Abstract:

Methods and compositions useful in the treatment or prevention of lysosomal storage diseases, such as Pompe's disease, Fabry's disease, Gaucher's disease, and Niemann-Pick disease, are provided. The treatment includes administering to a subject a farnesy transferase inhibitor compound. The treatment may also include enzyme replacement therapy or gene therapy.
INTERNATIONAL SEARCH REPORT

International application No
PCT/US 08/56162

A  CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 31/445 (2008.04)
USPC - 514/315
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 - 514/315

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)
PubMed (USPT, PGPB, EPAB, JPAB) and Google Patent/Scholar T farnesyl transferase inhibitor, lysosomal storage disease, prenyl, r15777 imidazole quinoline

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>Y</td>
<td>US 6 774 135 B2 (Fan et al) 10 Aug 2004 (10 08 2004), col 1, In 34-38</td>
<td>7, 12</td>
</tr>
</tbody>
</table>

D  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 claims(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
14 August 2008 (14 08 2008)

Date of mailing of the international search report
19 AUG 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 Help Desk 571-272-4300
PCTDBP 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2007)
INTERNATIONAL SEARCH REPORT

International application No
PCT/US 08/56162

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 1-16, 18-31, 86 because they relate to subject matter not required to be searched by this Authority, namely

2. [D] Claims Nos 2 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. [X] Claims Nos 160, 61 because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 64(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

Group I, claims 1-16, 18-31 and 86, drawn to a method comprising administering to a subject with a lysosomal storage disease a farnesyl transferase inhibitor

Group II, claims 17-31 and 87, drawn to a method comprising administering to a subject with a lysosomal storage disease a farnesyl transferase inhibitor of claim 17

Group III, claims 32-69 and 128-130, drawn to a method comprising administering to a subject a farnesyl transferase inhibitor of claim 32

[ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims

[ ] As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees

[ ] 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 1-16, 18-31, 86

[ ] 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 1-16, 18-31, 86

Remark on Protest

[ ] 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

Form PCT/ISA/210 (continuation of first sheet (2)) (April 2007)
Continuation of Box No III Observations where unity of invention is lacking

Group IV, claims 70, 72-77, 79-81, 83-85, drawn to a method comprising administering to a subject 6-[(4-chloro-phenyl)-hydroxy-(3-methyl-2Himidazol-4-yl)-methyl]-4-(3-ethyl-phenyl)-1-methylH-quinol in 2,3-dihydroxy butanedioate

Group V, claims 71-76, 78-80, 82-85, drawn to a method comprising administering to a subject 6-[(amino)-(6-chloro-pyr-din-3-y)]-(3-methyl-2H-imidazol-4-yl)-methyl]-4-(3-chloro- pheryl)-1-cyclopropylmethyl-1H-quinol-2-one

Group VI, claims 88-98, drawn to a method comprising administering to a subject a farnesyl transferase inhibitor of claim 88

Group VII, claims 99-106, 109-123, 151-159, 162-165, 179-184 and 187-193, wherein claim 151 is limited to Formula I

Group VIII, claims 107, 109-113, 151-159, 162-165, 185 and 187-193, wherein claim 151 is limited to Formula II

Group IX, claims 108-113, 151-159,162-165 and 186-193, wherein claim 151 is limited to Formula III

Group X, claims 124-127, drawn to a method comprising administering to a subject with a lysosomal storage disease 6-[(amino)-(4-chlorophenyl)-(1-methyl-2H-imidazol-5-yl)-methyl]-4-(3-chlorophenyl)-1-methyl-2-(1H)-quinolinone

Group XI, claims 131-134 and 136-140, drawn to a method comprising administering to a subject a farnesyl transferase inhibitor of claim 131

Group XII, claims 135-140, drawn to a method comprising administering to a subject a farnesyl transferase inhibitor of claim 135

Group XIII, claims 141-150, drawn to a method comprising administering to a subject a farnesyl transferase inhibitor of claim 141

Group XIV, claims 166-178, drawn to a method comprising administering to a subject a farnesyl transferase inhibitor of claim 166

Group XV, claim 194, drawn to a method comprising administering to a subject a farnesyl transferase inhibitor of claim 194

Group XVI, claim 195, drawn to a method comprising administering to a subject a farnesyl transferase inhibitor of claim 195

Group XVII, claim 196, drawn to a method comprising administering to a subject a farnesyl transferase inhibitor of claim 196

Group XVIII, claim 197, drawn to a method comprising administering to a subject a farnesyl transferase inhibitor of claim 197

The inventions listed as Groups I-VIII 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

As to Groups I-XV, XVII and XVIII, farnesyl transferase inhibitors of said groups do not include the inventive concept of a tricyclic skeleton, as required by Group XVI. In addition, the article entitled "Novel Tricyclic Inhibitors of Farnesyl Protein Transferase" by Bishop et al. (The Journal of Biological Chemistry Dec 1995, 270(S1) 30611-30618) teaches a tricyclic Inhibitor of farnesyl protein transferase having said tricyclic skeleton (pg 30613, col 1)

As to Groups XV, XVII and XVIII, farnesyl transferase inhibitors of said groups do not include the inventive concept of a quinoline core, as required by Groups I-XIV in addition, farnesyl transferase inhibitors of Groups XV, XVII and XVIII do not share common core structure Thus, no special technical feature exists among Groups I-XIV and XV, XVII and XVIII

As to Groups I-XIV, although said Groups do share a technical feature of a quinoline core, said skeleton does not represent a contribution over the prior art. Specifically, the article entitled "Characterization of the Antitumor Effects of the Selective Farnesyl Protein Transferase Inhibitor R 115777 in Vivo and in Vitro" by End et al. (Cancer Research Jan 2001, 61 131-137) teaches selective farnesyl protein transferase inhibitor R 115777 comprising said quinoline core (B)-6-[(amino)-4-chlorophenyl)-(1-methyl-2H-imidazol-5-yl)-methyl]-4-(3-chlorophenyl)-1-methyl-2(1H)-quinolinone (abstract, pg 132, col 2)

Groups I-XVIII therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.