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| 61/921,185 | 27 December 2013 (27.12.2013)  | US |
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| 62/027,042 | 21 July 2014 (21.07.2014)      | 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, BN, 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, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, 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.
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- 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))
- (88) **Date of publication of the international search report:**  
20 August 2015



(54) **Title:** BIOMARKER PROFILES FOR PREDICTING OUTCOMES OF CANCER THERAPY WITH ERBB3 INHIBITORS AND/OR CHEMOTHERAPIES

(57) **Abstract:** Provided are methods for optimizing therapy of, treating a patient having, or selecting (identifying) patients who will benefit from treatment for, a cancer (e.g., a non-hematological cancer; e.g., a gynecological cancer). The methods comprise determining whether the patient will benefit from treatment with an ErbB3 inhibitor (e.g., an anti-ErbB3 antibody), with or without either a taxane or an aromatase inhibitor, or with a taxane or an aromatase inhibitor in the absence of an ErbB3 inhibitor, based on levels of particular biomarkers and combinations of biomarkers measured in a biological sample obtained from the patient. The methods further comprise optimizing the patient's therapy, selecting the patient for treatment, or treating the patient accordingly. In various aspects the biological samples are sections of a biopsy (e.g., a formalin fixed paraffin embedded biopsy). In other aspects the biomarkers are proteins and/or nucleic acids. In other aspects the biomarkers function in ErbB-mediated signal transduction.

INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2014/072594

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, EMBASE, FSTA, PAJ, 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	WO 2012/177440 A1 (MERRIMACK PHARMACEUTICALS INC [US]; SANOFI SA [FR]; KUBASEK WILLIAM [U]) 27 December 2012 (2012-12-27) pages 2,3,6,12 pages 29,30	1-34
X	WO 2012/006552 A1 (EXELIXIS INC [US]; SANOFI SA [FR]; UNIV VANDERBILT [US]; ARTEAGA CARLO) 12 January 2012 (2012-01-12) pages 8,29,244	1-34
X	WO 2012/103341 A1 (MERRIMACK PHARMACEUTICALS INC [US]; SANOFI SA [FR]; MOYO VICTOR [US];) 2 August 2012 (2012-08-02) pages 2,18	1-34
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Further documents are listed in the continuation of Box C.

See patent family annex.

\* Special categories of cited documents :

<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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</p> <p>"&amp;" document member of the same patent family</p>
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Date of the actual completion of the international search  2 April 2015	Date of mailing of the international search report  29/06/2015
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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  Lunter, Pim
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## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2014/072594

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 2013/023043 A2 (MERRIMACK PHARMACEUTICALS INC [US]; SANOFI SA [FR]; MOYO VICTOR [US];) 14 February 2013 (2013-02-14) pages 8,20,52, page 71</p> <p style="text-align: center;">-----</p>	1-34
X	<p>NIE LIN ET AL: "Efficacy of MM121 in ER+ and triple negative breast cancer studies", AMERICAN ASSOCIATION FOR CANCER RESEARCH. PROCEEDINGS OF THE ANNUAL MEETING, AMERICAN ASSOCIATION FOR CANCER RESEARCH, US, vol. 51, 17 April 2010 (2010-04-17), page 436, XP001537417, ISSN: 0197-016X abstract</p> <p style="text-align: center;">-----</p>	1-34
X,P	<p>G MACBEATH ET AL: "A META-ANALYSIS OF BIOMARKERS IN THREE RANDOMIZED, PHASE 2 STUDIES OF MM-121, A LIGAND-BLOCKING ANTI-ERBB3 ANTIBODY, IN PATIENTS WITH OVARIAN, LUNG, AND BREAST CANCERS", ANNALS OF ONCOLOGY, vol. 25, no. S4, 1 September 2014 (2014-09-01), pages 313-47, XP055180759, DOI: 10.1093/annonc/mdu326.79 abstract</p> <p style="text-align: center;">-----</p>	1-34

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2014/072594

## 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.  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.:

1-34(partially)

### 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: 1-34(partially)

Method of selecting a therapy for a patient having cancer; method of improving or optimizing therapeutic efficacy of treatment; method of treating a cancer; method of ordering treatment; wherein the therapy comprises an ErbB3 inhibitor, comprising obtaining a score for ErbB2, or for ErbB2 and for heregulin.

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## 2. claims: 1-34(partially)

Method of selecting a therapy for a patient having cancer; method of improving or optimizing therapeutic efficacy of treatment; method of treating a cancer; method of ordering treatment; wherein the therapy comprises an ErbB3 inhibitor, comprising obtaining a score for ErbB3.

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## 3. claims: 1-34(partially)

Method of selecting a therapy for a patient having cancer; method of improving or optimizing therapeutic efficacy of treatment; method of treating a cancer; method of ordering treatment; wherein the therapy comprises an ErbB3 inhibitor, comprising obtaining a score for ErbB4.

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## 4. claims: 1-34(partially)

Method of selecting a therapy for a patient having cancer; method of improving or optimizing therapeutic efficacy of treatment; method of treating a cancer; method of ordering treatment, wherein the therapy comprises an ErbB3 inhibitor; comprising obtaining a score for heregulin.

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## 5. claims: 35-47(partially)

Method of selecting therapy for a patient having a non-hematological cancer; method of treating a non-hematological cancer; method of administering or ordering the administration of a therapy; wherein the therapy comprises an ErbB3 inhibitor and a taxane, comprising obtaining a score for ErbB2.

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## 6. claims: 35-47(partially)

Method of selecting therapy for a patient having a non-hematological cancer; method of treating a non-hematological cancer; method of administering or

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

ordering the administration of a therapy; wherein the therapy comprises an ErbB3 inhibitor and a taxane, comprising obtaining a score for ErbB3.

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7. claims: 35-47(partially)

Method of selecting therapy for a patient having a non-hematological cancer; method of treating a non-hematological cancer; method of administering or ordering the administration of a therapy; wherein the therapy comprises an ErbB3 inhibitor and a taxane, comprising obtaining a score for ErbB4.

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8. claims: 35-47(partially)

Method of selecting therapy for a patient having a non-hematological cancer; method of treating a non-hematological cancer; method of administering or ordering the administration of a therapy; wherein the therapy comprises an ErbB3 inhibitor and a taxane, comprising obtaining a score for heregulin.

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9. claims: 48-56

Method for administering a heregulin-neutral therapeutic agent, comprising obtaining a tumor heregulin level.

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2014/072594

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