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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))*

— *of inventorship (Rule 4.17(iv))*

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))*

— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:
18 May 2012

(54) Title: NOVEL ANTIGEN BINDING PROTEINS

(57) Abstract: The present disclosure relates to antigen binding proteins, such as antibodies, that bind to HER3, polynucleotides encoding such antigen binding proteins, pharmaceutical compositions comprising said antigen binding proteins and methods of manufacture. The present disclosure also concerns the use of such antigen binding proteins in the treatment or prophylaxis of diseases associated with breast cancer, ovarian cancer, prostate cancer, bladder cancer, pancreatic, gastric, melanoma and other cancers that overexpress HER3.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 11/50322

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C07K 16/18, C12P 21/08; C07H 21/00 (2011.01)
USPC - 530/387.1; 530/387.7; 536/23.53
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) - C07K 16/18, C12P 21/08; C07H 21/00 (2011.01)
USPC - 530/387.1; 530/387.7; 536/23.53

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
IPC(8) - C07K 16/18, C12P 21/08; C07H 21/00 (2011.01), USPC - 530/387.1; 530/387.7; 536/23.53, 530/387.3, 530/388.1, 530/388.15, 424/130.1, 424/133.1. 424/141.1, 424/155.1: keyword search, as below

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
USPTO PubWest (databases: PGPB,USPT,USOC,EPAB,JPAB), Thompson Innovation (core patent databases), Google Scholar -- Search Terms: Her3, erbB3, receptor, antibody, binding protein, immunoglobulin, asp tyr asn met asn, dynmn, nucleic acid, polynucleotide, vector, humanized, chimeric, chimaeric, fused, fusion, heavy, CDR, CDR3

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- A	US 2008/0269467 A1 (ALLAN et al.) 30 October 2008 (30.10.2008) para [0007]; [0017]; [0027];SEQ ID NO: 11	1, 2, 5, 6, 27 --- 75
A	US 2010/0183631 A1 (ROTHE et al.) 22 July 2010 (22.07.2010) abstract; para [0005]; [0031]; [0054]	75
A	US 2010/0074900 A1 (GHAYUR et al.) 25 March 2010 (25.03.2010) abstract; para [0014]; [0316]; SEQ ID NOs: 86, 92, 96.	75

☐ Further documents are listed in the continuation of Box C. ☐

* 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	Date of mailing of the international search report
17 March 2012 (17.03.2012)	27 MAR 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

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 11/50322

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.: 86, 115-126, and 136-137
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:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: Claims 1-2, 5-6, 27, 75, drawn to an antigen binding protein comprising a heavy chain variable region having at least one CDR with greater than 75% sequence identity to SEQ ID NO: 2 and its humanized equivalent as set forth in SEQ ID NO: 23.

---please see continuation on extra 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 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.:
1-2, 5-6, 27, 75, limited to SEQ ID NOs: 2 and 23

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.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 11/50322

Continuation of Box No. III Observations where unity of invention is lacking

Group II+: Claims 1-8, 17-18, 21, 22, 27-31, 39, 40, 42-49, 53-55, 58-71, 76, 77, 84-85, drawn to an antigen binding protein comprising a heavy chain variable region having at least one CDR with greater than 75% sequence identity to a sequence selected from any one of SEQ ID NOs: 3 and 4, and the humanized equivalents as set forth respectively in SEQ ID NOs: 24 and 25; or a light chain variable region having at least one CDR with greater than 75% sequence identity to a sequence selected from any one of SEQ ID NOs: 6, 7, and 8 and the humanized equivalents as set forth respectively in SEQ ID NOs: 27, 28, and 29; and
also drawn to an isolated nucleic acid encoding the antigen binding protein, expression vectors, host cells, compositions, uses, and methods related to the antigen binding protein.
-Please note that claims 3-4, 7-8, and 76-77 will be searched only if all of SEQ ID NOs: 2, 3, 4, 6, 7, 8 or all of their humanized equivalents SEQ ID NOs: 23, 24, 25, 27, 28, 29 are elected for search.
-Please note that claims 17-20 and their dependent claims will be searched only if SEQ ID NO: 7 or 8 is elected for search.
-Please note that claims 21, 22 and their dependent claims will be searched only if SEQ ID NO: 4 (which represents a fragment of sequences SEQ ID NOs: 1 and 22) is elected for search.-Please note that claims 28, 29, 31, 40 and 41 will be searched only if the nucleic acid sequences listed therein are elected for search.

Group III+: Claims 9-16, 23, 24, 26, 32-38, 42-46, 50-53, 56-68, 72-74, 78-79, 84-85, 87-114, 127-135, drawn to an antigen binding protein comprising a heavy chain variable region having at least one CDR with greater than 75% sequence identity to a sequence selected from any one of SEQ ID NOs: 45, 46, and 47 and the humanized equivalents as set forth in SEQ ID NOs: 31, 32, and 33 respectively, or a light chain variable region having at least one CDR with greater than 75% sequence identity to any one of SEQ ID NOs: 49, 50, and 51, and the humanized equivalents as set forth respectively in SEQ ID NOs: 35, 36, and 37;
an antigen binding protein comprising SEQ ID NOs: 44, 48, 30; and
also drawn to an isolated nucleic acid encoding the antigen binding protein, expression vectors, host cells, compositions, uses, and methods related to the antigen binding protein.
-Please note that claims 11-12, 15-16, and 78-79 will be searched only if all of SEQ ID NOs: 45, 46, 47, 49, 50, 51 or all of their humanized equivalents SEQ ID NOs: 31, 32, 33, 35, 36, 37 are elected for search.
-Please note that claims 23 and 26 and their dependent claims will be searched only if SEQ ID NO:47 (which represents a fragment of SEQ ID NOs: 30 and 44) and SEQ ID NO: 50 (which represents a fragment of SEQ ID NOs: 48 and 57) are elected for search.
-Please note that claims 24 and its dependent claims will be searched only if SEQ ID NO:47 (which represents a fragment of SEQ ID NO:3) is elected for search.
-Please note that claims 33-34, 36, and 38 will be searched only if the nucleic acid sequences listed therein are elected for search.
-Please note that claims 87-91 and 92-96 will be searched only if SEQ ID NO:51 (which represents amino acids 113-121 of SEQ ID NOs:104) is elected for search and one of SEQ ID NO: 45 (which represents amino acids 50-54 of SEQ ID NOs:100 and 102) or SEQ ID NO:47 (which represents amino acids 118-125 of SEQ ID NOs: 100 and 102)
-Please note that claims 97-98, 101-102, and their dependent claims will be searched only if SEQ ID NO:45 or 47 are elected for search.
-Please note that claims 99-100 and their dependent claims will be searched only if SEQ ID NO:51 is elected for search

Group IV+: Claims 17-20, 39-46, 53, 68, 80, 81, 84-85, drawn to an antigen binding protein comprising a heavy chain variable region having at least one CDR with greater than 75% sequence identity to SEQ ID NOs: 10, 11, and 12; or to a light chain variable region having at least one CDR with greater than 75% sequence identity to any one of SEQ ID NOs: 12, 18, 19, 20; and
also drawn to an isolated nucleic acid.encoding the antigen binding protein, expression vectors, host cells, compositions, uses, and methods related to the antigen binding protein.
-Please note that claims 19-20 will be searched only if all of SEQ ID NOs: 10,11, 12, 7, 8, 18, 19, 20 are elected for search.
-Please note that claims 80 and 81 will be searched only if all of the sequences listed therein are elected for search.
-Please note that claims 40 and 41will be searched only if the nucleic acid sequences listed therein are elected for search.

Group V+: Claims 25, 45, 46, 53, 68, 82-85, drawn to an antigen binding protein comprising SEQ ID NOs: 9, 13, and 17; and compositions, uses, and methods related thereto.

The inventions listed as Groups I, II+, III+, IV+, and V+ do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of Groups I, II+, III+, IV+, and V+ is an antigen binding protein comprising a heavy chain variable region having at least one CDR and/or a light chain variable region having at least one CDR. This special technical feature fails to provide a contribution over the prior art, as evidenced by US 2008/0262203 A1 to Clegg et al. (published 23 October 2008, hereinafter 'Clegg'). Clegg discloses an antigen binding protein comprising a heavy chain variable region having at least one CDR and a light chain variable region having at least one CDR (para [0048] - "a penta-specific antibody comprises heavy and light chain variable regions which comprise the CDR amino acid sequence"). In the absence of a contribution over the prior art, the shared technical feature is not a shared special technical feature. Without a shared special technical feature, the inventions lack unity with one another.

A further special technical feature of Groups I and II+ are the antigen binding proteins set forth in claims 1 and 5. This special technical feature fails to provide a contribution over Clegg. Clegg teaches claim 1, namely, an antigen binding protein comprising a heavy chain variable region having at least one CDR with greater than 75% sequence identity to an amino acid sequenceof SEQ ID NO: 2 (para [0048] - "a penta-specific antibody comprises at least four CDR sequences selected from the group consisting of: SEQ ID NOs: 19"; SEQ ID NO: 19 exhibits 100% identity with SEQ ID NO:2). Clegg also teaches claim 5, namely, an antigen binding protein comprising a heavy chain variable region having at least one CDR with greater than 75% sequence identity to an amino acid sequence of SEQ ID NO: 23 (para [0048] - "a penta-specific antibody comprises at least four CDR sequences selected from the group consisting of: SEQ ID NOs: 19"; SEQ ID NO: 19 exhibits 100% identity with SEQ ID NO:23; para [0200] - "humanized penta-specific antibody"). In the absence of a contribution over the prior art, the shared technical feature is not a shared special technical feature. Without a shared special technical feature, the inventions lack unity with one another.

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Continuation of previous extra sheet

Additionally, a further special technical feature of each of the inventions listed as Groups I, II+, III+, IV+ and V+ is the specific antigen binding protein sequence recited therein. Significant structural similarities cannot readily be ascertained among each of the unique antigen binding protein amino acid sequences. Without significant structural similarities, the antigen binding protein sequences do not have a shared special technical feature. In the absence of a shared special technical feature, the inventions lack unity with one another. If Applicant elects to have any of Groups II+, III+, IV+, or V+ searched, Applicant must specify the specific amino acid sequence(s) to be searched, and where applicable, the specific nucleic acid sequence(s) to be searched. Each unique sequence constitutes an inventive concept.

Unity of invention exists only when the same or corresponding technical feature is shared by the claimed inventions. With out a shared special technical feature, the inventions of Groups I, II+, III+, IV+ and V+ lack unity of invention.