

(51) International Patent Classification:  
*A61K 38/46* (2006.01) *C12N 9/16* (2006.01)

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(21) International Application Number:  
PCT/US2011/045011

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(22) International Filing Date:  
22 July 2011 (22.07.2011)

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
61/366,714 22 July 2010 (22.07.2010) US(71) Applicant (for all designated States except US):  
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(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK,

[Continued on next page]

(54) Title: MANUFACTURE OF ACTIVE HIGHLY PHOSPHORYLATED HUMAN N-ACETYL GALACTOSAMINE-6-SULFATASE AND USES THEREOF

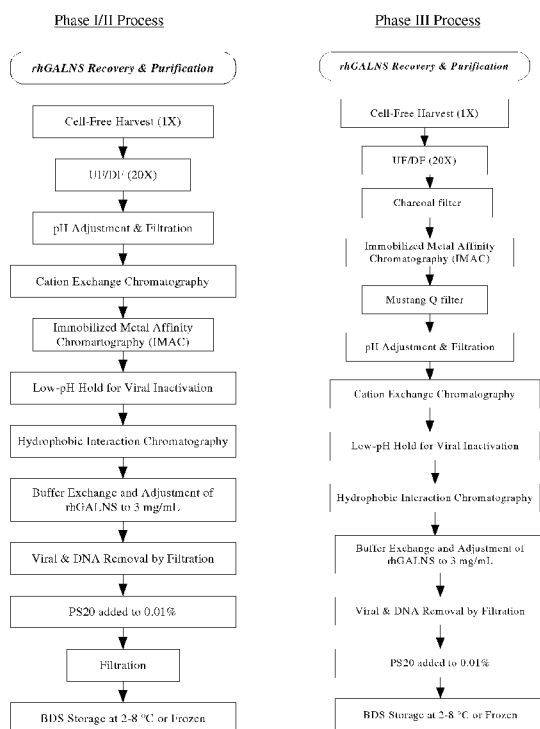


FIGURE 11

(57) Abstract: This invention provides compositions of active highly phosphorylated human N- acetylgalactosamine-6-sulfatase (GALNS), and pharmaceutical compositions and formulations thereof, methods of producing and purifying GALNS, and its use in the diagnosis, prophylaxis, or treatment of diseases and conditions, including particularly lysosomal storage diseases that are caused by, or associated with, a deficiency in the GALNS enzyme, e.g., Mucopolysaccharidosis IVa (MPS IVa or Morquio A syndrome).



SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

— *with sequence listing part of description (Rule 5.2(a))*

**Published:**

**(88) Date of publication of the international search report:**

5 April 2012

- *with international search report (Art. 21(3))*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2011/045011

A. CLASSIFICATION OF SUBJECT MATTER  
INV. A61K38/46 C12N9/16  
ADD.

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)

A61K C12N

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)

EP0-Internal, BIOSIS, EMBASE, FSTA, PAJ, WPI Data, Sequence Search

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                  | Relevant to claim No.    |
|-----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|
| X         | US 2010/068195 A1 (VELLARD MICHEL C [US]<br>ET AL VELLARD MICHEL CLAUDE [US] ET AL)<br>18 March 2010 (2010-03-18)<br>paragraphs [0019] - [0031], [0033] -<br>[0041]<br>paragraph [0275]                             | 1-17,<br>19-27,<br>29-46 |
| X         | US 2009/186011 A1 (VELLARD MICHEL CLAUDE<br>[US] ET AL) 23 July 2009 (2009-07-23)<br><br>paragraphs [0020] - [0022], [0095] -<br>[0096]<br>paragraphs [0175], [0176], [0280],<br>[0281], [0264]<br><br>-----<br>-/- | 1-17,<br>19-27,<br>29-46 |

☒ Further documents are listed in the continuation of Box C.

☒ See patent family 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

13 February 2012

Date of mailing of the international search report

17/02/2012

Name and mailing address of the ISA/  
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# INTERNATIONAL SEARCH REPORT

International application No

PCT/US2011/045011

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                                                                                                                                       | Relevant to claim No. |
|-----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| X         | <p>ALEXANDER RODRÍGUEZ ET AL: "Enzyme replacement therapy for Morquio A: an active recombinant N-acetylgalactosamine-6-sulfate sulfatase produced in Escherichia coli BL21", JOURNAL OF INDUSTRIAL MICROBIOLOGY &amp; BIOTECHNOLOGY, vol. 37, no. 11, 27 June 2010 (2010-06-27), pages 1193-1201, XP55018909, ISSN: 1367-5435, DOI: 10.1007/s10295-010-0766-x abstract<br/>page 1198 - page 1199; figure 4<br/>-----</p> | 19-27,<br>38-46       |
| X         | <p>BIELICKI J ET AL: "EXPRESSION, PURIFICATION AND CHARACTERIZATION OF RECOMBINANT HUMAN N-ACETYLGALACTOSAMINE-6-SULPHATASE", BIOCHEMICAL JOURNAL, THE BIOCHEMICAL SOCIETY, LONDON, GB, vol. 33, no. PART 01, 1 October 1995 (1995-10-01), pages 333-339, XP000600743, ISSN: 0264-6021 abstract<br/>figure 4; tables 2,3<br/>-----</p>                                                                                   | 19-27,<br>38-46       |
| X         | <p>TOMATSU ET AL: "Characterization and pharmacokinetic study of recombinant human N-acetylgalactosamine-6-sulfate sulfatase", MOLECULAR GENETICS AND METABOLISM, ACADEMIC PRESS, SAN DIEGO, CA, US, vol. 91, no. 1, 10 April 2007 (2007-04-10), pages 69-78, XP022020286, ISSN: 1096-7192, DOI: 10.1016/J.YMGME.2007.01.004 abstract<br/>figures 1,2; table 1<br/>-----</p>                                             | 19-27,<br>38-46       |

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2011/045011

### 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.:  
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:

see additional 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 an 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.:  
  
1-27, 29-46
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/ US2011/ 045011

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-18

methods of purification of GALNS

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2. claims: 19-27, 29-46

Composition and formulations comprising purified GALNS, uses thereof

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3. claim: 28

Method of preventing dephosphorylation of recombinant human GALNS

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2011/045011

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|-------------------------------------------|---------------------|----------------------------|---------------------|
| US 2010068195 A1                          | 18-03-2010          | NONE                       |                     |
| -----                                     |                     |                            |                     |
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|                                           |                     | WO 2009091994 A2           | 23-07-2009          |
| -----                                     |                     |                            |                     |