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C07K 16/28 (2006.01) *A61K 39/395* (2006.01)
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61/783,094 14 March 2013 (14.03.2013) US
- (71) **Applicant:** REGENERON PHARMACEUTICALS, INC. [US/US]; 777 Old Saw Mill River Road, Tarrytown, NY 10591 (US).
- (72) **Inventors:** MACDONALD, Lynn; 16 Gedney Way, White Plains, NY 10605 (US). MURPHY, Andrew, J.; 10 Newton Court, Croton-on-hudson, NY 10520 (US). PAPADOPOULOS, Nicholas, J.; 59 Heritage Lane, Lagrangeville, NY 12540 (US). STAHL, Neil; 48 Kent Shore Drive, Carmel, NY 10512 (US). ALESSANDRI-HABER, Nicole; 15 Bonwit Road, Rye Brook, NY 10573 (US).
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- (81) **Designated States** (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,

BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

- (84) **Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

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:**
4 December 2014

(54) **Title:** HUMAN ANTIBODIES TO NAV1.7

(57) **Abstract:** The present invention provides antibodies that bind to the human voltage gated sodium channel designated Nav1.7 and methods of using same. According to certain embodiments of the invention, the antibodies are fully human antibodies that bind to human Nav1.7 (hNav1.7). The antibodies of the invention are useful for the treatment of diseases and disorders associated with one or more Nav1.7 biological activities, including the treatment of acute or chronic pain conditions, or inflammatory conditions.



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/024336

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.:

1-9, 11, 15, 18-32(all 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.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/024336

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/28 A61K39/395
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, BIOSIS, EMBASE, 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	US 2011/307966 A1 (MACDONALD LYNN [US] ET AL) 15 December 2011 (2011-12-15) page 15,, paragraph 0178 page 13; example III page 15, paragraph 0182 -----	1-9,11, 15,18-32
X	EP 2 527 842 A1 (REGENERON PHARMA [US]) 28 November 2012 (2012-11-28) page 24, paragraph 0233 - paragraph 0234 page 25; table 1 ----- -/--	1-9,11, 15,18-32



Further documents are listed in the continuation of Box C.



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

7 July 2014

Date of mailing of the international search report

08/10/2014

Name and mailing address of the ISA/

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Malamoussi, A

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2014/024336

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2011/052350 A1 (KUREHA CORP [JP]; NAKAMURA TAKASHI [JP]; AMANO YOSHIKAZU [JP]) 5 May 2011 (2011-05-05) cited in the application abstract page 66, line 4 - line 9 page 65 - page 66; table 1 page 74, line 27 - line 32 figures 3B, 3C page 26, line 4 -----	1-9,11, 15,18-32
X	WO 2011/051349 A1 (UCB PHARMA SA [BE]; MILLER KAREN MARGRETE [BE]; DE RYCK MARC ROGER [BE]) 5 May 2011 (2011-05-05) page 63 - page 64; table 1 page 69, line 12 figure 3F page 26, line 1 - line 3 -----	1-9,11, 15,18-32
A	R-Y. BI ET AL: "Involvement of trigeminal ganglionic Na v 1.7 in hyperalgesia of inflamed temporomandibular joint is dependent on ERK1/2 phosphorylation of glial cells in rats", EUROPEAN JOURNAL OF PAIN, vol. 17, no. 7, 14 December 2012 (2012-12-14), pages 983-994, XP055127084, ISSN: 1090-3801, DOI: 10.1002/j.1532-2149.2012.00262.x abstract -----	1-9,11, 15,18-32
A	MARK L DALLAS ET AL: "Immunopharmacology: utilizing antibodies as ion channel modulators", EXPERT REVIEW OF CLINICAL PHARMACOLOGY, vol. 3, no. 3, 1 May 2010 (2010-05-01), pages 281-289, XP055127086, ISSN: 1751-2433, DOI: 10.1586/ecp.10.18 the whole document -----	1-9,11, 15,18-32
A	JEFFREY J CLARE: "Targeting voltage-gated sodium channels for pain therapy", EXPERT OPINION ON INVESTIGATIONAL DRUGS, ASHLEY PUBLICATIONS LTD., LONDON, GB, vol. 19, no. 1, 1 January 2010 (2010-01-01), pages 45-62, XP008156826, ISSN: 1354-3784, DOI: 10.1517/13543780903435340 the whole document -----	1-9,11, 15,18-32
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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/024336

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	S. D. SHIELDS ET AL: "Sodium Channel Nav1.7 Is Essential for Lowering Heat Pain Threshold after Burn Injury", JOURNAL OF NEUROSCIENCE, vol. 32, no. 32, 8 August 2012 (2012-08-08), pages 10819-10832, XP055127114, ISSN: 0270-6474, DOI: 10.1523/JNEUROSCI.0304-12.2012 abstract -----	1-9,11, 15,18-32
A	SULAYMAN D. DIB-HAJJ ET AL: "The Nav1.7 sodium channel: from molecule to man", NATURE REVIEWS NEUROSCIENCE, vol. 14, no. 1, 12 December 2012 (2012-12-12), pages 49-62, XP055127118, ISSN: 1471-003X, DOI: 10.1038/nrn3404 the whole document -----	1-9,11, 15,18-32

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2014/024336

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2011307966	A1	15-12-2011	NONE
EP 2527842	A1	28-11-2012	DK 2527842 T3 08-09-2013 EP 2527842 A1 28-11-2012 EP 2579039 A1 10-04-2013 EP 2631654 A1 28-08-2013 HK 1174387 A1 15-11-2013
WO 2011052350	A1	05-05-2011	TW 201127712 A 16-08-2011 WO 2011052350 A1 05-05-2011
WO 2011051349	A1	05-05-2011	CA 2778671 A1 05-05-2011 CN 102597002 A 18-07-2012 EP 2493928 A1 05-09-2012 JP 2013508443 A 07-03-2013 US 2012259096 A1 11-10-2012 WO 2011051349 A1 05-05-2011

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 2/4.

2. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 6/8.

3. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 10/12.

4. claims: 1-32(partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 14/16.

5. claims: 1-9, 11, 12, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 18/20.

6. claims: 1-32(partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 22/24.

7. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 26/28.

8. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 26/28.

9. claims: 1-32(partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 30/32.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

10. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 34/36.

11. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 38/40.

12. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 42/44.

13. claims: 1-9, 11, 12, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 46/48.

14. claims: 1-9, 11, 12, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 50/52.

15. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 54/56.

16. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 58/60.

17. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 62/64.

18. claims: 1-9, 11, 12, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 66/68.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

19. claims: 1-9, 11, 12, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 70/72.

20. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 74/76.

21. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 78/80.

22. claims: 1-9, 11, 12, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 82/84.

23. claims: 1-9, 11, 12, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 86/88.

24. claims: 1-9, 11, 12, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 90/92.

25. claims: 1-9, 11, 12, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 94/96.

26. claims: 1-32(partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 98/100.

27. claims: 1-9, 11, 12, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID No 102/104.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

28. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 106/108.

29. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 110/112.

30. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 681/683.

31. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 683/687.

32. claims: 1-9, 11, 12, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 689/691.

33. claims: 1-9, 11, 12, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 693/695.

34. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 697/699.

35. claims: 1-32(partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 701/703.

36. claims: 1-9, 11, 12, 15-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 705/707.

37. claims: 1-9, 11, 15, 18-32(all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 709/711.

38. claims: 1-32(partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 722/724.

39. claims: 1-32(partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 727/735.

40. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 743/751.

41. claims: 1-32(partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 759/767.

42. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 791/799.

43. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 807/815.

44. claims: 1-9, 11, 15, 18-32(all partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 823/831.

45. claims: 1-32(partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 860/862.

46. claims: 1-32(partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 864/866.

47. claims: 1-32(partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 868/870.

48. claims: 1-32(partially)

An isolated human antibody comprising HCVR/LCVR with SEQ ID
No 872/874.
