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(71) **Applicant**: **RUIYI INC.** [US/US]; 505 Coast Boulevard, Suite 300, La Jolla, CA 92037 (US).

(72) **Inventors**: **KRETZ-ROMMEL, Anke**; 4535 Kensington Drive, San Diego, CA 92116 (US). **SHI, Lei**; 4-602, 777 Biyun Road, Shanghai 201206 (CN). **FERRINI, Roger**; 325 S. Sierra Avenue, #23, Solana Beach, CA 92075 (US). **YANG, Teddy**; Rm. 2904, Building 7, 888 South Shaanxi Road, Shanghai 200000 (CN). **XU, Fei**; 1061 Vintner Boulevard, Palm Beach Gardens, FL 33410 (US). **CAMPION, Brian**; 630 Fern Glen, La Jolla, CA 92037 (US).

(74) **Agent**: **DEGIULIO, James, V.**; McDonnell Boehnen Hulbert & Berghoff LLP, 300 South Wacker Drive, Chicago, IL 60606 (US).

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(88) **Date of publication of the international search report**:
12 November 2015

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(54) **Title**: ANTIBODIES THAT BIND HUMAN CANNABINOID 1 (CB1) RECEPTOR

(57) **Abstract**: The present invention relates to novel antibodies and fragments thereof that binds cannabinoid 1 (CB1) receptor. The antibodies and fragments thereof as disclosed herein include humanized antibodies that bind CB1 receptor. The invention also includes uses of the antibodies for treating a disease or disorder responsive to antagonism or agonism of the CB1 receptor.

INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/28 A61K39/395 A61P3/00 A61P9/00
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)
C07K A61K

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, EMBASE, BIOSIS, Sequence Search, 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	XINGLIN KUANG ET AL: "A Novel Monoclonal Antibody Against Cannabinoid Receptor 1", HYBRIDOMA, vol. 31, no. 2, 1 April 2012 (2012-04-01), pages 131-136, XP055138991, ISSN: 1554-0014, DOI: 10.1089/hyb.2011.0099	1-8,10, 12,13, 17-22, 25-30
Y	abstract page 132, column 1 page 135, column 1 page 135, column 2 page 134,, column 2	14-16, 36-38

Y	WO 2012/007847 A2 (EPSHTEIN OLEG ILIICH [RU]; SERGEEVA SVETLANA ALEXANDROVNA [RU]; DOLGOV) 19 January 2012 (2012-01-19) claims 1, 2, 12	14-16, 36-38

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* 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
30 June 2015	24/09/2015

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Saame, Tina

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International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CHORVAT ROBERT J: "Peripherally restricted CB1 receptor blockers", BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 23, no. 17, 2013, pages 4751-4760, XP028690076, ISSN: 0960-894X, DOI: 10.1016/J.BMCL.2013.06.066 the whole document -----	38
A	DATABASE Geneseq [Online] 9 December 2010 (2010-12-09), "Mouse anti-amyloid beta monoclonal antibody AL-208 mature VL, SEQ 560.", XP002741601, retrieved from EBI accession no. GSP:AYL01861 Database accession no. AYL01861 abstract; sequence -----	21

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2015/023108

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.:

11, 20-22, 28-30(completely); 1-10, 12-19, 25-27, 36-38(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: 11, 20-22, 28-30(completely); 1-10, 12-19, 25-27, 36-38(partially)

Antibody (or antigen binding fragment thereof) binding to CB1 receptor with a Kd of 1 micromolar or less, wherein the antibody has a heavy chain variable region comprising SEQ ID No 2 and/or a light chain variable region comprising SEQ ID No 6 (antibody PA13R3-P1C4); methods of using this antibody including therapeutic and diagnostic methods; an antibody binding to CB1 receptor comprising the heavy chain and/or light chain CDRs represented by SEQ ID Nos 352-354 and 355-357 (antibody PA13R3-P1C4); an antibody having the same binding characteristics as the above antibodies; framework humanized variants of the above antibodies;

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2. claims: 1-10, 12-19(all partially)

Antibody (or antigen binding fragment thereof) binding to CB1 receptor with a Kd of 1 mM or less, wherein the antibody has a heavy chain variable region comprising SEQ ID Nos 10 or 18 and/or a light chain variable region comprising SEQ ID Nos 14 or 22 (chimeric and mouse antibody 36E12B6C2); methods of using this antibody including therapeutic and diagnostic methods; an antibody having the same binding characteristics as the above antibodies; framework humanized variants of the above antibodies;

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3. claims: 1-10, 12-19(all partially)

Antibody (or antigen binding fragment thereof) binding to CB1 receptor with a Kd of 1 mM or less, wherein the antibody has a heavy chain variable region comprising SEQ ID No 26 and/or a light chain variable region comprising SEQ ID No 30 (antibody PA2LR3-P4B5); methods of using this antibody including therapeutic and diagnostic methods; an antibody having the same binding characteristics as the above antibodies; framework humanized variants of the above antibodies;

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4. claims: 23(completely); 25-27, 36-38(partially)

Antibody (or antigen binding fragment thereof) binding to CB1 receptor wherein the antibody comprises a heavy chain CDR1 represented by any of SEQ ID Nos 443-463, a heavy chain CDR2 represented by any of SEQ ID Nos 464-557 and a heavy chain CDR3 represented by any of 578-625; humanized versions thereof; therapeutic methods of using these antibodies;

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

5. claims: 24(completely); 25-27, 36-38(partially)

Antibody (or antigen binding fragment thereof) binding to CB1 receptor wherein the antibody comprises a light chain CDR1 represented by any of SEQ ID Nos 626-661, a light chain CDR2 represented by any of SEQ ID Nos 662-742 and a light chain CDR3 represented by any of 742-824; humanized versions thereof; therapeutic methods of using these antibodies;

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6. claims: 31-35(completely); 36-38(partially)

An isolated humanized antibody (or antigen binding fragment thereof) which has a binding affinity Kd for CB1 receptor of 100nM or less; therapeutic methods of using this antibody

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2015/023108

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WO 2012007847 A2	19-01-2012	AR 082246 A1	21-11-2012
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