(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
24 August 2017 (24.08.2017)

WIPO | PCT

(10) International Publication Number
WO 2017/141104 A3

(51) International Patent Classification:
A61K 9/00 (2006.01) *A61P 9/00* (2006.01)
A61K 45/06 (2006.01) *A61P 31/12* (2006.01)
A61K 31/485 (2006.01) *A61P 37/00* (2006.01)
A61P 35/00 (2006.01)

(21) International Application Number:
PCT/IB2017/000124

(22) International Filing Date:
17 February 2017 (17.02.2017)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/296,759 18 February 2016 (18.02.2016) 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, DJ, 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, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, 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, ST, 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))*

(88) Date of publication of the international search report:
02 November 2017 (02.11.2017)

(54) Title: METHOD FOR INDUCING A SUSTAINED IMMUNE RESPONSE

(57) Abstract: A method for inducing a sustained immune response in humans or animal patient suffering from human immunodeficiency virus (HIV) acquired immune deficiency syndrome (AIDS, autoimmune disease, cancer, inflammation, and neurodegenerative diseases comprises daily administration to such patients a single oral tablet, rapidly dissolving film, capsule, liquid or cream dose of an Immediate release naltrexone composition comprising between about.01 to about l0mg of naltrexone. In order to provide a benefit the naltrexone must be an Immediate release composition comprising between about.01 and about l0mg of naltrexone.

WO 2017/141104 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2017/000124

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K9/00 A61K45/06 A61K31/485 A61P35/00 A61P9/00
A61P31/12 A61P37/00
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)
A61K A61P

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, WPI Data, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BURTON M. BERKSON ET AL: "The Long-term Survival of a Patient With Pancreatic Cancer With Metastases to the Liver After Treatment With the Intravenous [alpha]-Lipoic Acid/Low-Dose Naltrexone Protocol", INTEGRATIVE CANCER THERAPIES, vol. 5, no. 1, 1 March 2006 (2006-03-01), pages 83-89, XP55366095, US ISSN: 1534-7354, DOI: 10.1177/1534735405285901 abstract -----	1-11, 67-77
X	US 6 384 044 B1 (BIHARI BERNARD [US]) 7 May 2002 (2002-05-07) column 6, line 53; claims 9,12,13; examples 3,4 -----	1-11,13, 67-77
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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
11 September 2017	27/09/2017

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	Allnutt, Sarah

6

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LDN Research Trust: "Low-dose Naltrexone (LDN) Fact Sheet 2015 Suggested Method of Therapy", , 1 January 2015 (2015-01-01), XP055366331, Retrieved from the Internet: URL:https://www.ldnresearchtrust.org/sites/default/files/LDN%202015%20Fact%20Sheet.pdf [retrieved on 2017-04-21] page 7, paragraph 2	1-11, 13-25, 67-77
X	J Carnahan: "Low-dose Naltrexone (LDN) The new treatment you've never heard of... ¦ Jill C. Carnahan, MD ¦ Pulse ¦ LinkedIn", , 19 December 2015 (2015-12-19), XP055366304, Retrieved from the Internet: URL:https://www.linkedin.com/pulse/low-dose-naltrexone-ldn-new-treatment-youve-never-carnahan-md [retrieved on 2017-04-21] See page 3, paragraph under "Experimental and Off-label but well tolerated and promising"	15-25, 67-77
X	WO 2007/123865 A2 (SMITH JILL P [US]) 1 November 2007 (2007-11-01) See also Abstract on cover page; paragraphs [0025] - [0037]; claim 15 paragraph [0049]	15-25, 67-77
X	B Bihari: "Low Dose Naltrexone in the Treatment of HIV Infection (September 1996)", , 1 September 1996 (1996-09-01), XP55366284, Retrieved from the Internet: URL:http://www.lowdosenaltrexone.org/ldn_hiv_1996.htm [retrieved on 2017-04-21] the whole document	27-41
A	WO 01/85257 A2 (PAIN THERAPEUTICS INC [US]; EINSTEIN COLL MED [US]; SHERMAN BARRY [US]) 15 November 2001 (2001-11-15) claim 114; examples 1,3	1-100

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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.
X	"Low Dose Naltrexone", , 5 April 2010 (2010-04-05), XP002769413, Retrieved from the Internet: URL:http://www.skipspharmacy.com/wplog/services/low-dose-naltrexone/ [retrieved on 2017-04-21] This page was retrieved from the following link http://www.skipspharmacy.com/wplog/services/low-dose-naltrexone/ found when entering the search term "immediate" in the search field from the home page http://www.skipspharmacy.com/wplog/	15-25
A	WO 2011/144746 A2 (MOLTENI & C [IT]; ANGELI ROBERTO [IT]; RAFFAELI WILLIAM [IT]; RIGAMONT) 24 November 2011 (2011-11-24) example 1	1-100
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X	US 2012/252831 A1 (PISAK IBRAHIM MUSTAFA ISKENDER [TR] ET AL) 4 October 2012 (2012-10-04) example 1	15-25
X	US 5 013 739 A (BIHARI BERNARD [US] ET AL) 7 May 1991 (1991-05-07) column 6, lines 28-29,57,58; examples 1-3	15-21, 23-25, 27,29, 33-37, 39-41
X	US 2011/245278 A1 (PISAK IBRAHIM MUSTAFA ISKENDER [TR] ET AL) 6 October 2011 (2011-10-06) paragraphs [0011], [0043]; example 2	27-29, 33-41

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6

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011/082167 A1 (PISAK IBRAHIM MUSTAFA ISKENDER [TR] ET AL) 7 April 2011 (2011-04-07) paragraph [0032]; claims 1,4; example 1	27-29, 33-40
X	PRADEEP CHOPRA ET AL: "Treatment of Complex Regional Pain Syndrome (CRPS) Using Low Dose Naltrexone (LDN)", JOURNAL OF NEUROIMMUNE PHARMACOLOGY, vol. 8, no. 3, 2 April 2013 (2013-04-02), pages 470-476, XP55403142, Boston ISSN: 1557-1890, DOI: 10.1007/s11481-013-9451-y the whole document	43-53
X	PAPE W ET AL: "Low dose naltrexone in the treatment of dissociative symptoms", NERVENARZT, SPRINGER VERLAG, BERLIN, DE, vol. 86, no. 3, 26 November 2014 (2014-11-26), pages 346-351, XP035472706, ISSN: 0028-2804, DOI: 10.1007/S00115-014-4015-9 [retrieved on 2014-11-26] last 2 paragraphs of pg 347, col.1; page 347, column 1 page 351, column 1	43-53
X	JARRED YOUNGER ET AL: "The use of low-dose naltrexone (LDN) as a novel anti-inflammatory treatment for chronic pain", CLINICAL RHEUMATOLOGY., vol. 33, no. 4, 15 February 2014 (2014-02-15), pages 451-459, XP55366086, BE ISSN: 0770-3198, DOI: 10.1007/s10067-014-2517-2 page 455, column 1, paragraphs 2,3; figure 2	43-53
X	US 2007/259939 A1 (STEBBING FRANKLIN LEROY [US]) 8 November 2007 (2007-11-08) claims 8-16,19,20	43-53, 90-99
X	WO 2014/120936 A2 (PHARMORX THERAPEUTICS INC [US]) 7 August 2014 (2014-08-07) example 1	43-53

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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.
X	DEBASISH HOTA ET AL: "Off-Label, Low-Dose Naltrexone for Refractory Painful Diabetic Neuropathy", PAIN MEDICINE, 7 December 2015 (2015-12-07), page pnv009, XP055403281, US ISSN: 1526-2375, DOI: 10.1093/pm/pnv009 the whole document	43-53
A	WO 2005/079767 A2 (UNIVERSITAETSKLINIKUM MUENSTER [DE]; WEBER THOMAS [DE]) 1 September 2005 (2005-09-01) page 13, lines 26-29	55-66
X	WO 01/70031 A1 (ZAGAN IAN S [US]; BLEBEA JOHN [US]; MCLAUGHLIN PATRICIA J [US]) 27 September 2001 (2001-09-27) page 10, lines 16-26; claims 1,8,11 page 3, lines 20-24	79-84, 86,87

6

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2017/000124

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.:

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

Information on patent family members

International application No
PCT/IB2017/000124

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2017/000124

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		WO 0170031 A1	27-09-2001

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-14

An Immediate release pharmaceutical composition comprising between about 0.01mg and about 10.0 mg of naltrexone or a pharmaceutically acceptable salt thereof for use in a method for treating or preventing cancer in a mammal, wherein said Immediate release pharmaceutical composition is to be administered alone or in combination with one or more anti-cancer agents or radiation therapy.

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2. claims: 15-26

An Immediate release pharmaceutical composition comprising between about 0.01 mg and about 10.0 mg of naltrexone or a pharmaceutically acceptable salt thereof for use in a method for treating or preventing autoimmune and inflammatory diseases in a mammal.

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3. claims: 27-42

An Immediate release pharmaceutical composition comprising between about 0.01 mg and about 10.0 mg of naltrexone or a pharmaceutically acceptable salt thereof for use in a method for treating or preventing viral infections in a mammal, wherein said Immediate release pharmaceutical composition is to be administered alone or in combination with one or more anti-viral agents.

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4. claims: 43-54

An Immediate release pharmaceutical composition comprising between about 0.01 mg and about 10.0 mg of naltrexone or a pharmaceutically acceptable salt thereof for use in a method for treating or preventing disorders of the central nervous system in a mammal.

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5. claims: 55-66

An Immediate release pharmaceutical composition comprising between about 0.01 mg and about 10.0 mg of naltrexone or a pharmaceutically acceptable salt thereof for use in a method for treating or preventing cardiovascular disorders in a mammal.

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6. claims: 67-78

An Immediate release pharmaceutical composition comprising

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

between about 0.01 mg and about 10.0 mg of naltrexone or a pharmaceutically acceptable salt thereof for use in a method for modulating the length of telomeres in the cells of a mammal.

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7. claims: 79-89

An Immediate release pharmaceutical composition comprising between about 0.01 mg and about 10.0 mg of naltrexone or a pharmaceutically acceptable salt thereof for use in a method for inhibiting angiogenesis in a mammal.

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8. claims: 90-100

An Immediate release pharmaceutical composition comprising between about 0.01 mg and about 10.0 mg of naltrexone or a pharmaceutically acceptable salt thereof for use in a method for inducing a sustained immune response in a mammal.
