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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))*

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

(88) Date of publication of the international search report:
29 June 2017

WO 2017/085212 A3

(54) Title: SURFACE-MODIFIED NANOSPHERES ENCAPSULATING ANTIGEN-BINDING MOLECULES

(57) Abstract: The present invention relates to nanospheres which comprise a polymeric matrix and antigen-binding molecules esterase-releasably incorporated therein and are coated with targeting molecules which increase the cellular uptake of the nanospheres. The polymeric matrix is formed by poly(alkyl cyanoacrylates) and/or alkoxy derivatives thereof. The invention further relates to methods for preparing and compositions comprising such nanospheres.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2016/078057

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K47/62 A61K47/69
ADD. A61P37/00

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

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, 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	R. M. KOFFIE ET AL: "Nanoparticles enhance brain delivery of blood-brain barrier-impermeable probes for in vivo optical and magnetic resonance imaging", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 108, no. 46, 7 November 2011 (2011-11-07), pages 18837-18842, XP055110283, ISSN: 0027-8424, DOI: 10.1073/pnas.1111405108 abstract page 18838, right-hand column page 18840, right-hand column	1-24

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[X] Further documents are listed in the continuation of Box C.

[X] 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 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

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16 May 2017	29/05/2017

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Dullaart, Anwyn

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Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2009/135855 A2 (GLAXO GROUP LTD [GB]; PAPANICOLAOU IRENE [GB]) 12 November 2009 (2009-11-12) examples 5,7-13	1-24
X	WO 2009/135854 A2 (GLAXO GROUP LTD [GB]; FIDANBOYLU MEHMET [GB]; PAPANICOLAOU IRENE [GB]) 12 November 2009 (2009-11-12) examples 5-8	1-24
X	RYOUNG KIM H ET AL: "Low-density lipoprotein receptor-mediated endocytosis of PEGylated nanoparticles in rat brain endothelial cells", CMLS CELLULAR AND MOLECULAR LIFE SCIENCES, vol. 64, no. 3, 26 January 2007 (2007-01-26), pages 356-364, XP019488170, ISSN: 1420-9071, DOI: 10.1007/S00018-007-6390-X abstract figures page 360, paragraph Discussion - page 363	1-24
Y	SANJEEB K. SAHOO ET AL: "Enhanced Antiproliferative Activity of Transferrin-Conjugated Paclitaxel-Loaded Nanoparticles Is Mediated via Sustained Intracellular Drug Retention", MOLECULAR PHARMACEUTICS, vol. 2, no. 5, October 2005 (2005-10), pages 373-383, XP055372660, ISSN: 1543-8384, DOI: 10.1021/mp050032z abstract page 374, right-hand column - page 375, left-hand column page 376, left-hand column page 377; figure 1 page 379, paragraph Discussion; figure 3	1-24
Y	YASHWANT GUPTA ET AL: "Transferrin-conjugated solid lipid nanoparticles for enhanced delivery of quinine dihydrochloride to the brain", JOURNAL OF PHARMACY AND PHARMACOLOGY, vol. 59, no. 7, July 2007 (2007-07), pages 935-940, XP055372635, ISSN: 0022-3573, DOI: 10.1211/jpp.59.7.0004 abstract page 936 figures; tables page 940, left-hand column, paragraph Conclusion	1-24

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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.
Y	US 5 972 707 A (ROY KRISHNENDU [US] ET AL) 26 October 1999 (1999-10-26) example 2	1-24

X	JÖRG KREUTER: "Mechanism of polymeric nanoparticle-based drug transport across the blood-brain barrier (BBB)", JOURNAL OF MICROENCAPSULATION., vol. 30, no. 1, 7 June 2012 (2012-06-07), pages 49-54, XP055372945, ISSN: 0265-2048, DOI: 10.3109/02652048.2012.692491 abstract page 52 - page 53	1-24

Y	KUMAR PRITI ET AL: "Transvascular delivery of small interfering RNA to the central nervous system", NATURE, NATURE PUBLISHING GROUP, UNITED KINGDOM, vol. 448, no. 7149, 5 July 2007 (2007-07-05), pages 39-45, XP002499820, ISSN: 0028-0836, DOI: 10.1038/NATURE05901 abstract page 42, paragraph Discussion	1-24

Y	JA-YOUNG KIM ET AL: "Brain-targeted delivery of protein using chitosan- and RVG peptide-conjugated, pluronic-based nano-carrier", BIOMATERIALS, vol. 34, no. 4, 2013, pages 1170-1178, XP055372710, ISSN: 0142-9612, DOI: 10.1016/j.biomaterials.2012.09.047 abstract page 1171 figures tables page 1177, right-hand column, paragraph Conclusion	1-24

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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.
Y	HWANG D ET AL: "Development of brain targeted microRNA delivery system using RVG-PEI polymer nanoparticle", SOCIETY FOR NEUROSCIENCE ABSTRACT VIEWER AND ITINERARY PLANNER, [Online] vol. 40, 2010, XP002770183, & NEUROSCIENCE MEETING OF SOCIETY-FOR-NEUROSCIENCE; SAN DIEGO, CA, USA; 2010, Retrieved from the Internet: URL:http://www.abstractsonline.com/Plan/AbstractPrintView.aspx?mID=2554&sKey=dd5cfcdb-d0b9-4cc6-ad1b-ee8a757bf557&cKey=f13d1351-7680-4d50-83bf-41782e65a67e> [retrieved on 2017-05-15] abstract -----	1-24
X,P	WO 2015/181344 A1 (ABBVIE DEUTSCHLAND [DE]) 3 December 2015 (2015-12-03) examples claims -----	1-24

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2016/078057

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.:

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-24(partially)

   A nanosphere, a method for its preparation, and a pharmaceutical composition containing a plurality of these nanospheres, as defined in these claims, wherein the targeting polypeptide is an apolipoprotein, or its receptor binding domain.

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2. claims: 1-24(partially)

   A nanosphere, a method for its preparation, and a pharmaceutical composition containing a plurality of these nanospheres, as defined in these claims, wherein the targeting polypeptide is transferrin, or its receptor binding domain.

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3. claims: 1-24(partially)

   A nanosphere, a method for its preparation, and a pharmaceutical composition containing a plurality of these nanospheres, as defined in these claims, wherein the targeting polypeptide is rabies virus glycoprotein (GVP), or its receptor binding domain.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2016/078057

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2009135855 A2	12-11-2009	AU 2009245786 A1	12-11-2009
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