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(71) Applicant (for all designated States except US): RE-COPHARMA AB [SE/SE]; P.O. Box 7710, Drottninggatan 33, S-103 95 Stockholm (SE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): HOLGERSSON, Jan [SE/SE]; Venusvagen 6A, S-141 33 Huddinge (SE). GUSTAFSSON, Anki [SE/SE]; Blasutvagen 5, 4Tr, S-121 36 Johanneshov (SE).

(74) Agent: ASTON, Heidi, Francis; Mintz Levin Cohn Ferris Glosky & Popeo, Intellectual Property LLP, The Rectory, 9 Ironmonger Lane, London EC2V 8EY (GB).

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[Continued on next page]

(54) Title: PRODUCTION OF PROTEINS CARRYING OLIGOMANNOSE OR HUMAN-LIKE GLYCANS IN YEAST AND METHODS OF USE THEREOF

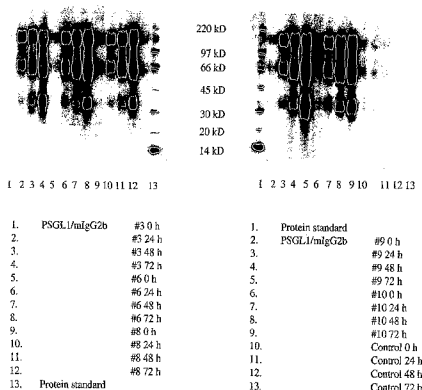


FIGURE 1

(57) Abstract: Cell lines having genetically modified glycosylation pathways that allow them to carry out a sequence of enzymatic reactions, which mimic the processing of glycoproteins in humans, have been developed. Recombinant proteins expressed in these engineered hosts yield glycoproteins more similar, if not substantially identical, to their human counterparts. The lower eukaryotes, which ordinarily produce high-mannose containing N-glycans, including unicellular and multicellular fungi are modified to produce O-glycans or other structures along human glycosylation pathways. This is achieved using a combination of engineering and/or selection of strains which: do not express certain enzymes which create the undesirable complex structures characteristic of the fungal glycoproteins, which express exogenous enzymes selected either to have optimal activity under the conditions present in the fungi where activity is desired, or which are targeted to an organelle where optimal activity is achieved, and combinations thereof wherein the genetically engineered eukaryote expresses multiple exogenous enzymes required to produce "human-like" glycoproteins.

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(15) **Information about Corrections:**

**Previous Corrections:**

see Notice of 6 November 2008

see Notice of 25 September 2008

## INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2007/004164

## A. CLASSIFICATION OF SUBJECT MATTER

INV. C07K14/47 C12N15/62 C12N9/10 C12P21/00  
 ADD. A61K39/39

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 C07K C12N C12P

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, EMBASE, 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	WO 03/088995 A (ABSORBER AB [SE]; HOLGERSSON JAN [SE]) 30 October 2003 (2003-10-30) the whole document	1-14
A	LAM JENNIFER S ET AL: "A model vaccine exploiting fungal mannosylation to increase antigen immunogenicity." JOURNAL OF IMMUNOLOGY (BALTIMORE, MD. : 1950) 1 DEC 2005, vol. 175, no. 11, 1 December 2005 (2005-12-01), pages 7496-7503, XP002481100 ISSN: 0022-1767 abstract	14

 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.

\*Z\* document member of the same patent family

Date of the actual completion of the international search

22 May 2008

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Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Wiame, Ilse

## INTERNATIONAL SEARCH REPORT

International application No

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C(Continuation): DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 177 256 B1 (MCKENZIE IAN F C [AU] ET AL) 23 January 2001 (2001-01-23)  the whole document	1-3, 8-10, 12-14
X	WO 03/089450 A (ABSORBER AB [SE]; HOLGERSSON JAN [SE]; LOFLING JONAS [SE]) 30 October 2003 (2003-10-30)  the whole document	1-10, 12-14
X	WO 03/010201 A (ABSORBER AB [SE]; LOFLING JONAS [SE]; HOLGERSSON JAN [SE]) 6 February 2003 (2003-02-06)  the whole document	1-5, 8-10, 12-14
X	POWERS D B ET AL: "Expression of single-chain Fv-Fc fusions in Pichia pastoris" JOURNAL OF IMMUNOLOGICAL METHODS, ELSEVIER SCIENCE PUBLISHERS B.V., AMSTERDAM, NL, vol. 251, no. 1-2, 1 May 2001 (2001-05-01), pages 123-135, XP004233079 ISSN: 0022-1759 abstract	1, 10, 13, 14
X	CHIBA A ET AL: "Structures of sialylated O-linked oligosaccharides of bovine peripheral nerve alpha-dystroglycan. The role of a novel O-mannosyl-type oligosaccharide in the binding of alpha-dystroglycan with laminin." THE JOURNAL OF BIOLOGICAL CHEMISTRY 24 JAN 1997, vol. 272, no. 4, 24 January 1997 (1997-01-24), pages 2156-2162, XP002481101 ISSN: 0021-9258 abstract	1, 2, 10
A	AEED P A ET AL: "Partial characterization of the N-linked oligosaccharide structures on P-selectin glycoprotein ligand-1 (PSGL-1)." CELL RESEARCH MAR 2001, vol. 11, no. 1, March 2001 (2001-03), pages 28-36, XP002481102 ISSN: 1001-0602 the whole document	1

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## INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2007/004164

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DI STASIO ENRICO ET AL: "A fast and accurate procedure to collect and analyze unfolding fluorescence signal: The case of dystroglycan domains." BIOPHYSICAL CHEMISTRY, vol. 107, no. 2, 1 February 2004 (2004-02-01), pages 197-211, XP002481103 ISSN: 0301-4622 page 209, column 1, line 14 - column 2, line 13; figure 1	1
A	HAMILTON S R ET AL: "Production of complex human glycoproteins in yeast" SCIENCE, WASHINGTON, DC, vol. 301, no. 5637, 29 August 2003 (2003-08-29), pages 1244-1246, XP002267832 ISSN: 0036-8075 abstract	
E	WO 2007/039788 A (RECOPHARMA AB [SE]; HOLGERSSON JAN [SE]; LIU JINING [SE]; GUSTAFSSON A) 12 April 2007 (2007-04-12) the whole document	1-11,13
L	WO 2007/087420 A (RECOPHARMA AB [SE]; HOLGERSSON JAN [SE]; GUSTAVSSON ANKI [SE]) 2 August 2007 (2007-08-02) Double patenting the whole document	

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IB2007/004164

## 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:  

Although claim 12 is 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 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 allsearchable 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.:
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.:

1-14

### 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-14

A fusion polypeptide comprising a first polypeptide operably linked to a second polypeptide wherein the first polypeptide is mannosylated and the second polypeptide comprises at least a region of an immunoglobulin polypeptide; an adjuvant composition comprising said fusion polypeptide; medical use thereof; and a yeast cell genetically engineered to produce said fusion polypeptide.

2. claims: 15-19

A genetically engineered lower eukaryotic cell producing human-like glycoproteins characterized as having O-linked glycans and a recombinant lower eukaryotic cell producing human-like glycoproteins wherein said cell comprises a nucleic acid molecule encoding N-acetylgalactosaminyltransferase(s).

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2007/004164

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 03088995	A	30-10-2003	AU 2003228067 A1 03-11-2003
			CA 2483473 A1 30-10-2003
			EP 1517700 A2 30-03-2005
			JP 2005530493 T 13-10-2005
US 6177256	B1	23-01-2001	NONE
WO 03089450	A	30-10-2003	AU 2003233008 A1 03-11-2003
			CA 2483476 A1 30-10-2003
			EP 1517923 A2 30-03-2005
			JP 2005532793 T 04-11-2005
WO 03010201	A	06-02-2003	AU 2002321760 B2 03-04-2008
			CA 2454469 A1 06-02-2003
			EP 1409542 A2 21-04-2004
			JP 2005503786 T 10-02-2005
			NO 20040249 A 18-03-2004
WO 2007039788	A	12-04-2007	AU 2005337047 A1 12-04-2007
			CA 2589422 A1 12-04-2007
			JP 2008517073 T 22-05-2008
WO 2007087420	A	02-08-2007	NONE