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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: SPACER MOIETY FOR POLY(ETHYLENE GLYCOL) -MODIFIED PEPTIDES

(57) Abstract: The present invention relates to a compound comprising a peptide moiety, a spacer moiety and a water-soluble polymer moiety such as a poly(ethylene glycol) moiety. The spacer moiety is between the peptide moiety and the water-soluble polymer moiety. The spacer moiety has the structure: $-NH-(CH_2)_\alpha-[O-(CH_2)_\beta]_\gamma-O_\delta-(CH_2)_\varepsilon-Y-$ wherein α, β, γ, δ,and ε are each integers whose values are independently selected.

WO 2004/100997 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/014887

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K47/48 A61K38/00

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)
IPC 7 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, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 179 337 A (DAVIS FRANK F ET AL) 18 December 1979 (1979-12-18) the whole document	1,5,7,9, 10,16, 20,22, 24,25, 33,35
X	WO 00/33881 A (ORSOLINI PIERO ; DEBIO RECH PHARMA SA (CH); CALICETI PAOLO (IT); SCHIA) 15 June 2000 (2000-06-15) the whole document	1,2,5,7, 9,10,12, 16,17, 20,22, 24,25, 27, 31-33,35

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

[X] Patent family members are listed in annex.

° Special categories of cited documents :

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Date of the actual completion of the international search	Date of mailing of the international search report
18 February 2005	21. 03. 05

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, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Vogt, T

Form PCT/ISA/210 (second sheet) (January 2004)

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 92/16555 A (ENZON INC) 1 October 1992 (1992-10-01) the whole document	1,2,5,7, 9,10,16, 17,20, 22,24, 25, 31-33,35
X	WO 00/24770 A (AMGEN INC) 4 May 2000 (2000-05-04) sequence 18	1,5,7,9, 11-13, 16,20, 22,24, 26-28, 30,33,35
X	WO 98/25965 A (GLAXO GROUP LTD ; BALASUBRAMANIAN PALANIAPPAN (US); DEPRINCE RANDOLPH) 18 June 1998 (1998-06-18) the whole document	1,5,7,9, 11-13, 15,16, 20,22, 24, 26-28, 30,33,35
X	WO 96/40772 A (JOHNSON & JOHNSON ; JOHNSON DANA L (US); ZIVIN ROBERT A (US)) 19 December 1996 (1996-12-19) the whole document	1,5,7,9, 10, 12-14, 16,17, 20,22, 24,25, 27-29, 33,35
A	WO 96/40750 A (GLAXO GROUP LTD ; GATES CHRISTIAN M (US); JOHNSON SHERRIL S (US); WRIG) 19 December 1996 (1996-12-19) the whole document	
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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.
X	GREENWALD R B ET AL: "Effective drug delivery by PEGylated drug conjugates" ADVANCED DRUG DELIVERY REVIEWS, AMSTERDAM, NL, vol. 55, no. 2, 10 February 2003 (2003-02-10), pages 217-250, XP002275066 ISSN: 0169-409X the whole document	1-3,5, 10,12, 16-18, 20,25, 27,33,35
X	GREENWALD RICHARD B ET AL: "Controlled release of proteins from their poly(ethylene glycol) conjugates: Drug delivery systems employing 1,6-elimination." BIOCONJUGATE CHEMISTRY, vol. 14, no. 2, 3 April 2003 (2003-04-03), pages 395-403, XP002318263 ISSN: 1043-1802 the whole document	1,2,5-7, 9,10,16, 17,20, 22,24, 25, 31-33,35
A	US 2002/015691 A1 (GREENWALD RICHARD B ET AL) 7 February 2002 (2002-02-07) the whole document	
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A	US 6 113 906 A (GREENWALD ET AL) 5 September 2000 (2000-09-05) the whole document	
A	WO 02/065988 A (ENZON, INC) 29 August 2002 (2002-08-29) the whole document	
P,X	WO 2004/014424 A (ENZON INC) 19 February 2004 (2004-02-19) the whole document	1-3,5, 10,12, 16-18, 20,25, 27,33,35
E	WO 2004/101600 A (AFFYMAX, INC; YIN, KEVIN; HOLMES, CHRIS; LALONDE, GUY; BALU, PALANI; T) 25 November 2004 (2004-11-25) the whole document	1-36

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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.
E	WO 2004/101606 A (AFFYMAX, INC; YIN, KEVIN; HOLMES, CHRIS; LALONDE, GUY; BALU, PALANI; S) 25 November 2004 (2004-11-25) the whole document	1-36
E	WO 2004/101611 A (AFFYMAX, INC; YIN, KEVIN; HOLMES, CHRISTOPHER; LALONDE, GUY; BALU, PAL) 25 November 2004 (2004-11-25) the whole document	1-36
E	WO 2004/108070 A (ENZON, INC; ZHAO, HONG; GREENWALD, RICHARD, B) 16 December 2004 (2004-12-16) the whole document	1-36

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/014887

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.: 1-36 (partly)
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

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. [X] 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.

[X] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

The specific specific peptide sequences disclosed in the examples of the present application have, according to PCT Rule 13ter.1.c, not been searched since the Sequence Listing as present in the description does not comply with WIPO Standard ST 25 prescribed in the administrative instructions under Rule 5.2. The Sequence Listing has been furnished neither in paper form nor in machine readable form as provided for in the same instructions and the applicant has not remedied the disclosed deficiencies within the time limit fixed in the invitation pursuant to PCT Rule 13ter.1.a.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

Invention 1: 1,2,5-17, 20-30, 33-36 (all partial), and 31 and 32 (complete)

A conjugate comprising a peptide, a spacer and a water soluble polymer, wherein the spacer moiety is of formula: -NH-(CH2)n-Y. (hence, both .gamma. and .delta. are equal to o).

Invention 2: claims 1,2,5-17 and 20-30, 33-36 (all partial), and claims 2-4 and 17-19 (complete)

A conjugate comprising a peptide, a spacer and a water soluble polymer, wherein the spacer moiety is of the formula: -NH-(CH2)a-'O-(CH2)b!g-Od-(CH2)e-Y, wherein at least one of .gamma. or .delta. is larger then, or equal to, 1, thus forming a spacer having at least one -O-.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US2004/014887

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International Application No
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