



(11) **EP 2 287 201 A3**

(12) **EUROPEAN PATENT APPLICATION**

(88) Date of publication A3:
04.04.2012 Bulletin 2012/14

(51) Int Cl.:
C07K 16/30 (2006.01) **G01N 33/53** (2006.01)
G01N 33/532 (2006.01)

(43) Date of publication A2:
23.02.2011 Bulletin 2011/08

(21) Application number: **08021299.6**

(22) Date of filing: **03.03.2003**

(84) Designated Contracting States:
**AT BE BG CH CY CZ DE DK EE ES FI FR GB GR
HU IE IT LI LU MC NL PT RO SE SI SK TR**

(30) Priority: **01.03.2002 US 360229 P**

(62) Document number(s) of the earlier application(s) in
accordance with Art. 76 EPC:
03743420.6 / 1 483 295

(71) Applicant: **Immunomedics, Inc.**
Morris Plains, NJ 07950 (US)

(72) Inventors:
• **Govindan, Serengulam**
Morris Plains, NJ 07950 (US)

- **Qu, Zhengxing**
Morris Plains, NJ 07950 (US)
- **Hansen, Hans J.**
Morris Plains, NJ 07950 (US)
- **Goldenberg, David**
Morris Plains, NJ 07950 (US)

(74) Representative: **Bohmann, Armin K.**
bohmann
Anwaltssozietät
Nymphenburger Strasse 1
80335 München (DE)

(54) **RS7 antibodies**

(57) This invention relates to monovalent and multivalent, monospecific binding proteins and to multivalent, multispecific binding proteins. One embodiment of these binding proteins has one or more binding sites where each binding site binds with a target antigen or an epitope on a target antigen. Another embodiment of these binding proteins has two or more binding sites where each binding site has affinity towards different epitopes on a target antigen or has affinity towards either a target antigen or

a hapten. The present invention further relates to recombinant vectors useful for the expression of these functional binding proteins in a host. More specifically, the present invention relates to the tumor-associated antigen binding protein designated RS7, and other EGP-1 binding-proteins. The invention further relates to humanized, human and chimeric RS7 antigen binding proteins, and the use of such binding proteins in diagnosis and therapy.

EP 2 287 201 A3



EUROPEAN SEARCH REPORT

Application Number
EP 08 02 1299

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	SHIH L B ET AL: "IN VITRO AND IN VIVO REACTIVITY OF AN INTERNALIZING ANTIBODY, RS7, WITH HUMAN BREAST CANCER", CANCER RESEARCH, vol. 55, no. 23, SUPPL, 1 December 1995 (1995-12-01), pages 5587S-5863S, XP000999121, ISSN: 0008-5472	1,2,15, 17-19, 49-53, 56-58, 73,79, 80, 88-91, 97-99, 105-109, 111-123	INV. C07K16/30 G01N33/53 G01N33/532
Y	* the whole document *	3-11,16, 20-25, 27-38, 54,55, 59-72, 81,82, 91,92, 95,109	
Y,D	QU Z ET AL: "Humanization of Immu31, an alpha-fetoprotein-specific antibody.", CLINICAL CANCER RESEARCH: AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH. UNITED STATES OCT 1999, vol. 5, no. 10 Suppl, October 1999 (1999-10), pages 3095S-3100S, XP001154527, ISSN: 1078-0432 * page 3096S, right-hand column, paragraph 2 - page 3097S, left-hand column, line 2 *	3-11,91, 92,109	TECHNICAL FIELDS SEARCHED (IPC) C07K G01N
Y	WO 98/42378 A (GOLDENBERG DAVID M ;IMMUNOMEDICS INC (US)) 1 October 1998 (1998-10-01) * page 13, line 18 - page 29, line 2 *	16, 20-25, 27-38, 54,55, 59-72, 81,82,95	
3 The present search report has been drawn up for all claims			
Place of search Munich		Date of completion of the search 4 November 2011	Examiner Mandl, Birgit
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

EPO FORM 1503 03.82 (P04C01)



EUROPEAN SEARCH REPORT

Application Number
EP 08 02 1299

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
Y	US 2002/006379 A1 (HANSEN HANS J ET AL) 17 January 2002 (2002-01-17) * claims 17-23 *	60-72	TECHNICAL FIELDS SEARCHED (IPC)
A	DE 100 34 607 A1 (JUNG GUNDRAM) 7 February 2002 (2002-02-07) * figure 1 * * paragraph [0014] - paragraph [0019] *	1-25, 27-38, 49-73, 79-82, 88-92, 95, 97-99, 105-109, 111-123	
A	SCHOONJANS R ET AL: "Fab chains as an efficient heterodimerization scaffold for the production of recombinant bispecific and trispecific antibody derivatives", JOURNAL OF IMMUNOLOGY, vol. 165, no. 12, 15 December 2000 (2000-12-15), pages 7050-7057, XP002207879, ISSN: 0022-1767 * figure 1 *	1-25, 27-38, 49-73, 79-82, 88-92, 95, 97-99, 105-109, 111-123	
A,D	LEUNG S O ET AL: "CHIMERIZATION OF LL2, A RAPIDLY INTERNALIZING ANTIBODY SPECIFIC FOR B CELL LYMPHOMA", HYBRIDOMA, vol. 13, no. 6, 1 December 1994 (1994-12-01), pages 469-476, XP000616008, ISSN: 0272-457X * abstract; figures 1,2 *	12,13	
-The present search report has been drawn up for all claims			
Place of search Munich		Date of completion of the search 4 November 2011	Examiner Mandl, Birgit
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

 3
EPO FORM 1503 03.82 (P04C01)



EUROPEAN SEARCH REPORT

Application Number
EP 08 02 1299

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	WO 98/12227 A (DARVEAU ANDRE ; FRADET YVES (CA); DIAGNOCURE INC (CA)) 26 March 1998 (1998-03-26) * page 6, line 26 - page 7, line 2 * -----	1-25, 27-38, 49-73, 79-82, 88-92, 95, 97-99, 105-109, 111-123	
A	WO 00/69914 A (OXFORD BIOMEDICA LTD ; REURS ANNEKE (NL); BEIBOER SIGRID HERMA WILM) 23 November 2000 (2000-11-23) * page 25, line 31 - page 28, line 10 * -----	1-25, 27-38, 49-73, 79-82, 88-92, 95, 97-99, 105-109, 111-123	
X,P	STEIN RHONA ET AL: "Therapy of a breast cancer xenograft using humanized RS7 labeled with residualizing iodine.", PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 43, March 2002 (2002-03), pages 88-89, XP001154183, ISSN: 0197-016X * abstract * -----	1-8,15, 17-19, 52,53, 56-58, 80,99	
The present search report has been drawn up for all claims			
Place of search Munich		Date of completion of the search 4 November 2011	Examiner Mandl, Birgit
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

3
EPO FORM 1503 03-02 (P04C01)



Application Number
EP 08 02 1299

CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing claims for which payment was due.

☒ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

☒ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

123(partial) 1-25, 28-38, 52-73(completely); 27, 49-51, 79-82, 88-92, 95, 97-99, 105-109, 111.

☐ The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).



LACK OF UNITY OF INVENTION
SHEET B

Application Number
EP 08 02 1299

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1-25, 28-38, 52-73(completely); 27, 49-51, 79-82, 88-92, 95, 97-99, 105-109, 111-123(partially)

Subject-matter relating to an antibody that binds to an EGP-1 glycoprotein and humanized derivatives thereof.

2. claims: 26, 39-48, 74-78, 83-87, 93, 94, 96, 100-104, 110, 124(completely); 27, 49-51, 79-82, 88-92, 95, 97-99, 105-109, 111-123(partially)

Subject-matter relating to multivalent, multispecific antibodies and antibody fusion proteins comprising one or more antigen-binding sites having affinity to a EGP-1 glycoprotein.

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 08 02 1299

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

04-11-2011

Patent document cited in search report		Publication date	Patent family member(s)	Publication date			
WO 9842378	A	01-10-1998	AT 297759 T	15-07-2005			
			AU 728325 B2	04-01-2001			
			AU 6761098 A	20-10-1998			
			CA 2284829 A1	01-10-1998			
			DE 69830570 D1	21-07-2005			
			DE 69830570 T2	03-11-2005			
			DK 0969866 T3	03-10-2005			
			EP 0969866 A1	12-01-2000			
			EP 1431311 A1	23-06-2004			
			EP 1459768 A2	22-09-2004			
			EP 2332576 A1	15-06-2011			
			ES 2241129 T3	16-10-2005			
			IN 189313 A1	08-02-2003			
			JP 4584363 B2	17-11-2010			
			JP 2001518930 A	16-10-2001			
			JP 2010031032 A	12-02-2010			
			WO 9842378 A1	01-10-1998			
			ZA 9802438 A	04-11-1998			

			US 2002006379	A1	17-01-2002	AU 2002256025 B2	31-07-2008
AU 2008201428 A1	24-04-2008						
AU 2010257348 A1	20-01-2011						
CA 2442839 A1	17-10-2002						
EP 1372718 A2	02-01-2004						
EP 2301581 A1	30-03-2011						
JP 4538062 B2	08-09-2010						
JP 2005503768 A	10-02-2005						
JP 2009022273 A	05-02-2009						
JP 2010209098 A	24-09-2010						
US 2002006379 A1	17-01-2002						
US 2006104899 A1	18-05-2006						
US 2008293921 A1	27-11-2008						
US 2009246131 A1	01-10-2009						
US 2010136626 A1	03-06-2010						
US 2010158803 A1	24-06-2010						
WO 02082041 A2	17-10-2002						

DE 10034607	A1	07-02-2002	AT 315585 T	15-02-2006			
			AU 7063701 A	05-02-2002			
			CA 2416572 A1	31-01-2002			
			DE 10034607 A1	07-02-2002			
			EP 1303540 A2	23-04-2003			
			ES 2256269 T3	16-07-2006			
			JP 2004504408 A	12-02-2004			
			PT 1303540 E	31-05-2006			
			US 2003232049 A1	18-12-2003			

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 08 02 1299

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

04-11-2011

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		WO 0208291 A2	31-01-2002
WO 9812227 A	26-03-1998	AU 4373197 A	14-04-1998
		WO 9812227 A1	26-03-1998
WO 0069914 A	23-11-2000	AU 4935000 A	05-12-2000
		WO 0069914 A2	23-11-2000

专利名称(译)	RS7抗体		
公开(公告)号	EP2287201A3	公开(公告)日	2012-04-04
申请号	EP2008021299	申请日	2003-03-03
[标]申请(专利权)人(译)	IMMUNOMEDICS , INC		
申请(专利权)人(译)	IMMUNOMEDICS INC.		
当前申请(专利权)人(译)	IMMUNOMEDICS INC.		
[标]发明人	GOVINDAN SERENGULAM QU ZHENGXING HANSEN HANS J GOLDENBERG DAVID		
发明人	GOVINDAN, SERENGULAM QU, ZHENGXING HANSEN, HANS J. GOLDENBERG, DAVID		
IPC分类号	C07K16/30 G01N33/53 G01N33/532 A61K51/10		
代理机构(译)	Bohmann , ARMIN K.		
优先权	60/360229 2002-03-01 US PCT/GB2003/000885 2003-03-03 WO		
其他公开文献	EP2287201A2 EP2287201B1		
外部链接	Espacenet		

摘要(译)

本发明涉及单价和多价单特异性结合蛋白和多价多特异性结合蛋白。这些结合蛋白的一个实施方案具有一个或多个结合位点，其中每个结合位点与靶抗原或靶抗原上的表位结合。这些结合蛋白的另一个实施方案具有两个或更多个结合位点，其中每个结合位点对靶抗原上的不同表位具有亲和力或对靶抗原或半抗原具有亲和力。本发明进一步涉及可用于在宿主中表达这些功能性结合蛋白的重组载体。更具体地，本发明涉及命名为RS7的肿瘤相关抗原结合蛋白和其他EGP-1结合蛋白。本发明还涉及人源化，人和嵌合RS7抗原结合蛋白，以及这种结合蛋白在诊断和治疗中的用途。

		EUROPEAN SEARCH REPORT		Application Number EP 08 02 1299	
 DOCUMENTS CONSIDERED TO BE RELEVANT					
Category	Citation of document with indication, where appropriate, of its relevance to the invention (Art. C)	Relevant documents	CLARIFICATION OF THE APPLICATION (Art. C)		
X	SHIH L B ET AL.: "IN VITRO AND IN VIVO REACTIVITY OF AN INTERFERON ANTIBODY. R57, WITH HUMAN BREAST CANCER". CANCER RESEARCH. vol. 55, no. 23, SUPPL., 1 December 1995 (1995-12-01), pages 55875-58635, XP000999121, ISSN: 0008-5472	1,2,15, 17-19, 49-53, 56-59, 73,79, 88-91, 91-92, 105-109, 91-92,105	INV C07K16/30 G01N33/73 G01N33/52		
Y	* the whole document *	20-25, 27-38, 54,55, 59-72, 81-82, 91,92, 95,105	3-11,16, 17-19, 20-25, 27-38, 54,55, 59-72, 81-82, 91,92, 95,105		
Y,D	QU Z ET AL.: "Humanization of 1Imu31, an alpha-fetoprotein-specific antibody", CLINICAL CANCER RESEARCH: AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, UNITED STATES OCT 1999, vol. 5, no. 10 Suppl., October 1999 (1999-10), pages 3095S-3100S, XP001154527, ISSN: 1078-0432 * page 3096S, right-hand column, paragraph - page 3097S, left-hand column, line 2 *	3-11,91, 92,109	TECHNICAL FIELD (IPC) C07K G01N		
Y	WO 98/42378 A (GOLDENBERG DAVID M : IMMUNOMEDICS INC (US)) 1 October 1998 (1998-10-01) * page 13, line 18 - page 29, line 2 * ----- --/--	16, 20-25, 27-38, 54,55, 59-72, 81,82,95			
-The present search report has been drawn up on file status-					
3	NAME OF APPLICANT Runitz		NAME OF INVENTOR OR INVENTORS 4 November 2013 Mandl, Birgit		CLASSIFICATION Mandl, Birgit
CATEGORY OF OTHER DOCUMENTS					
A	1 priority document(s) published in the name of the applicant or of one or more persons connected with him/her, after filing date: 2 document(s) filed by the applicant, after filing date: 3 document(s) filed by third parties, before or after filing date: 4 reference of the same patent family, corresponding document				