



(51) International Patent Classification:
G01N 33/574 (2006.01)

(21) International Application Number:
PCT/US2012/023691

(22) International Filing Date:
2 February 2012 (02.02.2012)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/438,918 2 February 2011 (02.02.2011) US

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO,

DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

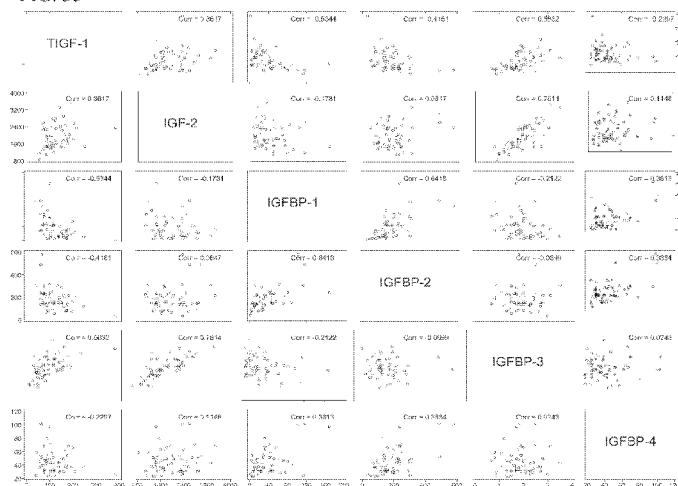
Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
- with sequence listing part of description (Rule 5.2(a))

[Continued on next page]

(54) Title: METHODS AND COMPOSITIONS RELATING TO INHIBITION OF IGF-1R

FIG. 35



(57) Abstract: The present invention provides, in part, methods for treating a tumor in a human subject comprising inhibiting IGF-1 receptor signaling, methods of determining whether a tumor is more or less likely to respond to such treatment, and compositions for practicing such methods. In particular embodiments, the invention provides fully human, humanized, or chimeric anti-IGF-1R antibodies that bind human IGF-1R, IGF-1R-binding fragments and derivatives of such antibodies, and IGF-1R-binding polypeptides comprising such fragments. Other embodiments provide nucleic acids encoding such antibodies, antibody fragments and derivatives and polypeptides, cells comprising such polynucleotides, methods of making such antibodies, antibody fragments and derivatives and polypeptides, and methods of using such antibodies, antibody fragments and derivatives and polypeptides, including methods of treating or diagnosing subjects having IGF-1R-related disorders or conditions, and kits for practicing the foregoing.

WO 2012/106556 A3

(88) Date of publication of the international search report:
26 October 2012

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER INV. G01N33/574 ADD.				
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) G01N				
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 practicable, search terms used) EPO-Internal, BIOSIS, 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	US 2009/093488 A1 (BUCK ELIZABETH A [US]) 9 April 2009 (2009-04-09) abstract paragraphs [0072], [0073] - [0077], [0193] - [0195], [0215], [0241], [0255] - [0258] -/--	1-9, 15, 16, 22, 31-42, 56-65, 71, 72, 76, 83-89, 135-138, 141, 142, 144, 148, 149, 152-162, 173-176, 179, 180, 182		
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none;"><input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.</td> <td style="width: 50%; border: none;"><input checked="" type="checkbox"/> See patent family annex.</td> </tr> </table>			<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.	<input checked="" type="checkbox"/> See patent family annex.
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.	<input checked="" type="checkbox"/> See patent family annex.			
* Special categories of cited documents :				
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none;"> "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent 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) "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 </td> <td style="width: 50%; border: none;"> "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 </td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent 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) "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	"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
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent 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) "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	"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	Date of mailing of the international search report			
13 July 2012	31/08/2012			
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Weijland, Albert			

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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.
A	<p style="text-align: center;">-----</p> <p>POLLAK MICHAEL N ET AL: "Insulin-like growth factors and neoplasia.", NATURE REVIEWS. CANCER JUL 2004 LNKD-PUBMED:15229476, vol. 4, no. 7, July 2004 (2004-07), pages 505-518, XP002674515, ISSN: 1474-175X</p> <p>abstract</p>	<p>1-9,15, 16,22, 31-41, 56-65, 71,72, 76, 83-89, 135-138, 141,142, 144,148, 149, 152-162, 173-176, 179,180, 182</p>
X	<p style="text-align: center;">-----</p> <p>WO 02/068960 A1 (BAYLOR COLLEGE MEDICINE [US]; SLAWIN KEVIN M [US]; SHARIAT SHAHROKH [U] 6 September 2002 (2002-09-06)</p> <p>abstract page 3, paragraph 2 page 8, paragraph 3 page 12, last paragraph; claims 1, 2, 13, 15, 20, 21, 28, 29, 34 and 35; example 2</p>	<p>1,23,43, 46-49, 52-55, 77,135, 136,139, 140,143, 145,163, 164, 167-170, 177,178, 181</p>
A	<p style="text-align: center;">-----</p> <p>WO 99/44062 A1 (US HEALTH [US]; KALLIONIEMI OLLI [US]; KONONEN JUHA [US]; LEIGHTON STE) 2 September 1999 (1999-09-02)</p> <p>abstract; claims 87-93</p> <p style="text-align: center;">-----</p>	<p>1-9,15, 16,22, 23, 31-43, 46-49, 56-65, 71,72, 76,77, 83-89, 135-145, 148,149, 152-164, 167-170, 173-182</p>

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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.:
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 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:

see additional sheet

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 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.:
4-8, 15, 16, 40-43, 46-49, 52-55, 71, 72, 76, 138-143, 145, 161-164
167-170, 176-181(completely); 1-3, 9, 22, 23, 31-39, 56-65, 77, 83-89
135-137, 144, 148, 149, 152-160, 173-175, 182(partially)
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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 40, 41, 138, 141, 142, 144, 161, 162, 176, 179, 180(completely); 1-9, 15, 16, 22, 31-39, 56-65, 71, 72, 76, 83-89, 135-137, 148, 149, 152-160, 173-175, 182(partially)

methods and kit for determining whether a cancerous condition is likely to respond to a treatment that reduces signalling using IGF-1 (total or free) as biomarker and its inhibitors

2. claims: 42, 43, 52, 53, 139, 141, 143, 144, 163, 164, 177, 179, 181(completely); 1-9, 15, 16, 22, 31-39, 56-65, 71, 72, 76, 83-89, 135-137, 148, 149, 152-160, 173-175, 182(partially)

As invention 1 using IGF-2 (total or free) as marker

- 3-9. claims: 1-182(partially)

As invention 1 and 2 using IGFBP-1, IGFBP-2, IGFBP-3, IGFBP-4, IGFBP-5, IGFBP-6, IGFBP-7 as marker

10. claims: 90-134, 146, 147

methods and kit for determining whether a cancerous condition is likely to respond to a treatment that reduces signalling, determining the exposure of the patient to an inhibitor

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/US2012/023691

Patent document cited in search report	A1	Publication date	Patent family member(s)	Publication date
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			WO 9944062 A1	02-09-1999
