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- (74) **Agent: HALSTEAD, David, P. et al.;** Foley Hoag LLP, 155 Seaport Boulevard, Boston, MA 02210-2600 (US).
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Declarations under Rule 4.17:

— of inventorship (Rule 4.17(iv))

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(54) **Title:** CDPK1 INHIBITORS, COMPOSITIONS AND METHODS RELATED THERETO

(57) **Abstract:** The invention relates to inhibitors of calcium-dependent protein kinase 1 (CDPK1) and pharmaceutical preparations thereof. The invention further relates to methods of treatment of parasitic infections, such as *T. gondii*, *T. cruzi*, *P. falciparum*, *T. brucei*, or *L. major* infections, using the novel inhibitors of the invention.



INTERNATIONAL SEARCH REPORT

International application No.

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A. CLASSIFICATION OF SUBJECT MATTER IPC (2018.01) C07D 487/04, A61K 31/519, A61P 33/02, A61P 33/06 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) IPC (2018.01) C07D 487/04, A61K 31/519, A61P 33/02, A61P 33/06 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) Databases consulted: CAPLUS, MEDLINE, MARPAT, REGISTRY, Google Scholar, DWPI Search terms used: protoz*, "calcium-dependent protein kinase", CDPK*1, inhib*, gondii, brucei, T*cruzi, L*major, falciparum, infect*, BK1, "bumped kinase".		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2009/062118 A2 (FOLDRX PHARMACEUTICALS INC [US]) 14 May 2009 (2009/05/14) Compounds 73, 74, 77, 113, 221, 228, 253 and 314.	1-8,10,11,14-19,27, 28,33
X	US 2012/0077827 A1 (Prabha N. Ibrahim et al. [US]) 29 Mar 2012 (2012/03/29) Compounds 1a-1c, 2a-2d, 3a-3d, 4a-4d and more.	1-4,6-8,14-18,27,28, 33
X	WO 2006/068760 A2 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA [US]) 29 Jun 2006 (2006/06/29) Compound 63	1,2,4,6-8,14,16,18, 27
X	WO 2010/045542 A2 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA [US]) 22 Apr 2010 (2010/04/22) Intermediate compounds on page 59 lines 22-23 and 26-27, as well as final products BB9 and BB10/cmpd3.	1,2,4,6,14,16,18,27
X	WO 2011/153553 A2 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA [US]) 08 Dec 2011 (2011/12/08) Example 28, compounds 38 and 17.	1,2,4,6,14,16,18,27, 28,33
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> See patent family annex.		
<p>* Special categories of cited documents:</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> <p>"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</p> <p>"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</p> <p>"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</p> <p>"&" document member of the same patent family</p>		
Date of the actual completion of the international search 11 Dec 2018		Date of mailing of the international search report 11 Dec 2018
Name and mailing address of the ISA: Israel Patent Office Technology Park, Bldg.5, Malcha, Jerusalem, 9695101, Israel Facsimile No. 972-2-5651616		Authorized officer SOMECH Erez Telephone No. 972-2-5651762

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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	WO 2013/010136 A2 (PHARMACYCLICS INCE [US]) 17 Jan 2013 (2013/01/17) Page 64 and more.	1-4,10,14,16-18,27
X	Okuzumi T et al. Synthesis and evaluation of indazole based analog sensitive Akt inhibitors. Molecular Biosystems (28 June 2010); 6(8), pages: 1389-402. Retrieved from URL: < https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2932704/ >. 28 Jun 2010 (2010/06/28) Compound XIi.	1,2,4,6-8,14,16,18,27
X	US 2013/0018040 A1 (VAN VOORHIS W.C. et al. [US]) 17 Jan 2013 (2013/01/17) See [0008], [0233], [0617]-[0619], formulae (Ib), (IIc) and (IIe), compounds 5f (page 30) and 13 (page 38),	1-37
Y	Lourido S et al. Optimizing small molecule inhibitors of calcium-dependent protein kinase 1 to prevent infection by Toxoplasma gondii. Journal of medicinal chemistry (26 March 2013); 56 (7), pages: 3068-3077. Retrieved from URL: < https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3625458/ >. 26 Mar 2013 (2013/03/26) Whole document.	1-37

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US2018/022595

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
WO 2009/062118 A2	14 May 2009	WO 2009062118 A2	14 May 2009
		WO 2009062118 A3	30 Dec 2009
		AU 2008323694 A1	14 May 2009
		BR PI0820342 A2	26 May 2015
		CA 2705303 A1	14 May 2009
		CN 101917999 A	15 Dec 2010
		EA 201070572 A1	30 Dec 2010
		EP 2217239 A2	18 Aug 2010
		JP 2011503103 A	27 Jan 2011
		US 2010331297 A1	30 Dec 2010
		ZA 201003725 B	30 Mar 2011
US 2012/0077827 A1	29 Mar 2012	US 2012077827 A1	29 Mar 2012
		US 8642606 B2	04 Feb 2014
WO 2006/068760 A2	29 Jun 2006	WO 2006068760 A2	29 Jun 2006
		WO 2006068760 A3	07 Dec 2006
		EP 1831225 A2	12 Sep 2007
		JP 2012087152 A	10 May 2012
		JP 5746985 B2	08 Jul 2015
		JP 2015003926 A	08 Jan 2015
		JP 6127034 B2	10 May 2017
		JP 2008520744 A	19 Jun 2008
		US 2009124638 A1	14 May 2009
		US 9512125 B2	06 Dec 2016
		US 2011144134 A1	16 Jun 2011
WO 2010/045542 A2	22 Apr 2010	WO 2010045542 A2	22 Apr 2010
		WO 2010045542 A3	19 Aug 2010
		AU 2009305669 A1	22 Apr 2010
		AU 2016202455 A1	12 May 2016

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US2018/022595

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
		AU 2018201842 A1	12 Apr 2018
		CA 2740885 A1	22 Apr 2010
		CA 2740885 C	03 Apr 2018
		DK 2358720 T3	06 Jun 2016
		EP 2358720 A2	24 Aug 2011
		EP 2358720 A4	15 Aug 2012
		EP 2358720 B1	02 Mar 2016
		ES 2570429 T3	18 May 2016
		JP 2012505916 A	08 Mar 2012
		JP 5819195 B2	18 Nov 2015
		JP 2014193925 A	09 Oct 2014
		US 2011275651 A1	10 Nov 2011
		US 8697709 B2	15 Apr 2014
WO 2011/153553 A2	08 Dec 2011	WO 2011153553 A2	08 Dec 2011
		WO 2011153553 A3	29 Mar 2012
		US 2013137708 A1	30 May 2013
		US 9353116 B2	31 May 2016
WO 2013/010136 A2	17 Jan 2013	WO 2013010136 A2	17 Jan 2013
		WO 2013010136 A3	04 Jul 2013
		AU 2012283775 A1	23 Jan 2014
		AU 2012283775 A8	20 Feb 2014
		BR 112014000653 A2	14 Feb 2017
		CA 2841080 A1	17 Jan 2013
		CN 103857396 A	11 Jun 2014
		EA 201490265 A1	30 Dec 2014
		EP 2731612 A2	21 May 2014
		EP 2731612 A4	08 Apr 2015
		JP 2014520863 A	25 Aug 2014
		KR 20140048968 A	24 Apr 2014

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US2018/022595

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
		MX 2014000518 A	30 May 2014
		NZ 619642 A	29 Apr 2016
		US 2013018032 A1	17 Jan 2013
		US 9138436 B2	22 Sep 2015
		US 2015329550 A1	19 Nov 2015
		US 9862722 B2	09 Jan 2018
		ZA 201400012 B	27 Jan 2016
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US 2013/0018040 A1	17 Jan 2013	US 2013018040 A1	17 Jan 2013
		US 9765037 B2	19 Sep 2017
		EP 2528919 A1	05 Dec 2012
		EP 2528919 B1	02 Nov 2016
		US 2018022709 A1	25 Jan 2018
		WO 2011094628 A1	04 Aug 2011
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