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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))

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8 May 2014

(54) Title: BIOMARKERS FOR PREDICTING AND ASSESSING RESPONSIVENESS TO LENVATINIB COMPOUNDS

(57) Abstract: Biomarkers are provided that are predictive of a subject's responsiveness to a therapy comprising lenvatinib or a pharmaceutically acceptable salt thereof (e.g., lenvatinib mesylate). The biomarkers, compositions, and methods described herein are useful in selecting appropriate treatment modalities for a subject having cancer (e.g., thyroid cancer, kidney cancer), suspected of having cancer, or at risk of developing cancer.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/40183

| A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - C12Q 1/68; G01N 33/50 (2012.01) USPC - 435/6.14, 436/63, 436/64 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(8) - C12Q 1/68; G01N 33/50 (2012.01) USPC - 435/6.14, 436/63, 436/64 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched 435/6.1 Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) WEST - DB=PGPB,USPT,USOC,EPAB,JPAB; PLUR=YES; OP=ADJ; Google Scholar search terms: Vegfr, vegfr\$, inhib\$, lenvatinib, E7080, thyroid, kidney, renal, cancer, cancer\$, tumor, tumor\$, malignan\$, amount, ratio, increas\$, decreas\$, reduc\$, measur\$, level, diagnos\$, prognos\$, profil\$, thyroglobulin, AITD3, TGN, FLT4, fit-4, mutat\$, mutant, | | |
| C. DOCUMENTS CONSIDERED TO BE RELEVANT | | |
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| Y | US 2007/0254295 A1 (HARVEY et al.) 01 November 2007 (01.11.2007) para [0010]-[0012]; [0027]; [0028]; [0030]-[0033]; [0051]-[0053]; [0058]; [0065]-[0067]; [0133]. | 1-5 |
| Y | US 2011/0118298 A1 (FRITZ et al.) 19 May 2011 (19.05.2011) para [0015]; [0024]; [0047]; [0095]; [0247]; [0734]; Table 7; claim 20. | 1-16 |
| Y | US 2004/0018528 A1 (MORIMOTO et al.) 29 January 2004 (29.01.2004) abstract; para [0055]; [0095]; [0104]-[0109]; [0116]; [0117]; [0120]; [0121]; [0382]; [0521]; [0574]; Table 20. | 6-11 |
| Y | US 2009/0311175 A1 (BROSE M.) 17 December 2009 (17.12.2009) para [0012]; [0023]; [0061]; [0147]; [0148]; [0195]; [0196]; [0200]; [0218]; [0235]. | 12-16 |
| A | Cooper et al. Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer. Throid 2006 vol 16 no. 2 pg 1-33. entire document | 11 |
| <input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> | | |
| * 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 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 10 August 2012 (10.08.2012) | | Date of mailing of the international search report 04 SEP 2012 |
| Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201 | | Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774 |

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/40183

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.: 17-21
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 all searchable claims.
- 2. As all searchable claims could be searched without effort justifying 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.