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Declaration under Rule 4.17:

— of inventorship (Rule 4.17(iv))

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(54) Title: NEUTRALIZATION OF CD95 ACTIVITY BLOCKS INVASION OF GLIOBLASTOMA CELLS *IN VIVO*

(57) Abstract: The present invention relates to methods for treating an individual with high grade glioblastoma multiforme by preventing or disrupting the binding of CD95 to its ligand, CD95L, *in vivo*, whereupon that neutralization of CD95 activity reduces undesirable glial cell migration and invasion into body tissue.



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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2007/011461

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61P35/00 C07K16/28 A61K39/395

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 , BIOSIS, EMBASE, Sequence Search, 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	SUSANNE KLEBER: "Gamma-Bestrahlung führt zur CD95-abhängiger Invasivität in apoptotischen Glioblastomzellen." 3 January 2006 (2006-01-03), , HEIDELBERG , XP002483066 the whole document	1-7,10, 11,13-15
Y		8,9
X	WO 2004/085478 A (APOGENIX BIOTECHNOLOGY AG [DE]; WALCZAK HENNING [DE] APOGENIX BIOTECHN) 7 October 2004 (2004-10-07) figures 3A,3B claims 26,40	13,14
Y		8,9



Further documents are listed in the continuation of Box C.



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)

O¹ 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

5 June 2008

Date of mailing of the international search report

24/06/2008

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Uilbrecht , Matthi as

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2007/011461

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BARNHART BRYAN C ET AL: "CD95 ligand induces motility and invasiveness of apoptosis-resistant tumor cells." THE EMBO JOURNAL 4 AUG 2004, vol . 23, no. 15, 4 August 2004 (2004-08-04) , pages 3175-3185 , XP002483063 ISSN: 0261-4189- cited in the application abstract page 3184, left-hand column , last paragraph - right-hand column , paragraph 1	13, 14
Y	-----	8,9
X	"BD Biosciences Product Catalog Pharmingen 2003" 2003, BD BIOSCIENCES , XP002483067 page 363	13, 14
Y	-----	8,9
X	wo 99/55134 A (UNIV MICHIGAN. [US]) 4 November 1999 (1999-11-04) page 4, line 23 - line 30	15
X	US 6 060 238 A (DIXIT VISHVA M [US]) 9 May 2000 (2000-05-09) claim 1	15
X	HAUPTSCHN ROBERT S ET AL: "Functional proteomic screen identifies a modulating role for CD44 in death receptor-mediated apoptosis." CANCER RESEARCH 1 MAR 2005, vol . 65, no. 5, 1 March 2005 (2005-03-01) , pages 1887-1896, XP002483064 ISSN: 0008-5472 abstract figure 1	15
A	WELLER M ET AL: "Anti-Fas/APO-1 antibody-mediated apoptosis of cultured human glioma cells. Induction and modulation of sensitivity by cytokines." THE JOURNAL OF CLINICAL INVESTIGATION SEP 1994, vol . 94, no. 3, September 1994 (1994-09) , pages 954-964, XP002483065 ISSN: 0021-9738 the whole document	1-15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2007/011461

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.: 12
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.: 12
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 FURTHER INFORMATION sheet PCT/ISA/210
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 allsearchable 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.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2007/011461

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

a. type of material

☒

a sequence listing

☐

table(s) related to the sequence listing

b. format of material

☒

on paper

☒

in electronic form

c. time of filing/furnishing

☒

contained in the international application as filed

☒

filed together with the international application in electronic form

☐

furnished subsequently to this Authority for the purpose of search

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 1-12 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.

Continuation of Box II.2

Claims Nos. : 12

Claim 12 defined the method of treating a high grade glioma in terms of a result to be achieved, namely of preventing the interaction between CD95 and the protein p18 of PI3K. It appears that this effect is a property of the agent used. This agent is structurally not limited and the application fails to disclose any instance of such an agent. Hence, no meaningful search of claim 12 could be performed (Art. 6 PCT).

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.2), should the problems which led to the Article 17(2)PCT declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2007/011461

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			WO 9625501 A2	22-08-1996
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