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[Continued on next page]

(54) Title: DOSING FOR TREATMENT WITH ANTI-EGFL7 ANTIBODIES

(57) Abstract: The present invention concerns dosing of anti-EGFL7 antibodies for cancer therapy.

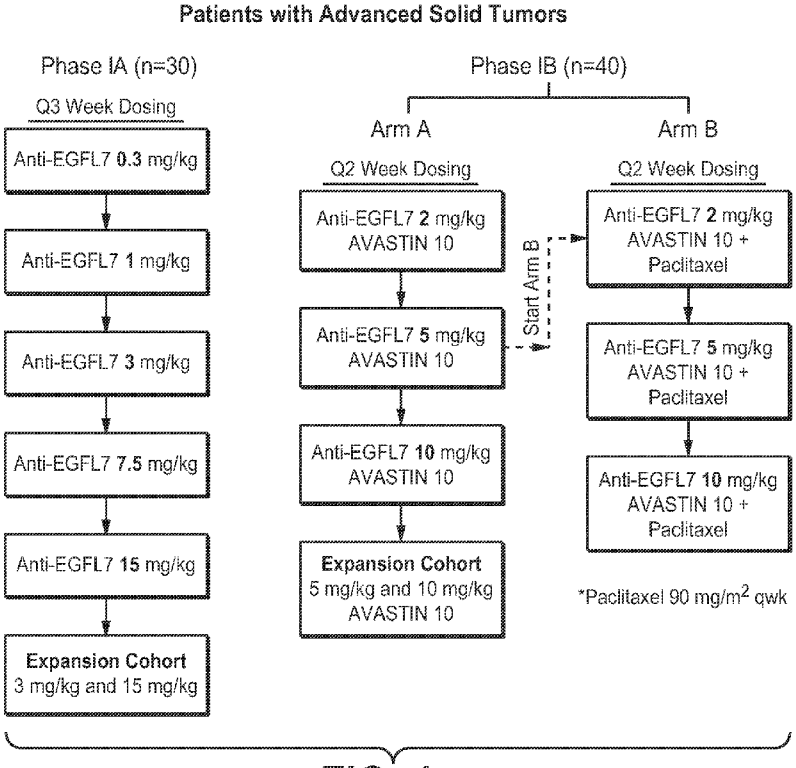

FIG. 1

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— *with international search report (Art. 21(3))*

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

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1 November 2012

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 12/23547

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 39/395, A61P 35/00 (2012.01)
USPC - 424/133.1; 424/174.1, 424/155.1
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) - A61K 39/395, A61P 35/00 (2012.01)
USPC - 424/133.1; 424/174.1, 424/155.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
424/141.1, 424/130.1

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST - DB=PGPB,USPT,USOC,EPAB,JPAB; PLUR=YES; OP=ADJ; Google Scholar; GenCore 6.3
search terms: EGFL7, EGFL-7, EGFL 7, EGF, like, domain, protein, 7, NEU1, ZNEU1, Vascular endothelial statin, antibod$, ab, anti, immunog$, cycling, dose, dosing, paclitaxel, carboplatin, bevacizumab, oxaliplatin, fluorourcail, 5-FU, mg/ml, mg/kl, heavy, light, v

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2010/0285009 A1 (YE et al.) 11 November 2010 (11.11.2010) para [0008]-[0010]; [0013]-[0017]; [0029]-[0031]; [0035]; [0046]; [0047]; [0111]; [0115]; [0120]; [0353]; [0359]; [0360]; [0393]; SEQ ID NOs: 7, 12, 34, 35, 76-87, 100-105, 130-145, 193-196.	1-11, 13, 14, 16, 17, 30-46, 48, 49, 51, 52
A	US 2010/0203041 A1 (YE et al.) 12 August 2010 (12.08.2010) para [0024]; [0029]; [0030]; [0080]; [0307].	1-11, 13, 14, 16, 17, 30-46, 48, 49, 51, 52

☐ 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
11 July 2012 (11.07.2012)	16 AUG 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 12/23547

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.: 12, 15, 18-29, 47, 50, and 53
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 and 30-34, drawn to a method and article of manufacture wherein an anti-EGFL7 antibody is administered at a dose of between 1 mg/kg and 15 mg/kg.

Group II: Claims 2-4 and 35-37, drawn to a method and article of manufacture wherein an anti-EGFL7 antibody is administered at a flat dose selected from the group consisting of: (a) 375-400 mg every two weeks and (b) 550-600 mg every three weeks.

Group III: Claims 5-11, 13-14, and 16-17, drawn to a method wherein an anti-EGFL7 antibody is administered in a first dose and a second dose.

---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.:

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 12/23547

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

Group IV: Claims 38-46, 48-49, and 51-52, drawn to a method wherein an anti-EGFL7 antibody is administered in a dosing regimen comprising treatement cycles.

The inventions listed as Groups I-IV 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 shared technical feature of the inventions listed as Groups I-IV is an anti-EGFL7 antibody is administered to a patient. This shared technical feature fails to provide a contribution over the prior art, as evidenced by US 2010/0203041 A1 to Ye et al. (published 12 August 2010; hereinafter 'Ye'). Ye discloses a method for the treatment of cancer in a human patient comprising administering an anti-EGFL7 antibody (para [0030] and [0080]), the method comprising administering the antibody at a dose of between 1 mg/kg and 15 mg/kg (para [0307]). In the absence of a contribution over the prior art, the shared technical feature is not a shared special technical feature.

The shared technical feature of the inventions listed as Groups II-IV is the administration of anti-EGFL7 antibody in multiple doses. This shared technical feature fails to provide a contribution over Ye, which further teaches a method for the treatment of cancer in a human patient comprising administering an anti-EGFL7 antibody (para [0030] and [0080]), the method comprising administering the antibody at a flat dose consisting of: (b) 550-600 mg every three weeks (para [0307] - "For repeated administrations over several days or longer, depending on the condition, the treatment is sustained until a desired suppression of disease symptoms occurs. One exemplary dosage of the antibody would be in the range from about 0.05 mg/kg to about 10 mg/kg. Thus, one or more doses of about 0.5 mg/kg, 2.0 mg/kg, 4.0 mg/kg or 10 mg/kg (or any combination thereof) may be administered to the patient. Such doses may be administered intermittently, e.g. every week or every three weeks (e.g. such that the patient receives from about two to about twenty, e.g. about six doses of the antibody)" ? for patient with weights between 54 and 91 kg (120-200 lbs), the dose of 5-10 mg/kg would be in the range of 550-600 mg). In the absence of a contribution over the prior art, the shared technical feature is not a shared special technical feature.

Further, the special technical feature of the inventions listed as Group IV is administration of anti-EGFL7 antibody in a dosing regimen comprising treatement cycles. This special technical feature is not shared by the inventions of Groups I-III.

Groups I-IV therefore lack unity under PCT Rule 13.2 because they do not share a same or corresponding special technical feature.