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(54) Title: PHARMACEUTICAL FORMULATIONS FOR THE TREATMENT AND PREVENTION OF TRAUMA-INDUCED NEUROPATHOLOGY AND NEURODEGENERATION

(57) Abstract: Novel multi-component formulations, procedures and methods for use in treating neuropathology and neurodegeneration incident to trauma are provided. Multi-component formulations of the invention comprise biologically active forms of any two, any three, or all four of at least one neurosteroid or neuroactive steroid, such as progesterone or synthetic progestin, at least one anti-epileptic or anticonvulsant, such as gabapentin, pregabalin or valproic acid, at least one NK-1 receptor antagonist, such as aprepitant, casopitant or vestipitant, at least one lithium-containing or lithium-related drug. The provided formulations are configured or adapted to prevent or reduce the incidence and severity of neurological damage caused by trauma, or the risk of such damage. Formulations, procedures and methods of the invention advantageously effect both neuroprotective actions to prevent or reduce secondary injuries, and neurotrophic actions to repair and restore cells and tissues affected by the trauma, and are especially useful in treating injury or trauma to nerve cells, to neural support cells and to neural support tissues.

## INTERNATIONAL SEARCH REPORT

International application No.

**PCT/IB2014/000606**

A. CLASSIFICATION OF SUBJECT MATTER IPC: <i>A61K 31/573</i> (2006.01), <i>A61K 31/19</i> (2006.01), <i>A61K 31/197</i> (2006.01), <i>A61K 31/445</i> (2006.01), <i>A61K 31/495</i> (2006.01), <i>A61K 31/5377</i> (2006.01), <i>A61K 31/57</i> (2006.01), <i>A61K 33/00</i> (2006.01), <i>A61K 33/14</i> (2006.01), <i>A61P 25/00</i> (2006.01), <i>A61P 25/28</i> (2006.01)		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols) A61K		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used) TotalPatent, Canadian Patent Database, EPOQUE: anticonvulsant, antiepileptic, neurosteroid, trauma, gabapentin, pregabalin, valproic, progesterone, methylprednisolone, medroxyprogesterone, trauma, neuro		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011/0288059 A1 (MARX, et al.) 24 November 2011 (24-11-2011) Claim 9, abstract	1-3, 6-12, 15-24
X	WO 2010/107815 A1 (ROSE, et al.) 23 September 2010 (23-09-2010) claims 17, 20	1-3, 6-12, 15-24
X	US 2011/0301133 A1 (WU, et al.) 8 December 2011 (08-12-2011) claims 25, 28	1-3, 6-12, 15-24
X	WO 2010/077680 A2 (WU, et al.) 8 July 2010 (08-07-2010) claims 25, 28	1-3, 6-12, 15-24
X	US 2011/0046090 A1 (BARLOW, et al.) 24 February 2011 (24-02-2011) claims 1, 4, 5, page 146, paragraph [1160] to page 147	1-3, 6-12, 15-24
X	WO 2012/112340 A2 (PAN) 23 August 2012 (23-08-2012) claims 1, 9, 39-46	1-3, 6-12, 15-24
X	WO 2009/089024 A1 (MARX, et al.) 16 July 2009 (16-07-2009) claim 4, page 93, line 8, example 16; claim 8, abstract	1-3, 6-12, 15-24
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> See patent family annex.		
* "A" "E" "L" "O" "P"	Special categories of cited documents: document defining the general state of the art which is not considered to be of particular relevance earlier application or patent but published on or after the international filing date 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) document referring to an oral disclosure, use, exhibition or other means document published prior to the international filing date but later than the priority date claimed	"T" "X" "Y" "&"
Date of the actual completion of the international search 4 June 2014 (04-06-2014)	Date of mailing of the international search report 23 July 2014 (23-07-2014)	
Name and mailing address of the ISA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001-819-953-2476	Authorized officer  Karol Gajewski (819) 934-6734	

**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the 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.  Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claim 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.  Claim 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:

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 claim 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 claim Nos.: Claims 1-3, 6-12, 15-24, all in part  
The search is restricted to the embodiment relating to a combination of an anticonvulsant or antiepileptic with a neurosteroid or neuroactive steroid.

**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/IB2014/000606**

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
US2011288059A1	24 November 2011 (24-11-2011)	US2011288059A1 AU2009204429A1 CA2711605A1 EP2249840A1 US2009074677A1 US2009203658A1 WO2009089024A1 WO2009089024A8 WO2010107815A1 US2013210783A1	24 November 2011 (24-11-2011) 16 July 2009 (16-07-2009) 16 July 2009 (16-07-2009) 17 November 2010 (17-11-2010) 19 March 2009 (19-03-2009) 13 August 2009 (13-08-2009) 16 July 2009 (16-07-2009) 21 October 2010 (21-10-2010) 23 September 2010 (23-09-2010) 15 August 2013 (15-08-2013)
WO2010107815A1	23 September 2010 (23-09-2010)	WO2010107815A1 AU2009204429A1 CA2711605A1 EP2249840A1 US2009074677A1 US2009203658A1 WO2009089024A1 WO2009089024A8 US2011288059A1 US2013210783A1	23 September 2010 (23-09-2010) 16 July 2009 (16-07-2009) 16 July 2009 (16-07-2009) 17 November 2010 (17-11-2010) 19 March 2009 (19-03-2009) 13 August 2009 (13-08-2009) 16 July 2009 (16-07-2009) 21 October 2010 (21-10-2010) 24 November 2011 (24-11-2011) 15 August 2013 (15-08-2013)
US2011301133A1	08 December 2011 (08-12-2011)	US2011301133A1 AU2009333537A1 CA2746220A1 CN102292338A EP2376495A2 EP2376495A4 JP2012511054A KR20110114565A MX2011006108A RU2011128013A WO2010077680A2 WO2010077680A3	08 December 2011 (08-12-2011) 28 July 2011 (28-07-2011) 08 July 2010 (08-07-2010) 21 December 2011 (21-12-2011) 19 October 2011 (19-10-2011) 31 October 2012 (31-10-2012) 17 May 2012 (17-05-2012) 19 October 2011 (19-10-2011) 18 November 2011 (18-11-2011) 20 January 2013 (20-01-2013) 08 July 2010 (08-07-2010) 14 October 2010 (14-10-2010)
WO2010077680A2	08 July 2010 (08-07-2010)	WO2010077680A2 WO2010077680A3 AU2009333537A1 CA2746220A1 CN102292338A EP2376495A2 EP2376495A4 JP2012511054A KR20110114565A MX2011006108A RU2011128013A US2011301133A1	08 July 2010 (08-07-2010) 14 October 2010 (14-10-2010) 28 July 2011 (28-07-2011) 08 July 2010 (08-07-2010) 21 December 2011 (21-12-2011) 19 October 2011 (19-10-2011) 31 October 2012 (31-10-2012) 17 May 2012 (17-05-2012) 19 October 2011 (19-10-2011) 18 November 2011 (18-11-2011) 20 January 2013 (20-01-2013) 08 December 2011 (08-12-2011)
US2011046090A1	24 February 2011 (24-02-2011)	US2011046090A1 AU2006308889A1 CA2625210A1 EP1942879A1 EP2314289A1 JP2009513672A US2007112017A1 WO2007053596A1	24 February 2011 (24-02-2011) 10 May 2007 (10-05-2007) 10 May 2007 (10-05-2007) 16 July 2008 (16-07-2008) 27 April 2011 (27-04-2011) 02 April 2009 (02-04-2009) 17 May 2007 (17-05-2007) 10 May 2007 (10-05-2007)

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WO2012112340A2	23 August 2012 (23-08-2012)	WO2012112340A2	23 August 2012 (23-08-2012)
		WO2012112340A3	17 April 2014 (17-04-2014)
		AU2012218094A1	29 August 2013 (29-08-2013)
		CA2827715A1	23 August 2012 (23-08-2012)
		CN103764136A	30 April 2014 (30-04-2014)
		EP2675447A2	25 December 2013 (25-12-2013)
		MX2013009544A	26 September 2013 (26-09-2013)
		US2013324608A1	05 December 2013 (05-12-2013)
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WO2009089024A1	16 July 2009 (16-07-2009)	WO2009089024A1	16 July 2009 (16-07-2009)
		WO2009089024A8	21 October 2010 (21-10-2010)
		AU2009204429A1	16 July 2009 (16-07-2009)
		CA2711605A1	16 July 2009 (16-07-2009)
		EP2249840A1	17 November 2010 (17-11-2010)
		US2009074677A1	19 March 2009 (19-03-2009)
		US2009203658A1	13 August 2009 (13-08-2009)
		WO2010107815A1	23 September 2010 (23-09-2010)
		US2011288059A1	24 November 2011 (24-11-2011)
		US2013210783A1	15 August 2013 (15-08-2013)