

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
26 October 2006 (26.10.2006)

PCT

(10) International Publication Number
WO 2006/113151 A3

(51) International Patent Classification:

A61K 31/47 (2006.01) A61K 31/5377 (2006.01)
A61K 31/4706 (2006.01) A61K 45/06 (2006.01)
A61K 31/4709 (2006.01) A61P 35/00 (2006.01)

(21) International Application Number:

PCT/US2006/012877

(22) International Filing Date: 7 April 2006 (07.04.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/671,287 14 April 2005 (14.04.2005) US

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
11 January 2007

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: USE OF AN EPIDERMAL GROWTH FACTOR RECEPTOR KINASE INHIBITOR (EGFR) IN GEFITINIB RESISTANT PATIENTS

(57) Abstract: This invention discloses method of treating or inhibiting cancer in a human having at least one of an Exon 19 del E746-A750 and/or an Exon 21 point mutation comprising administering to said human gefitinib and/or irressa alone or in combination with other cytotoxic agents or chemotherapeutic agents and an effective amount of EGFR kinase inhibitor.



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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K31/47 A61K31/4706 A61K31/4709 A61K31/5377 A61K45/06
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)

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, WPI Data, PAJ, BIOSIS, EMBASE, CHEM ABS Data, SCISEARCH, PASCAL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 2006/084058 A (THE GENERAL HOSPITAL CORPORATION; WYETH; HABER, DANIEL; BELL, DAPHNE W) 10 August 2006 (2006-08-10) page 4, paragraph 11 page 4, paragraph 13 - page 5, paragraph 14 page 5, paragraph 18 page 6, paragraph 21 page 10, paragraph 31 - page 11, paragraph 34 ----- -/--	1-7

☒ 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)

"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

24 August 2006

Date of mailing of the international search report

15/11/2006

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INTERNATIONAL SEARCH REPORT

International application No

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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.
P,X	WO 2005/094357 A (THE GENERAL HOSPITAL CORPORATION; DANA-FARBER CANCER INSTITUTE, INC; B) 13 October 2005 (2005-10-13) page 6, paragraph 18 - page 7, paragraph 19 page 10, paragraph 34 page 59, paragraph 219 - paragraph 220 page 64, paragraph 232 - paragraph 233 page 68, paragraph 248 - page 69, paragraph 249	1-7
P,X	----- YOSHIMURA ET AL: "EKB-569, a new irreversible epidermal growth factor receptor tyrosine kinase inhibitor, with clinical activity in patients with non-small cell lung cancer with acquired resistance to gefitinib" LUNG CANCER, ELSEVIER, AMSTERDAM, NL, vol. 51, no. 3, March 2006 (2006-03), pages 363-368, XP005350966 ISSN: 0169-5002 the whole document	1-4,7
Y	----- WO 2004/014426 A (ASTRAZENECA AB; ASTRAZENECA UK LIMITED; WEDGE, STEPHEN, ROBERT) 19 February 2004 (2004-02-19) page 2, line 24 - line 25 page 6, line 28 - line 30 page 14, line 14 page 14, line 21 - line 24	1-7
Y	----- WO 2005/018677 A (WYETH HOLDINGS CORPORATION; GREENBERGER, LEE, MARTIN; DISCAFANI-MARRO,) 3 March 2005 (2005-03-03) page 2, line 18 - page 6, line 7 page 8, line 9 - line 11	1-4,7
Y	----- WO 2005/028443 A (WYETH A CORPORATION OF THE STATE OF DELAWARE, USA; WISSNER, ALLAN; RAB) 31 March 2005 (2005-03-31) page 1, line 3 - line 9 claims 3,9	1,2,5-7
Y	----- RABINDRAN S K ET AL: "Antitumor Activity of HKI-272, an Orally Active, Irreversible Inhibitor of the HER-2 Tyrosine Kinase" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 64, no. 11, 2004, pages 3958-3965, XP002318446 ISSN: 0008-5472 figure 3	1,2,5-7
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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/012877

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	FRY D W: "INHIBITION OF THE EPIDERMAL GROWTH FACTOR RECEPTOR FAMILY OF TYROSINE KINASES AS AN APPROACH TO CANCER CHEMOTHERAPY: PROGRESSION FROM REVERSIBLE TO IRREVERSIBLE INHIBITORS" PHARMACOLOGY AND THERAPEUTICS, ELSEVIER, GB, vol. 82, no. 2/3, 1999, pages 207-218, XP001014432 ISSN: 0163-7258 page 212, column 2, paragraph 2 page 213, column 1, paragraph 2 -----	1-7
Y	LYNCH THOMAS J ET AL: "Activating mutations in the epidermal growth factor receptor underlying responsiveness of non-small-cell lung cancer to gefitinib" NEW ENGLAND JOURNAL OF MEDICINE, vol. 350, no. 21, 20 May 2004 (2004-05-20), pages 2129-2139, XP002359960 ISSN: 0028-4793 the whole document -----	1-7
X	KOBAYASHI S ET AL: "EGFR mutation and resistance of non-small-cell lung cancer to gefitinib" NEW ENGLAND JOURNAL OF MEDICINE 24 FEB 2005 UNITED STATES, vol. 352, no. 8, 24 February 2005 (2005-02-24), pages 786-792, XP002395764 ISSN: 0028-4793 cited in the application	1,2,7
Y	page 790, column 1, paragraph 1 - page 791, column 2, paragraph 2 -----	3-6
A	PAO W ET AL: "Acquired resistance of lung adenocarcinomas to gefitinib or erlotinib is associated with a second mutation in the EGFR kinase domain" PLOS MEDICINE, XX, XX, vol. 2, no. 3, March 2005 (2005-03), pages 225-235, XP002359961 ISSN: 1549-1676 cited in the application the whole document ----- -/--	1-7

INTERNATIONAL SEARCH REPORT

International application No
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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	KURATA T ET AL: "Effect of re-treatment with gefitinib ('Iressa', ZD1839) after acquisition of resistance [1]" ANNALS OF ONCOLOGY 2004 UNITED KINGDOM, vol. 15, no. 1, 2004, page 173, XP002395765 ISSN: 0923-7534 cited in the application the whole document -----	1-7

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Box 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.: 1-7
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-7 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.
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 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 an additional fee, this Authority did not invite payment of any additional fee.
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.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2006/012877

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
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