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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- with sequence listing part of description published separately in electronic form and available upon request from the International Bureau

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

3 April 2008

(54) Title: USE OF EXENDINS AND GLP-I RECEPTOR AGONISTS FOR ALTERING LIPOPROTEIN PARTICLE SIZE AND SUBCLASS COMPOSITION

(57) Abstract: The present invention relates to altering the concentration of various lipid molecules, specifically for example by shifting from small LDL particles to large LDL and HDL particles. The present invention also relates to methods for increasing average lipid particle size and methods for improving the cardiovascular risk profile of a subject by altering lipid particle sizes or concentrations or both.



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## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/017540

A. CLASSIFICATION OF SUBJECT MATTER  
 INV. A61K38/22 A61P3/06 A61P3/10

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 A61P

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, FSTA, BIOSIS, EMBASE, 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 01/66135 A (NOVO NORDISK A/S)<br>13 September 2001 (2001-09-13)                            | 1-7,<br>11-34,<br>37-42,<br>58-61,<br>73-80,<br>84,89,<br>91-100<br>1-100 |
| Y         | * See the whole document (GLP-1 agonists<br>to increase HDL/lower LDL) *<br><br>-----<br>-/-- |                                                                           |
|           |                                                                                               |                                                                           |

☒ 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

30 January 2008

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11/02/2008

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## 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         | FORMAN ET AL (EDITOR): "ADA PREVIEW;<br>ABSTRACT HIGHLIGHTS; JUNE 10 CONFERENCE<br>CALL; SAN DIEGO, CA, 10-14 JUNE, 2005"<br>INDUSTRY UPDATE / WR HAMBRECHT+CO,<br>7 June 2005 (2005-06-07), pages 1-24,<br>XP002466765<br>Retrieved from the Internet:<br>URL:www.wrhambrecht.com/sector/pharm/notes<br>/ir20050607.pdf> [retrieved on 2008-01-29]              | 1-7, 10,<br>12-34,<br>37-45,<br>73-80,<br>84,<br>91-100 |
| Y         | * See in particular page 7 (exendin-4<br>= exenatide -> LDL reduction, HDL<br>increase) *                                                                                                                                                                                                                                                                        | 1-100                                                   |
| Y         | GEDULIN ET AL: "Exenatide (exendin-4)<br>improves insulin sensitivity and beta-cell<br>mass in insulin-resistant obese fa/fa<br>Zucker rats independent of glycemia and<br>body weight"<br>ENDOCRINOLOGY,<br>vol. 146, 2005, pages 2069-2076,<br>XP002466767<br>* See page 2069 (end of left column)<br>and page 2071 (Table 1/HDL) *                            | 1-100                                                   |
| Y         | BUSE ET AL: "Effects of exenatide<br>(exendin-4) on glycaemic control over 30<br>weeks in sulfonylurea-treated patients<br>with type 2 diabetes"<br>DIABETES CARE,<br>vol. 27, 2004, pages 2628-2635,<br>XP002431949<br>* See page 2632 (LDL/HDL) *                                                                                                              | 1-100                                                   |
| P, X      | KAPITZA ET AL: "Long-term treatment with<br>exenatide was associated with improved<br>post-prandial glycaemic control and a<br>shift from small to large HLD and LDL<br>particles"<br>DIABETES MEDICINE (SUPPLEMENT 4/2006),<br>vol. 23, December 2006 (2006-12), page<br>532, XP002466768<br>* See Abstract P1493 (compare<br>the Example of the Application) * | 1-100                                                   |

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

Continuation of Box II.1

Although Claims 1-100 are directed to a method of treatment of the human body, the search has been carried out and been based on the alleged effects of the compounds/compositions.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2007/017540

## 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:  
see FURTHER INFORMATION sheet PCT/ISA/210
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:

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 reportcovers 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

Information on patent family members

International application No  
PCT/US2007/017540

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date    |
|-------------------------------------------|---------------------|----------------------------|------------------------|
| WO 0166135                                | A                   | 13-09-2001                 | AT 309818 T 15-12-2005 |
|                                           |                     | AU 3725401 A               | 17-09-2001             |
|                                           |                     | DE 60114996 D1             | 22-12-2005             |
|                                           |                     | DE 60114996 T2             | 10-08-2006             |
|                                           |                     | EP 1263458 A1              | 11-12-2002             |
|                                           |                     | ES 2253353 T3              | 01-06-2006             |
|                                           |                     | JP 2003525908 T            | 02-09-2003             |
| <hr/>                                     |                     |                            |                        |