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(71) Applicant: **ANAPTYSBIO, INC.** [US/US]; 10421 Pacific Center Court, Suite 200, San Diego, California 92121 (US).

(72) Inventors: **VERDINO, Petra**; 3831 Camino Lindo, San Diego, California 92122 (US). **BOWERS, Peter**; 10025 Tree Haven Court, San Diego, California 92131 (US). **KING, David**; 310 Cole Ranch Road, Encinitas, California 92024 (US).

(74) Agents: **KOLOM, Melissa E.** et al.; Leydig, Voit & Mayer, Ltd., 180 N. Stetson Ave., Suite 4900, Chicago, Illinois 60601-6731 (US).

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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))*

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

(88) Date of publication of the international search report:
8 January 2015

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(54) Title: ANTIBODIES DIRECTED AGAINST ACTIVIN RECEPTOR TYPE II (ACTRII)

(57) Abstract: The invention relates to an isolated immunoglobulin heavy chain polypeptide and an isolated immunoglobulin light chain polypeptide that bind to an activin receptor type II (ActRII) protein (e.g., either or both of ActRIIA and/or ActRIIB). The invention provides an ActRII-binding agent that comprises the aforementioned immunoglobulin heavy chain polypeptide and immunoglobulin light chain polypeptide. The invention also provides related vectors, compositions, and methods of using the ActRII-binding agent to treat an ActRII-mediated disease.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US14/34344

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 39/395; C12N 15/00 (2014.01)
CPC - A61K 48/00; C07K 16/18; C12N 15/86; A61K 38/00, 2309/505
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; C12N 15/00 (2014.01)
CPC: A61K 48/00; C07K 16/18; C12N 15/86; A61K 38/00, 2309/505; USPC: 424/158.1, 130.1; 435/320.1, 386, 380, 350

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)
MicroPatent (US-G, US-A, EP-A, EP-B, WO, JP-bib, DE-C,B, DE-A, DE-T, DE-U, GB-A, FR-A); Google; Google Scholar; Dialog ProQuest; Entrez Pubmed; NCBI BLAST (protein); immunoglobulin, antibody, 'heavy chain variable,' 'CDR,' 'complementarity determining region'

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 2011/0064751 A1 (MOSSNER, E et al.) March 17, 2011; paragraphs [0024], [0028], [0115], [0148], [0158]; SEQ ID NO: 81	16 ----- 1-4, 17
A	US 2011/0052582 A1 (AUER, J et al.) March 3, 2011; paragraph [0195]; SEQ ID NO: 7	8-10
A	US 2007/0087000 A1 (WALSH, FS et al.) April 19, 2007; paragaphs [0021], [0023]; SEQ ID NO: 7	12-14
A	US 2010/0272734 A1 (BERGER, C et al.) October 28, 2010; abstract	1-4, 8-10, 12-14, 16, 17

☐ 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
22 October 2014 (22.10.2014)	19 NOV 2014

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Shane Thomas 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/US14/34344

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing filed or furnished:

   a. (means)

   ☐ on paper

   ☒ in electronic form

   b. (time)

   ☒ in the international application as filed

   ☐ together with the international application in electronic form

   ☐ subsequently to this Authority for the purposes of search

2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US14/34344

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.: 5-7, 11, 15, 21-27, 38-53
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:

-***-Please See Supplemental Page-***-

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.:

Group I: Claims 1-4, 8-10, 12-14, 16, 17

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.

-***-Continued from Box No. III: Observations Where Unity Of Invention Is Lacking:

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 1-4, 8-10, 12-14, 16 and 17 are directed toward an isolated immunoglobulin heavy chain polypeptide which comprises an amino acid sequence that is at least 90% identical to any one of SEQ ID NO: 1-68, SEQ ID NO: 115, SEQ ID NO: 116, SEQ ID NO: 117, SEQ ID NO: 118, or SEQ ID NO: 119; an isolated immunoglobulin comprising a CDR having a sequence of any one of SEQ ID NOs: 1-68, or 115-119; and isolated immunoglobulins having residues replaced and/or inserted, wherein the immunoglobulins comprise SEQ ID NOs: 1, 34, and 55.

Group II: Claims 18-20 and 28-37 are directed toward an isolated immunoglobulin light chain polypeptide which comprises an amino acid sequence that is at least 90% identical to an amino acid sequence of any one of SEQ ID NO: 69-97, SEQ ID NO: 101-104, SEQ ID NO: 120, SEQ ID NO: 121, or SEQ ID NO: 122; an isolated immunoglobulin comprising a CDR having a sequence of any one of SEQ ID NOs: 69-97, 101-104, or 120-122; and isolated immunoglobulins having residues replaced and/or inserted, wherein the immunoglobulins comprise SEQ ID NOs: 69, 101 and 103.

The inventions listed as Groups I-II 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 features of Group I include SEQ ID NOs: 1-68, and 115-119, which are not present in Group II, the special technical features of Group II including SEQ ID NOs: 69-97, 101-104, and 120-122.

Groups I-II share the technical features including an isolated immunoglobulin polypeptide comprising an amino acid sequence, and a complementarity determining region (CDR) having a sequence.

However, these shared technical features are previously disclosed by US 2010/0272734 A1 to Berger, et al. (hereinafter 'Berger'). Berger discloses an isolated immunoglobulin polypeptide comprising an amino acid sequence (an isolated immunoglobulin polypeptide comprising an amino acid sequence; paragraph [0021]), and a complementarity determining region (CDR) having a sequence (a complementarity determining region (CDR) having a sequence; paragraph [0021]).

Since none of the special technical features of the Groups I-II inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Berger reference, unity of invention is lacking.