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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, 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, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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Declarations under Rule 4.17:

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

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

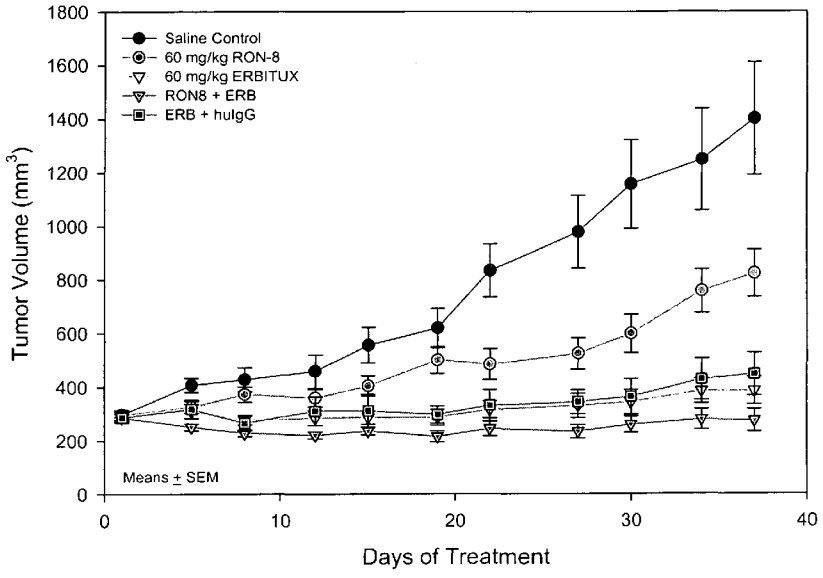
Published:

— *with international search report (Art. 21(3))*

[Continued on next page]

(54) Title: INHIBITION OF MACROPHAGE-STIMULATING PROTEIN RECEPTOR (RON) AND METHODS OF TREATMENT THEREOF

FIG. 4E



(57) Abstract: The invention provides antibodies or fragments thereof, including human antibodies, specific for Macrophage-Stimulating Protein Receptor (MSP-R or RON), which inhibit RON activation. Also provided are methods to inhibit RON, particularly the use of RON antibodies to treat diseases such as cancer.

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— *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))*

(88) Date of publication of the international search report:
20 August 2009

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/013130

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/18 C07K16/00 A61K39/395 A61P35/00

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)
C07K

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, WPI Data, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2005/120557 A (IMCLONE SYSTEMS INC [US]; PEREIRA DANIEL [US]) 22 December 2005 (2005-12-22) the whole document pages 36-42 figure 1 ----- -/--	1-52

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

[X] 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)

"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
25 June 2009	01/07/2009

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, Fax: (+31-70) 340-3016	Fellows, Edward

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/013130

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	O'TOOLE JENNIFER M ET AL: "Therapeutic implications of a human neutralizing antibody to the macrophage-stimulating protein receptor tyrosine kinase (RON), a c-MET family member" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD.; US, vol. 66, no. 18, 15 September 2006 (2006-09-15), pages 9162-9170, XP009102372 ISSN: 0008-5472 the whole document pages 9164-8; figures 5a,b,c	1-52
A	RAMSAY CAMP E ET AL: "RON, a Tyrosine Kinase Receptor Involved in Tumor Progression and Metastasis" ANNALS OF SURGICAL ONCOLOGY, SPRINGER-VERLAG, NE, vol. 12, no. 4, 1 April 2005 (2005-04-01), pages 273-281, XP019369668 ISSN: 1534-4681 the whole document	1-52

INTERNATIONAL SEARCH REPORT

International application No.
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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. [X] 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 reportcovers 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.

[X] 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: 1 (partially), 8-13, 14-19 (partially), 20 and 21-52 (partially)

   Aspects related to antibody anti-RON 6, or fragment thereof, that specifically binds to a RON protein comprising a CDR selected from SEQ ID NOs: 17, 19, 21, 23, 25, and 27 or variable regions SEQ ID NOs 6 and 8.

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2. claims: 1 (partially), 2-7, 14-19 and 21-52 (all partially)

   Aspects related to antibody RON 8, or fragment thereof, that specifically binds to a RON protein comprising a CDR selected from SEQ ID NOs: 29, 31, 33, 35, 37 and 39 or variable regions SEQ ID NOs 2 and 4.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2008/013130

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005120557 A	22-12-2005	CA 2566647 A1	22-12-2005
		EP 1773881 A2	18-04-2007
		JP 2008508858 T	27-03-2008