Title: TARGETED NANOCARRIER SYSTEMS FOR DELIVERY OF ACTIVES ACROSS BIOLOGICAL MEMBRANES

Abstract: Disclosed herein are nanoparticle, micelle and/or liposome compositions, each comprising a therapeutic agent encapsulated in one or more polymer(s), wherein a vitamin B12 or a derivative thereof is attached to the one or more polymer(s) via a linker group, as well as methods for making and using same.

FIG. 1
Declarations under Rule 4.17:

- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(in))

Published:

- 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))

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

14 March 2013
INTERNATIONAL SEARCH REPORT

PCT/US2012/028138

A. CLASSIFICATION OF SUBJECT MATTER
A61K47/48
A61P5/48 A61P35/02

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
A61K

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)
EPO-Internal , BIOSIS, EMBASE, CHEM ABS Data, DISSERTATION ABS, PASCAL, WPI Data

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>
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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 application or patent but published on or after the international filing date
* "L" document(s) of which the priority claim(s) on which the international application is based
* "O" document referring to an oral disclosure, use, exhibition or other special reason (as specified)

*"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

"A" document member of the same patent family

Date of the actual completion of the international search
4 September 2012

Date of mailing of the international search report
11/01/2013

Name and mailing address of the ISA/
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk
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Dul laart, Anwyn

Form PCT/ISA2/210 (second sheet) (April 2005)
### 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. ☐ 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.:

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.:

   see annex

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

1. claims: 1-10, 23-41 (all partially)
   Nanoparticle or micelle as defined in these claims, wherein the polymer is dextrans or carboxymethyl dextran
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2. claims: 1-10, 23 (all partially)
   Nanoparticle or micelle as defined in these claims, wherein the polymer is chitosan or trimethyl chitosan
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3. claims: 1-10, 23-41 (all partially)
   Nanoparticle or micelle as defined in these claims, wherein the polymer is a polyester selected from poly(lactide-co-glycolide) (PGLA), polylactide acid (PLA) or polyglycolide acid (PGA)
   ---

4. claims: 1-10, 23-41 (all partially)
   Nanoparticle or micelle as defined in these claims, wherein the polymer is polyvinylalcohol (PVA)
   ---

5. claims: 1-10, 23-41 (all partially)
   Nanoparticle or micelle as defined in these claims, wherein the polymer is a polyanhydride
   ---

6. claims: 1-10, 23-41 (all partially)
   Nanoparticle or micelle as defined in these claims, wherein the polymer is a polyacylate
   ---

7. claims: 1-10, 23-41 (all partially)
   Nanoparticle or micelle as defined in these claims, wherein the polymer is a polyacylamide
   ---

8. claims: 1-10, 23-41 (all partially)
   Nanoparticle or micelle as defined in these claims, wherein the polymer is polymethacrylate
   ---

9. claims: 1-10, 23-41 (all partially)
Nanoparticle or micelle as defined in these claims, wherein the polymer is cellulose or hypromellose
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10. claims: 1-10, 23-41 (partially)

Nanoparticle or micelle as defined in these claims, wherein the polymer is starch
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11. claims: 1-10, 23-41 (partially)

Nanoparticle or micelle as defined in these claims, wherein the polymer is a dendrimer
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12. claims: 1-10, 23-41 (partially)

Nanoparticle or micelle as defined in these claims, wherein the polymer is a peptide or a protein
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13. claims: 1-10, 23-41 (partially)

Nanoparticle or micelle as defined in these claims, wherein the polymer is a polyethylene glycol
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14. claims: 1-10, 23-41 (partially)

Nanoparticle or micelle as defined in these claims, wherein the polymer is a poly(ethylene glycol-co-propylene glycol)
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15. claims: 1-19, 23-41 (partially)

Nanoparticle or micelle as previously defined, further comprising a polymer coating encompassing the nanoparticle or micelle
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16. claims: 20 (completely); 1-19, 23-41 (partially)

Nanoparticle or micelle as previously defined, further comprising a polymer coating encompassing the nanoparticle or micelle, and comprising a targeting agent other than vitamin B12
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17. claims: 21, 22 (completely); 23-31 (partially)

Liposome as defined in these claims
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<th>Relevant to claim No.</th>
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<td>wo 02/067995 AI (COUNCIL SCI ENT IND RES [IN] ; CHALASANI KISHORE BABU [IN] ; DIWAN PRAKAS) 6 September 2002 (2002-09-06) page 18 - page 22</td>
<td>1-10, 23-41</td>
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<td>CHALASANI ET AL: &quot;Effecti ve oral deli very of insulin in animal model s usi ng v i tamin B12-coated dextran nanoparti cles&quot;, JOURNAL OF CONTROLLED RELEASE, vol. 122, no. 2, 5 September 2007 (2007-09-05), pages 141-150, XP022230608, ISSN: 0168-3659, DOI: 10.1016/J.JCONREL.2007.05.019 abstract page 142, right-hand column page 144, left-hand column, paragraph 2.3 - right-hand column, paragraph 2.5 page 147, left-hand column, paragraph 3.3.2 - page 148, left-hand column, line 11 page 149, left-hand column, paragraph 3.3.7</td>
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<td>RUSSELL-JONES G J: &quot;Use of targeting agents to increase uptake and localization of drugs to the intestinal epithelium&quot;, JOURNAL OF DRUG TARGETING - CELLULAR ASPECTS OF TARGETING IN THE GASTROINTESTINAL TRACT, vol. 12, no. 2, 2004, pages 113-123, XP008155552, ISSN: 1061-186X, DOI: 10.1080/10611860410001693760 page 118 - page 119 ----</td>
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<td>wo 2012/030745 AI (ACCESS PHARMAECUTICALS INC [US]; ZARZYCKI RYSZARD [US]; SOOD PAUL [US]) 8 March 2012 (2012-03-08) examples 1-4 claims ----</td>
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