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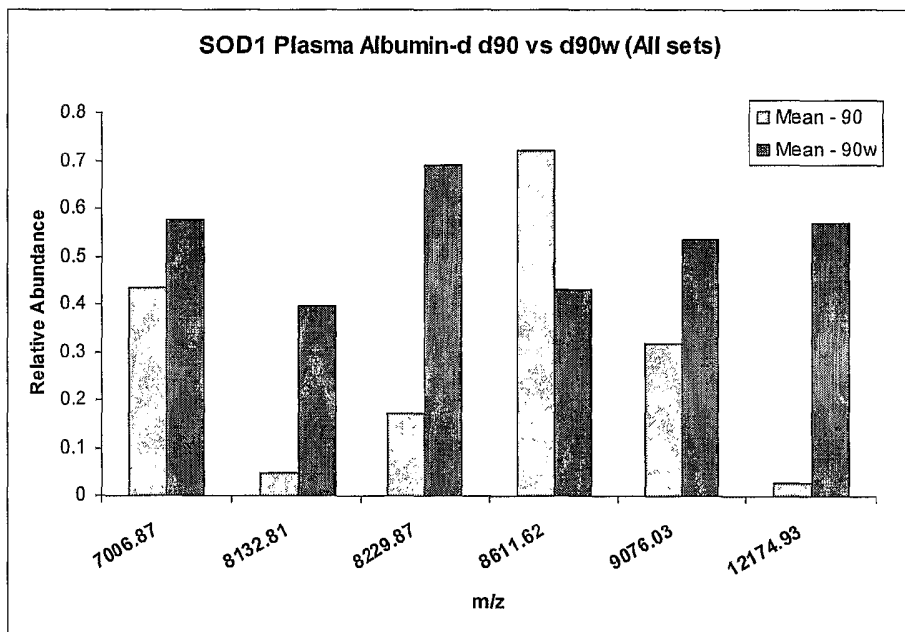
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[Continued on next page]

(54) Title: PROTEIN BIOMARKERS AND THERAPEUTIC TARGETS IN AN ANIMAL MODEL FOR AMYOTROPHIC LATERAL SCLEROSIS



(57) Abstract: The invention provides a method for determining the onset and/or progression of ALS in an animal. The method comprises (a) obtaining a sample from the animal, (b) analyzing the proteins in the sample by mass spectroscopy, and (c) determining a mass spectral profile for the sample. The invention also provides isolated protein biomarkers of ALS.

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— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

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3 August 2006

## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/044018

A. CLASSIFICATION OF SUBJECT MATTER  
 INV. G01N33/68 C07K14/47

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)  
 G01N C07K

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, BIOSIS, EMBASE, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>BOWSER ROBERT PAUL ET AL: "Protein profiling of amyotrophic lateral sclerosis patients by mass spectrometry."            FASEB JOURNAL,            vol. 17, no. 4-5, March 2003 (2003-03),            pages Abstract No. 406.6 URL-http://ww,            XP002378306            &amp; FASEB MEETING ON EXPERIMENTAL BIOLOGY:            TRANSLATING THE GENOME; SAN DIEGO, CA,            USA; APRIL 11-15, 2003            ISSN: 0892-6638            abstract</p> <p style="text-align: center;">----- -/--</p>	1-8

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.

"&" document member of the same patent family

Date of the actual completion of the international search

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European Patent Office, P.B. 5818 Patentlaan 2  
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## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/044018

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	POMPL P N ET AL: "PHARMACOTHERAPEUTIC BIOMARKER DISCOVERY IN A MOUSE MODEL OF AMYOTROPHIC LATERAL SCLEROSIS." SOCIETY FOR NEUROSCIENCE ABSTRACT VIEWER AND ITINERARY PLANNER, vol. 2002, 2002, pages Abstract No. 888.2 URL-http://sf, XP002378307 & 32ND ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE; ORLANDO, FLORIDA, USA; NOVEMBER 02-07, 2002 abstract	1-8
P,A	----- RANGANATHAN SRIKANTH ET AL: "Proteomic profiling of cerebrospinal fluid identifies biomarkers for amyotrophic lateral sclerosis." JOURNAL OF NEUROCHEMISTRY. DEC 2005, vol. 95, no. 5, December 2005 (2005-12), pages 1461-1471, XP002378308 ISSN: 0022-3042 abstract; figures 1,2; table 1 -----	1

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2005/044018

## Box 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.: 1-2, 9-13  
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 FURTHER INFORMATION sheet PCT/ISA/210
  
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 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 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.:

### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 1-2, 9-13

Although claims 1 and 2 are directed to a diagnostic method practised on the human/animal body, the search has been carried out in as far as it concerns in vitro methods.

The present claims 9-13 relate to an extremely large number of possible proteins. Support and disclosure in the sense of Article 6 and 5 PCT is to be found however for none of the proteins. The non-compliance with the substantive provisions is to such an extent, that no search has been carried out at all.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: invention 1: Claims 1-2, 6-9 (all partially)

A marker for ALS, wherein the marker is a 4369 Da protein.

1.1. claims: inventions 2-50: Claims 1-2 and 6-9 (for inventions 2-12, all partially); Claims 1, 3, 6-8 and 10 (for inventions 13-20, all partially); Claims 1, 4-8 and 13 (for inventions 21-33, all partially); Claims 1, 6-8 and 11-12 (for inventions 34-50, all partially):

A marker for ALS, wherein the marker is a 6840 Da protein (invention 2), a 6865 Da protein (invention 3)... up to a 16777 Da protein (invention 50).

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