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(71) Applicant (for all designated States except US): **UNIVERSITY OF MANITOBA** [CA/CA]; 631 Drake Centre, Winnipeg, Manitoba R3T 5V4 (CA).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **SCHWEIZER, Frank** [CA/CA]; 631 Drake Centre, Winnipeg, Manitoba R3T 5V4 (CA). **ZHANEL, George, G.** [—/CA]; 631 Drake Centre, Winnipeg, Manitoba R3T 5V4 (CA). **BERA, Smritilekha** [—/CA]; 631 Drake Centre, Winnipeg, Manitoba R3T 5V4 (CA).

(81) Designated States (unless otherwise indicated, for every

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1 April 2010

(54) Title: TRIAZOLE-BASED AMINOGLYCOSIDE-PEPTIDE CONJUGATES AND METHODS OF USE

(57) Abstract: Aminoglycoside-amino acid and -peptide conjugates comprising a triazolyl linker are provided along with efficient methods of their preparation. The aminoglycoside may be an aminoglycoside antibiotic. Conjugates comprising an aminoglycoside antibiotic may exhibit antimicrobial activities against Gram-positive and/or Gram-negative strains and display significantly enhanced activity against multi-drug resistant MRSA and MRSE when compared to their unconjugated aminoglycoside antibiotic counterparts.



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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the 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. Claim Nos. : 52-58, 109-115
because they relate to subject matter not required to be searched by this Authority, namely :

Claims 52-58, 109-115 are directed to a method for treatment of the human or animal body by surgery or therapy which the International Search Authority is not required to search. However, this Authority has carried out a search based on the alleged effects or purposes/uses of the product defined in claims.
2. Claim Nos. : 1-20, 22, 39-49, 59-77, 79, 81, 95-104, 107, 108
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 :

See extra sheet (page 6)
3. Claim 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 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 claim 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 claim 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

International application No.
PCT/IB2008/003486

A. CLASSIFICATION OF SUBJECT MATTER IPC: <i>C07H 19/056</i> (2006.01), <i>A61K 31/7028</i> (2006.01), <i>A61K 45/00</i> (2006.01), <i>A61K 47/48</i> (2006.01), <i>A61P 31/04</i> (2006.01), <i>C07G 11/00</i> (2006.01), <i>C07G 3/00</i> (2006.01), <i>C07K 1/06</i> (2006.01), <i>C07K 4/00</i> (2006.01), <i>C07K 5/078</i> (2006.01), <i>C07K 5/097</i> (2006.01), <i>C07K 5/117</i> (2006.01), <i>C07K 9/00</i> (2006.01) 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) <i>C07H 19/056</i> (2006.01), <i>A61K 31/7028</i> (2006.01), <i>A61K 45/00</i> (2006.01), <i>A61K 47/48</i> (2006.01), <i>A61P 31/04</i> (2006.01), <i>C07G 11/00</i> (2006.01), <i>C07G 3/00</i> (2006.01), <i>C07K 1/06</i> (2006.01), <i>C07K 4/00</i> (2006.01), <i>C07K 5/078</i> (2006.01), <i>C07K 5/097</i> (2006.01), <i>C07K 5/117</i> (2006.01), <i>C07K 9/00</i> (2006.01)		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used) Canadian Patent Database, STN, Delphion, Scopus (triazole, antibiotic, aminoglycoside, glycopeptide)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Kuijpers, B. H. M., et al., Expedient synthesis of triazole-linked glycosyl amino acids and peptides, <i>Org. Lett.</i> , 2004, vol. 6, no. 18, pp. 3123-3126 Whole document; Compounds 18-20	1-51, 59-108
X	Macmillan, D. and Blanc, J., A novel neoglycopeptide linkage compatible with native chemical ligation, <i>Org. Biomol. Chem.</i> , 2006, vol. 4, pp. 2847-2850 Compounds 12, 13	1-51, 59-108
X, P	WO 2008/001109 (MACMILLAN, D., et al.) 03 January 2008 (03-01-2008) Claims, Example page 40-41	1-51, 59-108
A	Quader, S., et al., Multisite modification of neomycin B: Combined Mitsunobu and click chemistry approach, <i>J. Org. Chem.</i> , 2007, vol. 72, pp. 1962-1979 Whole document; Compounds 17-19	1-115
[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.		
* Special categories of cited documents:	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"&"	document member of the same patent family
"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		
Date of the actual completion of the international search 16 April 2009 (16-04-2009)	Date of mailing of the international search report 28 May 2009 (28-05-2009)	
Name and mailing address of the ISA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001-819-953-2476	Authorized officer Michael Ganton 819-994-3425	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2008/003486

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Bera, S., et al., Design, synthesis, and antibacterial activities of neomycin-lipid conjugates: Polycationic lipids with potent gram-positive activity, J. Med. Chem., 2008, vol. 51, pp. 6160-6164 Whole document; Compounds 13-19	1-115
A	Pietrzik, N., et al., Efficient synthesis of glycosylated asparaginic acid building blocks via click chemistry, Synthesis, 2008, vol. 4, pp. 519-526 Whole document; Compounds 5a, 5b, 5d, 5e, 5f	1-51, 59-108

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2008/003486

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
WO 2008001109A2	03-01-2008	EP 2046810A2	15-04-2009
		GB 0613147D0	09-08-2006
		GB 2440388A	30-01-2008
		WO 2008001109A3	26-06-2008

Continuation of Box II.2

Claims 1-20, 22, 39-49, 59-77, 79, 81, 95-104, 107, 108 relate to an extremely large number of possible compounds. There are such a large number of possibilities for compounds that are defined broadly as "aminoglycoside-(amino acid/peptide) conjugate(s)" which comprise a "triazolymethyl linker" that a meaningful search of the claims 1-20, 22, 39-49, 59-77, 79, 81, 95-104, 107, 108 is impossible. Consequently, the search has been carried out for the compounds representing the subject matter of claims 21, 23, 24, 36, 50, 78, 80, 82, 94 and 105.