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Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
- with sequence listing part of description (Rule 5.2(a))

(88) Date of publication of the international search report:
7 October 2010

(54) Title: NA/K-ATPASE-DERIVED PEPTIDE SRC INHIBITORS AND OUABAIN ANTAGONISTS AND USES THEREOF

(57) Abstract: A novel Src inhibitor that targets the Na/K-ATPase/Src receptor complex and antagonizes ouabain-induced protein kinase cascades and uses thereof are disclosed.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 09/67845

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 38/04 (2010.01)

USPC - 514/2

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 38/04 (2010.01)

USPC: 514/2

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

USPC: 514/2, 514/12, 530/328, 530/327, 530/326

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PubWest, Google Scholar: fusion, GST, HIV, cancer, vascular disease, cardiovascular disease, heart disease, bone disease, prostate cancer, breast cancer, neuroblastoma, cardiac hypertrophy, tissue fibrosis, congestive heart failure, ischemia, hyperfusion, injury, osteoporosis, permeate\$2, plasma, membrane\$2, CTS, kinase, Src, inhibit\$4, Na+/K+-ATPase

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2008/054792 A2 (XIE et al.) 08 May 2008 (08.05.2008); para [0003], [0004], [00017]-[00020], [00022], [00024], [000113], [000316], [000138], [000319], [000156], [000224], [000316], [000319], Figure 24A, SEQ ID NO:2	1-4, 8, 16-25, 56, 58, 71-72, 77, 79, 82-86, 107-108
A	US 2002/0091085 A1 (KAY et al.) 09 Mar 2004 (09.03.2004); para [0041], [0101]	1-4, 8, 16-25, 56, 58, 71, 72, 77, 79, 82-86 and 107-108

☐ 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

27 July 2010 (27.07.2010)

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 09/67845

Box No. 1 Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing filed or furnished:

a. (means)

☐

on paper

☒

in electronic form

b. (time)

☐

in the international application as filed

☒

together with the international application in electronic form

☐

subsequently to this Authority for the purposes of search

2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.

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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.:
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:
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.

Group I: Claims *1-25, 56, 58, 71, 72, 77, 79, 82-86, 107, and 108 drawn to compositions of matter, where the first named invention will be searched and includes a search for SEQ ID NO: 3, i.e. claims 1-4, 8-25, 56, 58, 71, 72, 77, 79, 82-86, 107, and 108 wherein claims 3, 4, and 71 are limited to SEQ ID NO: 3. Applicant may have additional sequences searched for an additional search fee per sequence.

Group II: Claims *1, 2, 26-46, 57, 67, 68, 69, 78, 80, 81, 97, 98, 102, and 109 drawn to compositions of matter and methods of treatment and methods of binding a kinase domain.

Group III: Claims 47-55, 87, 88, 99-101, and 106, drawn to methods for screening or identifying agents or compositions.

****Continued in Supplemental Page****

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.:
1-4, 8, 16-25, 56, 58, 71, 72, 77, 79, 82-86 and 107-108 wherein claims 3, 4, and 71 are limited to SEQ ID NO: 3

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

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Continuation of Box III:

Group IV: Claims 59-66, 73, 74, and 75 are drawn to cell penetrating conjugates and methods of use.

Group V: Claims 70 and 76, drawn to methods of determining physiological and pathological significance of signaling function.

Group VI: Claims 89-96, drawn to methods of diagnosis, evaluating treatment efficacy, and determination of risk for developing a disease.

Group VII: Claims 103-105, drawn to antibodies.

*Note on claims 1 and 2: Claims 1 and 2 have been included "in part" with both Groups I and II to the extent that they encompass the dependent claims in the the respective Groups.

The groups listed above 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.

Groups I-VII share one or more of the following technical features:

- 1) an Na/KATPase polypeptide such as SEQ ID NO 3.
- 2) an Na/KATPase polypeptide or other agent which binds and inhibits an Src and antagonizes CTS-induced protein kinase cascades.
- 3) a method of treating a cardiac disease or cancer by administering an Na/KATPase polypeptide;
- 4) a method of detecting the level of Na/KATPase polypeptide; Na/KATPase binding, or Src activity.

However, none of these represent improvements over the prior art. Xie et al. (WO 2008/054792; May 2008) teach shared feature 1) an Na/KATPase polypeptide such as SEQ ID NO 3 (SEQ ID NO: 2; claim 27, Fig 24A) and also teach shared features 2)-4) (para [0010]; [0011]; [0014]; [0021]; and [0037])

Accordingly, unity of invention is lacking.

***Additionally claims 9-15 depend from claims not designated in claim group 1 and thus were not included in this search.