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- (74) Agents: **HSI, Jeffrey, D.** et al.; Edwards & Angell, LLP, P.O. Box 55874, Boston, MA 02205 (US).
- (21) International Application Number: PCT/US2004/026485
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- (71) Applicant (*for all designated States except US*): **SYNOVO GMBH** [DE/DE]; Paul-Ehrlich-Strasse 15, 72076 Tübingen (DE).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): **GUTKE, Hans-Jurgen** [DE/DE]; Sauerampferweg 14a, 70599 Stuttgart (DE). **FLOHR, Christian** [GE/GE]; Harzstrasse 57, 72074 Tübingen (GE). **BECK, Albert** [DE/DE]; Talstrasse 8, 72147 Nehren (DE). **MARGUTTI, Simona** [IT/DE]; Dorfackerstrasse 18, 72074 Tübingen (DE). **EGGERS, Mary** [US/DE]; Blasenbergstrasse 29, 72119 Ammerbuch (DE). **GUSE, Jan-Hinrich** [DE/DE]; Ziegelhüttestrasse 68, 72072 Tübingen-Bühl (DE). **KHOBZAOUI, Moussa** [FR/DE]; Raichbergstrasse 40A, 72072 Tübingen (DE). **BURNET, Michael** [US/DE]; August-Lammle-Strasse 2, 72127 Kusterdingen (DE).
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- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: CONJUGATES OF BIOLOGICALLY ACTIVE COMPOUNDS, METHODS FOR THEIR PREPARATION AND USE, FORMULATION AND PHARMACEUTICAL APPLICATIONS THEREOF

(57) Abstract: This invention features a compound of the following formula: T-(L-C)<sub>m</sub>, T is a transportophore, L is a bond or a linker having a molecular weight up to 240 dalton, C is a non-antibiotic therapeutic agent, and m is 1, 2, 3, 4, 5, 6, 7, or 8, in which the transportophore has an immune selectivity ratio of at least 2, the transportophore is covalently bonded to the non-antibiotic therapeutic agent via the bond or the linker, and the compound has an immune selectivity ratio of at least 2.



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**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US04/26485

<p><b>A. CLASSIFICATION OF SUBJECT MATTER</b>                  IPC(7) : C07G 11/00; C07H 15/00, 17/08; A01N 43/04                  US CL : 514/ 25, 27, 28, 29; 536/4.1, 7.1, 7.2                  According to International Patent Classification (IPC) or to both national classification and IPC</p>												
<p><b>B. FIELDS SEARCHED</b></p> <p>Minimum documentation searched (classification system followed by classification symbols)                  U.S. : 514/ 25, 27, 28, 29; 536/4.1, 7.1, 7.2</p> <p>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched                  Medline Plus</p> <p>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)                  STN, Registry, CAPLUS, Google, PALM, EAST</p>												
<p><b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b></p> <table border="1"> <thead> <tr> <th>Category *</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X</td> <td>US 5,466,681 (KRIVAN et al.) 14 November 1995 (14.11.1995), whole document, especially column 6, line 53).</td> <td>1-13, 16, 25, and 27</td> </tr> <tr> <td>X</td> <td>US 5,928,868 (LIU et al.) 27 July 1999 (27.07.1999) whole document, especially figure 7B.</td> <td>1-3, 5, 14, 18, 25-26, and 28</td> </tr> </tbody> </table>			Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X	US 5,466,681 (KRIVAN et al.) 14 November 1995 (14.11.1995), whole document, especially column 6, line 53).	1-13, 16, 25, and 27	X	US 5,928,868 (LIU et al.) 27 July 1999 (27.07.1999) whole document, especially figure 7B.	1-3, 5, 14, 18, 25-26, and 28	
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<p><input type="checkbox"/> Further documents are listed in the continuation of Box C.      <input type="checkbox"/> See patent family annex.</p>												
<p>* Special categories of cited documents:</p> <table border="0"> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"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</td> </tr> <tr> <td>"E" earlier application or patent published on or after the international filing date</td> <td>"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</td> </tr> <tr> <td>"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)</td> <td>"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</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td>"&amp;" document member of the same patent family</td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance	"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	"E" earlier application or patent published on or after the international filing date	"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	"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)	"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	"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	"P" document published prior to the international filing date but later than the priority date claimed	
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<p>Date of the actual completion of the international search                  19 March 2005 (19.03.2005)</p>		<p>Date of mailing of the international search report  <b>27 APR 2005</b></p>										
<p>Name and mailing address of the ISA/US                  Mail Stop PCT, Attn: ISA/US                  Commissioner for Patents                  P.O. Box 1450                  Alexandria, Virginia 22313-1450                  Facsimile No. (703) 305-3230</p>		<p>Authorized officer <i>James O. Wilson</i>                  James O. Wilson                  Telephone No. 571-272-0700</p>										

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/26485

**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.: 15,17,21 and 24  
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:  
Claims 15, 17, 21, and 24 all intend to limit subject matter in claim 1 which was not claimed in claim 1, and as such, it is unclear as to what applicants are intending in claims 15, 17, 21, and 24.
  
- 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 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.  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.  
 No protest accompanied the payment of additional search fees.