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(54) Title: IMPROVING RESISTANCE TO SKELETAL MUSCLE FATIGUE

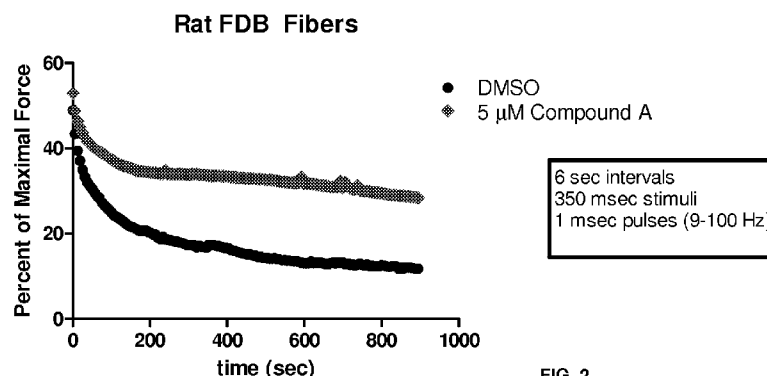


FIG. 2

(57) Abstract: Provided are compounds, compositions and methods for improving resistance to skeletal muscle fatigue comprising administering an effective amount of a skeletal muscle troponin activator. Also provided are methods for improving resistance to fatigue, improving physical endurance, or reducing exercise intolerance in a subject suffering from a condition associated with muscle fatigue or weakness, such as heart failure.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US13/36114

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C12N 5/00 (2013.01)

USPC - 435/4, 375

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): C07D 471/00; C12N 5/00; C12Q 1/00 (2013.01)

USPC: 435/4, 375; 544/350

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 practicable, search terms used)

MicroPatent (US-G, US-A, EP-A, EP-B, WO, JP-bib, DE-C,B, DE-A, DE-T, DE-U, GB-A, FR-A); DialogPro; IP.com; Google Scholar; skeletal*, muscle*, fatigu*, weakness*, bone* troponin*, activator*, anti*platelet*, diuretic*, calcium*, channel*, block*, beta*, block*, statin*, aldosterone*, angiotensin*, antagonist*

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US 2009/0029345 A1 (RUSSELL, A et al.) 29 January 2009; abstract; paragraphs [0007], [0027], [0036]-[0037], [0039], [0056], [0075]-[0078], [0080], [0082], [0097], [0168]-[0170]	1-4, 14-17, 18/14-17 --- 5/1-4, 7/1-3, 8/7/1-3, 9/7/1-3, 10/7/1-3, 11/7/1-3, 12/7/1-3, 13/7/1-3, 19/18/14-17, 20/19/18/14-17, 21/18/14-17, 28-34
Y	HIATT, WR et al. 'Efficacy and Tolerability of the Novel Fast Skeletal Muscle Troponin Activator, CK-2017357, in Patients with Claudication.' 22nd Annual Sessions of the Society for Vascular Medicine, Boston, MA, June 2011 [poster presentation]; [Retrieved on 2013-08-20]. Retrieved from the Internet at <URL: www.cytokinetics.com/pdf/4022-20110531-rev004.pdf>; introduction, paragraphs 1-2, figure 1; methods, lines 1-7, 18-28; clinical results, figures 4A-C, paragraph 1	5/1-4, 7/1-3, 8/7/1-3, 9/7/1-3, 10/7/1-3, 11/7/1-3, 12/7/1-3, 13/7/1-3, 28-34
Y	WO 2011/133888 A1 (YANG, Z et al.) 27 October 2011; page 71, line 21-33	19/18/14-17, 20/19/18/14-17, 21/18/14-17

☐ 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

29 October 2013 (29.10.2013)

Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US13/36114

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.: 6, 22-27
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 1-4, 5/1-4, 7/1-3, 8-17, 18/14-17, 19/18/14-17, 20/19/18/14-17 and 21/18/14-17 are directed to improving skeletal muscle fatigue.

Group II: Claims 28-34 are directed to determining the efficacy of a skeletal muscle troponin activator.

---Continued Within the Next Extra Sheet Below---

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.:

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

International application No.

PCT/US13/36114

-Continued From Box III: Observations where unity of invention is lacking-

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 special technical features of Group I include treating exercise intolerance, improving physical endurance performance, increasing the function, activity, efficiency, sensitivity to calcium of a patient suffering from heart failure, which are not present in Group II; and the special technical features of Group III include determining the efficacy of a skeletal muscle troponin activator in a subject, comprising; instructing the subject to perform heel raises at regular intervals; and measuring one or more parameters selected from time to claudication onset, number of heel raises to claudication onset, work to claudication onset, time to maximal claudication fatigue, number of heel raises to maximal claudication fatigue, and work to maximal claudication fatigue, wherein an increase in one or more of the parameters indicates an improvement in resistance to skeletal muscle fatigue in the subject, which are not present in Group I.

The common technical features of Groups I-II are improving resistance to skeletal muscle fatigue; and administering to the subject a therapeutically effective amount of a skeletal muscle troponin activator.

These common technical features are disclosed by US 2009/0029345 A1 to Russell, et al. (hereinafter 'Russell'). Russell discloses improving resistance to skeletal muscle fatigue (methods for increasing time to skeletal muscle fatigue and enhancing skeletal muscle efficiency; paragraph [0075], [0077]); and administering to the subject a therapeutically effective amount of a skeletal muscle troponin activator (administered to a human or non-human patient, a therapeutically effective amount sufficient to treat a disease responsive to activation of skeletal muscle, including administering to said patient an effective amount of a compound that selectively binds the troponin complex of fast skeletal muscle fiber or sarcomere (skeletal muscle troponin activator); abstract; paragraph [0039], [0075]).

Since the common technical features are previously disclosed by the Russell, these common features are not special, and thus Groups I and II lack unity.