Title: COMPOSITIONS AND METHODS FOR TREATING NEURODEGENERATIVE DISEASES

Abstract: Compositions and methods for treating subjects with preexisting neuronal damage are disclosed. The compositions and methods use adeno-associated virus (AAV)-based gene delivery systems for delivering glial cell line-derived neurotrophic factor (GDNF) to subjects with neurodegenerative conditions such as Parkinson’s disease.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/864 A61K48/00 C12N15/12 A61P25/00 C07K14/475

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 7 A61K

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)

WPI Data, PAJ, EPO-Internal, MEDLINE, BIOSIS, EMBASE, CHEMABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>MANDEL ET AL: &quot;Recombinant adeno-associated viral vector-mediated glial cell line-derived neurotrophic factor gene transfer protects nigral dopamine neurons after onset of progressive degeneration in a rat model of Parkinson's disease.&quot; EXPERIMENTAL NEUROLOGY, vol. 160, 1999, pages 205-214, XP001148187 page 205 abstract page 206, right-hand column, paragraph 4 -page 207, left-hand column, paragraph 1 page 208, right-hand column, paragraph 2 page 210, left-hand column, paragraph 2 page 212, left-hand column, paragraph 3 —right-hand column, paragraph 1</td>
<td>1-13</td>
</tr>
</tbody>
</table>

X

Further documents are listed in the continuation of box C.

Patent family members are listed in 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 published on or after the international filing date

"L" document which may throw doubts on priority claims 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 data claimed

*I* 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.

*S* document member of the same patent family

Date of the actual completion of the international search

7 February 2003

Date of mailing of the international search report

27/02/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5815 Patentlaan 2 NL-2280 HV Rijswijk
Tel: (31-70) 340-2040, Tx: 31 661 epo nl
Fax: (31-70) 340-3815

Authorized officer

Sitch, W
<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>DURING M J ET AL: &quot;Neuroprotection and neuroregeneration in rodent and primate Parkinsonian models using AAV vectors expressing GDNF.&quot; SOCIETY FOR NEUROSCIENCE ABSTRACTS, vol. 21, no. 1-3, 1995, page 542 XP001109631 25th Annual Meeting of the Society for Neuroscience; San Diego, California, USA; November 11-16, 1995 ISSN: 0190-5295 abstract 225.9</td>
<td>1-13</td>
</tr>
</tbody>
</table>
### INTERNATIONAL SEARCH REPORT

#### C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1993</td>
<td></td>
</tr>
</tbody>
</table>
**INTERNATIONAL SEARCH REPORT**

**Box I  Observations where certain claims were found unsearchable (Continuation of item 1 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. **X** Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
   
   Although claims 1-13 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 compound/composition.

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 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:

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.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1966)