US009409988B2

(12) **United States Patent**
Robert et al.

(10) **Patent No.: US 9,409,988 B2**
(45) **Date of Patent: Aug. 9, 2016**

(54) **ANTI-AXL ANTIBODIES AND USES THEREOF**

(75) Inventors: **Bruno Robert**, Montpellier (FR); **Benedicte Fauvel**, Montpellier (FR); **Gwenael Cheve**, Montpellier (FR); **Aziz Yasri**, Montpellier (FR); **Christel Larbouret**, Montpellier (FR); **Wilhem Leconet**, Montpellier (FR); **Thierry Chardes**, Montpellier (FR); **Christian Larroque**, Montpellier (FR); **Andre Pelegrin**, Montpellier (FR)

(73) Assignees: **INSERM (Institut National De La Sante Et De La Recherche Medicale)** (FR); **ORIBASE Pharma** (FR); **UNIVERSITE De Montpellier 1** (FR); **INSTITUT Regional Du Cancer De Montpellier-Val D'Aurelle** (FR)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **14/127,416**

(22) PCT Filed: **Jun. 22, 2012**

(86) PCT No.: **PCT/EP2012/062115**

§ 371 (c)(1),
(2), (4) Date: **Apr. 24, 2014**

(87) PCT Pub. No.: **WO2012/175692**

PCT Pub. Date: **Dec. 27, 2012**

(65) **Prior Publication Data**

US 2014/0227283 A1 Aug. 14, 2014

Related U.S. Application Data

(60) Provisional application No. 61/504,256, filed on Jul. 4, 2011.

(30) **Foreign Application Priority Data**

Jun. 22, 2011 (EP) 11305792

(51) **Int. Cl.**

C07K 16/40	(2006.01)
C07K 16/28	(2006.01)
C07K 16/32	(2006.01)
G01N 33/574	(2006.01)
G01N 33/68	(2006.01)
A61K 39/00	(2006.01)

(52) **U.S. Cl.**

CPC ***C07K 16/28*** (2013.01); ***C07K 16/32*** (2013.01); ***G01N 33/57492*** (2013.01); ***G01N 33/6872*** (2013.01); *A61K 2039/505* (2013.01); *C07K 2317/33* (2013.01); *C07K 2317/34* (2013.01); *C07K 2317/565* (2013.01); *C07K 2317/73* (2013.01); *C07K 2317/76* (2013.01); *C07K 2317/92* (2013.01)

(58) **Field of Classification Search**

CPC C07K 16/00–16/468

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2012/0014870	A1 *	1/2012	Aburatani	C07K 5/1008 424/1.49
2014/0302041	A1 *	10/2014	Robert	C07K 16/2863 424/139.1

FOREIGN PATENT DOCUMENTS

EP	1 382 969		1/2004
EP	2 228 392		9/2010
EP	2 270 053		1/2011
EP	2 270 053	A1	1/2011
WO	2009/062690		5/2009
WO	2009/063965		5/2009
WO	WO2009/062690	A1 *	5/2009
WO	2010/131733		11/2010
WO	2011/014457		2/2011

OTHER PUBLICATIONS

Chan and Carter, Nature Reviews Immunology, 2010; 10:301-316.*
Li et al., Oncogene 2009; 28:3442-55.*
Lemke and Rothlin, Nat. Rev. Immunol. 2008; 8:327-36.*
V.A. Korshunov, Clin. Sci. 2012; 122:361-68.*
Brand et al., Arthritis Rheum., 2013; 65:671-80.*
Brindley et al., Virology. 2011; 415:83-94.*
Bartolazzi et al., The Lancet 2008; 9:543-49.*
Verma et al., Mol. Cancer Therapeutics 2011; 10(10):1763-73.*
E. A. Padlan, Adv Prot Chem 49:57-133; 1996.*
Corada et al., Blood, 2001; 97:1679-84.*

* cited by examiner

Primary Examiner — Jessica H Roark
(74) *Attorney, Agent, or Firm* — McAndrews, Held & Malloy, Ltd.

(57) **ABSTRACT**

The present invention relates to anti-Axl antibodies and uses thereof in diagnostic and therapeutic methods. More particularly, the present invention relates to a monoclonal antibody having specificity for Axl comprising an heavy chain variable region comprising SEQ ID NO:2 in the H-CDR1 region, SEQ ID NO:3 in the H-CDR2 region and SEQ ID NO:4 in the H-CDR3 region; and a light chain variable region comprising SEQ ID NO: 6 in the L-CDR1 region, SEQ ID NO:7 in the L-CDR2 region and SEQ ID NO:8 in the L-CDR3 region. Said monoclonal antibody binds to the extracellular domain of Axl via, SEQ ID NO:9 and SEQ ID NO: 10.

17 Claims, 12 Drawing Sheets