Abstract: The present invention provides methods for the regulation of osteopontin activity in a subject as well as for treating or preventing conditions associated with an increased activity of osteopontin activity in a subject.
### A CLASSIFICATION OF SUBJECT MATTER

| IPC(8) - | C07C 281/18, A61 K 31/155 (2008 04) |
| USPC - | 564/227, 514/632 |

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)

| USPC | 564/227, 514/632 |

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

| USPC | 564/227, 514/632 |

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

- PubWEST(PGPB,USPT,USOC,EPAB,JPAB), Google, PubMed
- Search terms: MGBG, osteopontin, polyamine, s-adenosyl methionine decarboxylase, amyotrophic lateral sclerosis, monocyte

### 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>
</table>

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: 25 August 2008 (25 08 2008)

Date of mailing of the international search report: 02 SEP 2008

Name and mailing address of the ISA/US

- Mail Stop PCT, Attn ISA/US, Commissioner for Patents
- P O Box 1450, Alexandria, Virginia 22313-1450
- Facsimile No 571-273-3201
- Authorized officer: Lee W Young
- PCT Helpdesk 571-272-4300
- PCT OSP 571-272-7774

Form PCT/ISA/2 10 (second sheet) (April 2007)
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 64(a):

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:

—See extra 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 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. 1-6, 13-23, and 30 directed to method of treating or preventing a condition associated with an increased activity of osteopontin using MGBG.

Remark on Protest

D The additional search fees were accompanied by the applicant’s protest and, where applicable, the payment of a protest fee.

D 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.

D No protest accompanied the payment of additional search fees.
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 1-6, 13-23, 30 directed to a method of decreasing the activity of osteopontin in a cell, and a method of treating or preventing a condition associated with an increased activity of osteopontin using MGBG, or a salt thereof.

Group II Claims 7-12 and 24-29 are directed to a method of treating or preventing a condition associated with an increased activity of osteopontin comprising administering to a subject in need of such treatment an effective amount of an agent wherein the agent is not MGBG.

The inventions listed as Groups I- II 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:

The common technical feature of Groups I and II is an agent that inhibits S-adenosyl methionine decarboxylase ("AMDr"), inhibits polyamine biosynthesis, increases adenosine in the cell or modulates macrophage proliferation. However, this is not an improvement over the prior art of US 2005/0159493 A1 to McGrath (21 July 2005 (21.07.2005)) that teaches MGBG inhibits S-adenosyl methionine decarboxylase which, in turn, is required for the production of polyamines (abstract, para [0124]).

Therefore, the inventions listed as Groups I and II lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.