(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

PCT

(43) International Publication Date
24 July 2008 (24.07.2008)

(10) International Publication Number
WO 2008/089135 A3

(51) **International Patent Classification:**
GOIN 33/566 **(2006.01)** ***A61K 49/00*** **(2006.01)**
GOIN 33/574 **(2006.01)**

(21) **International Application Number:**
PCT/US2008/050994

(22) International Filing Date: 14 January 2008 (14.01.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/884,634 12 January 2007 (12.01.2007) US

(71) **Applicant** *(for all designated States except US):* **UNIVERSITY OF SOUTH FLORIDA** [US/US]; 3802 Spectrum Blvd., Suite 100, Tampa, FL 33612 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only):* **HAURA, Eric, B.** [US/US]; 2608 West Wyoming Avenue, Tampa, FL 33611 (US).

(74) Agent: MCGAW, Michael, M.; 180 Pine Avenue North, Oldsmar, FL 34677 (US).

(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, SV, SY, 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, 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, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, 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*

(88) Date of publication of the international search report:
18 September 2008

WO 2008/089135 A3

(54) Title: IDENTIFICATION OF BIOMARKERS PREDICTIVE OF DASATINIB EFFECTS IN CANCER CELLS

(57) Abstract: A method of predicting response to treatment with inhibitors of EGFR and SRC by screening for status of key biomarkers such as EGFR. Dasatinib is a drug that can inhibit a group of proteins called SRC proteins. In addition, other experiments have suggested that other important signaling proteins are affected by dasatinib. Early phase trials of dasatinib are ongoing in cancer patients. It will be important to determine which patients receive a clinical benefit of dasatinib. Predetermination of treatment benefit can be performed by assessing biomarkers in patients tumors prior to treatment with dasatinib or other inhibitors of EGFR and SRC. Patients that have positive biomarkers for treatment could then be treated with higher confidence of benefit while those not possessing these predictive biomarkers would avoid ineffective and potentially toxic therapy. Additionally, treatment can be tailored according to predetermined sensitivity by evaluating indicated biomarkers correlating with sensitivity to one or more agents.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US 08/50994

A CLASSIFICATION OF SUBJECT MATTER
IPC(8) - G01N 33/566, G01N 33/574, A61K 49/00 (2008.04)
USPC - 436/501, 435/7.23, 424/9.1
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) - G01N 33/566, G01N 33/574, A61K 49/00 (2008 04)
USPC - 436/501, 811, 64. 435/7 23, 424/9 1, 530/827

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
PUBWEST, GOOGLE SCHOLAR

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PUBWEST(PGPB ,USPT ,USOC ,EPAB ,JPAB), GOOGLE SCHOLAR **gefitinib, βrlotinib, egfr, resistant, status, mutation, dasatinib, sprycel, bms-354825, inhibitor, antagonist, src, aal, cml, leukemia, bcr, abl**

C DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropπate, of the relevant passages	Relevant to claim No
X --- Y	WO **2005/117888 A1 (Green et al) 15 December 2005 (15 12 2005) pg 6, In 3-19 and In 26-32, pg 17, In 13-16, pg 18, In 3-8 and In 29-30, pg 22, In 17-21 and In 25-28, and pg 27, In 5-15 and In 28-30**	14, 15, 17, 24, and 25 --- 16
X --- Y	SONG **ET AL Dasatinib (BMS-354825) Selectively Induces Apoptosis in Lung Cancer Cells Dependent on Epidermal Growth Factor Receptor Signaling for Survival Cancer Research June 2006, Vol 66 No 11 pages 5542-5548, especially pg 5542, col 1 and 2, pg 5543, col 2-pg5545, col 1, pg 5546, fig 3, pg 5548, col 1 and 2, and the abstract**	1-10, 12-13, and 18-23 --- 11 and 16
Y	**US 2006/0235006 A1 (Lee et al) 19** October **2006 (19 10 2006) para [0003]**	11

☐ **Further documents are listed in the continuation of Box C** **D**

- **Special categoπes 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 pnoπty 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 pπor 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
18 Apr 2008 (18 04 2008)

Date of mailing of the international search report
27 JUN 200S

Name and mailing address of the ISA/US
Mail Stop PCT, Attn ISA/US, Commissioner for Patents
P O Box 1450, Alexandπa, Virginia 22313-1450
Facsimile No 571-273-3201

Authorized officer
Lθθ W Young
PCTH βlpdβsk 571-272-4300
PCT OSP 571-272 7774

Form PCT/ISA/210 (second sheet) (April 2007)