. The compositions comprise antisense compounds, particularly antisense oligonucleotides, targeted to nucleic acids encoding Nav1.3. Methods of using these compounds for modulation of Nav1.3 expression and for treatment of diseases associated with expression of Nav1.3 are provided.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/25465

A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : C07H 21/04; A61K 48/00 US CL : 536/24.5; 514/44 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) U.S. : 536/24.5; 514/44 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 practicable, search terms used) Please See Continuation Sheet		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6,124,133 (TAYLOR et al.) 26 September 2000 (26.09.2000) (see entire document, in particular col. 3-10; col. 12-25; col. 40, example 15; col. 41, table 1).	1-4, 6-15 16
E,X — E,Y	US 6,610,539 (WRIGHT et al.) 26 August 2003 (26.08.2003) (see entire document, in particular col. 5; col. 7-9; col. 12, table 3, SEQ ID NO: 161; col. 17-19)	1-4, 6-8, 10, 12, 13-15 9, 11
P,Y	US2004/0170608 A1 (BARBER et al.) 02 September 2004 (02.09.2004) (see entire document, in particular pg. 1, [0005]; pg. 11-12, [0178-0193], [0196], pg. 13, [0216-0220]; pg. 17, [0300]; pg. 19, example 8 and pg. 20, example 10).	1-3, 6-16
Y	BAKER et al. Involvement of Na ⁺ channels in pain pathways. Trends in Pharmacological Sciences. January 2001, Vol. 22(1):pp. 27-31 (see entire document, in particular pgs. 30 and 31).	16-18 and 21
☐ 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	"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
"B"	earlier application or patent published on or after the international filing date	"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
"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)	"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
"O"	document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed	
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Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner of Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230		Authorized officer Jon R. Ashen Telephone No. 703-308-1235

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/25465

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim 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. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation 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.: 1-21 and SEQ ID NO: 1

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

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BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

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 must be paid.

Groups 1-9094, claim(s) 1-21, drawn to antisense compounds targeted to NAV1.3. Claims 1-21 are generic and include SEQ ID NOs: 1-9094. Each sequence comprises a separate invention. SEQ ID NO: 1, listed in claims 4 and 5 and comprised within the subject matter of generic claims 1-21, comprises the first invention. SEQ ID NOs: 2-9094 listed in claims 4 and 5 and comprised within the subject matter of generic claims 1-21, comprise inventions 2-9094.

The inventions listed as Groups 1-9094 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:

This international searching authority has found 9094 inventions claimed in the international application covered by the claim(s) indicated below:

This international searching authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

According to the guidelines in Section (f)(i)(a) of Annex B of the PCT Administrative Instructions, the special technical feature as defined by PCT Rule 13.2 shall be considered to be met when all the alternatives of a Markush-group are of similar nature. For chemical alternatives, such as the claimed polynucleotide sequences, the Markush group shall be regarded as being of similar nature when:

(A) all alternatives have a common property or activity and

(B)(1) a common structure is present, i.e., a significant structure is shared by all of the alternatives or

(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to an art recognized class of compounds in the art to which the invention pertains.

The instant antisense sequences are considered to be each separate inventions for the following reasons:

The sequences do not meet the criteria of (A), common property or activity or (B)(2), art recognized class of compounds. Although the antisense sequences of the instant application all target and modulate expression of the same gene, each antisense sequence behaves in a different way in the context of the claimed invention. Each sequence targets a different and specific region of NAV1.3 and each sequence modifies (either increases or decreases) the expression of the gene to varying degrees (as shown by the variation in binding and T_m in Table I). Each member of the class cannot be substituted, one for the other, with the expectation that the same intended result would be achieved.

Further, although the instant antisense sequences target the same gene, the sequences do not meet the criteria of (B)(1), as they do not share, one with another, a common core structure. Accordingly, unity of invention between the antisense sequences of the instant application is lacking and each antisense sequence claimed is considered to constitute a special technical feature.

As the polynucleotide sequences of the instant invention are recited in the first claimed invention, Applicants will obtain a search of the first sequence listed in the claim. For every other sequence applicants wish to have searched, applicants need to elect the sequence and pay an additional fee.

If the sequences are recited in the second or subsequent claimed invention, Applicants will need to elect the group and pay the fee to obtain a search of the first sequence listed in the claims encompassed by the second or subsequent group. For every other sequence in the second/subsequent group that applicants wish to have searched, applicants need to elect the sequence and pay an additional fee.

The special technical feature of groups 1-9094 is considered to be an antisense compound comprising a nucleic acid sequence of SEQ ID NO: 1-9094.

INTERNATIONAL SEARCH REPORT

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Continuation of B. FIELDS SEARCHED Item 3:

EAST and STN: medline, biosis, embase, caplus

STIC: SEQ ID NO: 1

Search Terms: Nav1.3, scn3a, antisense, disease, expression, treatment, inhibit, pain