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— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

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19 July 2007

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(54) Title: FC-FUSION CONSTRUCTS BINDING TO PHOSPHATIDYLSERINE AND THEIR THERAPEUTIC USE

(57) Abstract: Disclosed are new phosphatidylserine binding constructs with surprising combinations of properties, and a range of diagnostic and therapeutic conjugates thereof. The new constructs effectively bind phosphatidylserine targets in disease and enhance their destruction, and can also specifically deliver attached imaging or therapeutic agents to the disease site. Also disclosed are methods of using the new construct compositions, therapeutic conjugates and combinations thereof in tumor vasculature targeting, cancer diagnosis and treatment, and for treating viral infections and other diseases.

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# INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/46 A61K38/48 A61K38/37

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)
C07K 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 practical, search terms used)
EPO-Internal, Sequence Search, BIOSIS, WPI Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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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 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 | Date of mailing of the international search report |
|---|---|
| 25 April 2007 | 18/05/2007 |

| Name and mailing address of the ISA/ | Authorized officer |
|---|---|
| European Patent Office, P.B. 5818 Patentlaan 2<br>NL – 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,<br>Fax: (+31-70) 340-3016 | Lechner, Oskar |

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

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| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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# INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/002964

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| A | PHILIP E. THORPE: "Antibodies to Anionic Phospholipids as Vascular Targeting Agents for Cancer Treatment" EUROCONFÉRENCES- ANGIOGENESIS 2, [Online] 19 June 2003 (2003-06-19), - 20 June 2003 (2003-06-20) XP002430977 Paris, FR. Retrieved from the Internet: URL:http://www.pasteur.fr/applications/eur oconf/angio2/12Thorpe.pdf> abstract | 1,5-72 |
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# INTERNATIONAL SEARCH REPORT

International application No.
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**Box 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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 54-72 are 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 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 fee, this Authority did not invite payment of any additional fee.

3. [X] 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, 2, 15-72 (all partially only aas far as relating to invention 1) 1
15-72 (partially as far as realting to invention 14)
5-14 (in full as being restricted to b2GPI, i.e. invention 14)

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.

[X] 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, 2, 15-72 (all in part)

A construct comprising an Ab Fc region operatively attached to at least a first phosphatidylserine binding protein, said protein being protein C, and therapeutic uses thereof

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2. claims: 1, 2, 15-72 (all in part)

A construct comprising an Ab Fc region operatively attached to at least a first phosphatidylserine binding protein, said protein being protein S, and therapeutic uses thereof

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3. claims: 1, 2, 15-72 (all in part)

A construct comprising an Ab Fc region operatively attached to at least a first phosphatidylserine binding protein, said protein being factor II (prothrombin), and therapeutic uses thereof

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4. claims: 1,2,15-72 (all in part)

A construct comprising an Ab Fc region operatively attached to at least a first phosphatidylserine binding protein, said protein being factor Vand therapeutic uses thereof.

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5. claims: 1,2,15-72 (all in part)

A construct comprising an Ab Fc region operatively attached to at least a first phosphatidylserine binding protein, said protein being factor VII, and therapeutic uses thereof.

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6. claims: 1,2,15-72 (all in part)

A construct comprising an Ab Fc region operatively attached to at least a first phosphatidylserine binding protein, said protein being factor IX and therapeutic uses thereof.

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7. claims: 1,2,15-72 (all in part)

A construct comprising an Ab Fc region operatively attached to at least a first phosphatidylserine binding protein, said protein being factor X, and therapeutic uses thereof.

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8. claims: 1,2,15-72 (all in part)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A construct comprising an Ab Fc region operatively attached to at least a first phosphatidylserine binding protein, said protein being mer proto-oncogene tyrosine kinase (Mer), and therapeutic uses thereof

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9. claims: 1,3,15-72 (all in part)

A construct comprising an Ab Fc region operatively attached to at least a first phosphatidylserine binding protein, said protein being PS-binding scavenger receptor, and therapeutic uses thereof

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10. claims: 1,3,15-72 (all in part)

A construct comprising an Ab Fc region operatively attached to at least a first phosphatidylserine binding protein, said protein being alpha3beta3 integrin, and therapeutic uses thereof

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11. claims: 1,3,15-72 (all in part)

A construct comprising an Ab Fc region operatively attached to at least a first phosphatidylserine binding protein, said protein being complement receptor CR3, and therapeutic uses thereof

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12. claims: 1,3,15-72 (all in part)

A construct comprising an Ab Fc region operatively attached to at least a first phosphatidylserine binding protein, said protein being complement receptor CR4, and therapeutic uses thereof

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13. claims: 1,4,15-72 (all in part)

A construct comprising an Ab Fc region operatively attached to at least a first phosphatidylserine binding protein, said protein being phosphatidylserine receptor (PSr), and therapeutic uses thereof

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14. claims: 1-72 (all in part)

A construct comprising an Ab Fc region operatively attached to at least a first phosphatidylserine binding protein, said protein being beta2-glycoprotein (2beta-GPI), and therapeutic uses thereof

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2006/002964

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
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