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(54) Title: USE OF MYOSTATIN (GDF8) INHIBITORS IN CONJUNCTION WITH CORTICOSTEROIDS FOR TREATING NEUROMUSCULAR DISORDERS

(57) Abstract: The disclosure provides methods for treating neuromuscular disorders in mammals. The disclosed methods include administering therapeutically effective amounts of a GDF-8 inhibitor and a corticosteroid to a subject susceptible to, or having, a neuromuscular disorder, so as to maintain desirable levels of muscle function.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/017049

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K39/395 A61P21/00
//(A61K39/395,31:57)

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)

EPO-Internal, BIOSIS, 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>KHURANA TEJVIR S ET AL: "Pharmacological strategies for muscular dystrophy." NATURE REVIEWS. DRUG DISCOVERY. MAY 2003, vol. 2, no. 5, May 2003 (2003-05), pages 379-390, XP009039735 ISSN: 1474-1776 abstract table 1 page 384, right-hand column, last paragraph - page 385, left-hand column, paragraph 1 page 387; figure 5</p> <p style="text-align: center;">----- -/--</p>	1-29

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 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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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/017049

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WAGNER KATHRYN R ET AL: "Loss of myostatin attenuates severity of muscular dystrophy in mdx mice." ANNALS OF NEUROLOGY, vol. 52, no. 6, December 2002 (2002-12), pages 832-836, XP009039801 ISSN: 0364-5134 abstract	1-29
Y	WHITTEMORE LISA-ANNE ET AL: "Inhibition of myostatin in adult mice increases skeletal muscle mass and strength." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 300, no. 4, 24 January 2003 (2003-01-24), pages 965-971, XP002305259 ISSN: 0006-291X abstract	1-29
Y	HILL JENNIFER J ET AL: "The myostatin propeptide and the follistatin-related gene are inhibitory binding proteins of myostatin in normal serum" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 277, no. 43, 25 October 2002 (2002-10-25), pages 40735-40741, XP002305260 ISSN: 0021-9258 the whole document	1-29
Y	LEE SE-JIN ET AL: "Regulation of myostatin activity and muscle growth" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 98, no. 16, 31 July 2001 (2001-07-31), pages 9306-9311, XP002281005 ISSN: 0027-8424 the whole document	1-29
Y	WO 02/29105 A (NORTH SHORE LONG ISLAND JEWISH) 11 April 2002 (2002-04-11) abstract	1-29
Y	US 2002/150577 A1 (MCPHERRON ALEXANDRA C ET AL) 17 October 2002 (2002-10-17) abstract claims 33-48	1-29
Y	WO 03/027248 A (DUNHAM WILLIAM J LM; BRIDGES KRISTIE GROVE ; BOUXSEIN MARY (US); O'HAR) 3 April 2003 (2003-04-03) the whole document	1-29
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/017049

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>HUDECKI M S ET AL: "Strength and endurance in the therapeutic evaluation of prednisolone-treated MDX mice." RESEARCH COMMUNICATIONS IN CHEMICAL PATHOLOGY AND PHARMACOLOGY. JAN 1993, vol. 79, no. 1, January 1993 (1993-01), pages 45-60, XP009039770 ISSN: 0034-5164 abstract</p>	1-6,8-29
Y	<p>MERLINI LUCIANO ET AL: "Early prednisone treatment in Duchenne muscular dystrophy." MUSCLE AND NERVE, vol. 27, no. 2, February 2003 (2003-02), pages 222-227, XP009039797 ISSN: 0148-639X abstract</p>	1-6,8-29
Y	<p>GRANCHELLI J A ET AL: "Pre-clinical screening of drugs using the mdx mouse." NEUROMUSCULAR DISORDERS : NMD. JUN 2000, vol. 10, no. 4-5, June 2000 (2000-06), pages 235-239, XP002305261 ISSN: 0960-8966 abstract</p>	1-6,8-29
Y	<p>MUNTONI FRANCESCO ET AL: "Steroids in Duchenne muscular dystrophy: from clinical trials to genomic research." NEUROMUSCULAR DISORDERS : NMD. OCT 2002, vol. 12 Suppl 1, October 2002 (2002-10), pages S162-S165, XP002305263 ISSN: 0960-8966 abstract page S163, left-hand column, paragraphs 3,4</p>	1-6,8-29
Y	<p>LANG CHARLES H ET AL: "Regulation of myostatin by glucocorticoids after thermal injury" FASEB JOURNAL, vol. 15, no. 10, August 2001 (2001-08), pages 1807-1809, XP002305301 ISSN: 0892-6638 the whole document</p>	7,12-25

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/017049

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:

Although claims 1-29 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 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:

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/017049

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