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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
20 November 2014 (20.11.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/184662 A3

(51) International Patent Classification:
A61K 31/4178 (2006.01) *A61K 9/52* (2006.01)
A61K 9/20 (2006.01)

(21) International Application Number:
PCT/IB2014/001589

(22) International Filing Date:
14 March 2014 (14.03.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/782,395 14 March 2013 (14.03.2013) US

(71) Applicant: **REDHILL BIOPHARMA LTD.** [IL/IL]; 21 Ha'arba'a Street, 64739 Tel Aviv (IL).

(72) Inventors; and
(71) Applicants : **GOSSELIN, Patrick** [CA/CA]; 200 Armand-Frappier, Laval, QC H7V 4A6 (CA). **GOLDBERG, Guy** [IL/IL]; Dizengof 6, Apartment 2, Tel Aviv (IL).

(72) Inventors: **FATHI, Reza**; 88 North Franklin Turnpike, Hohokus, NJ 07423 (US). **RADAY, Gilead**; 4025 Middlefield Road, Palo Alto, CA 94303 (US).

(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))*

(88) Date of publication of the international search report:
2 April 2015

(54) Title: ANTIEMETIC EXTENDED RELEASE SOLID DOSAGE FORMS

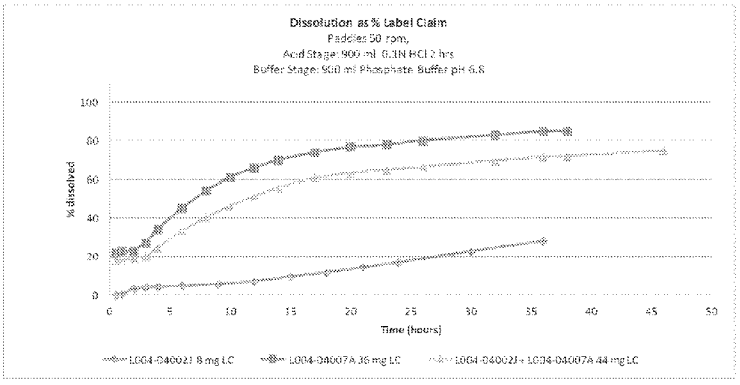


FIG. 19

(57) Abstract: A pharmaceutical formulation includes (1) a first dosage component comprising: a core comprising a non-ionic polymer matrix, a first amount of ondansetron or an equivalent amount of an ondansetron salt thereof dispersed within the matrix, and an electrolyte dispersed within the matrix; a first seal coat surrounding the core, the first seal coat comprising a non-ionic polymer matrix; and an immediate release drug layer surrounding the first seal coat, wherein the immediate release drug layer comprises a non-ionic polymer and a second amount of ondansetron or an equivalent amount of an ondansetron salt thereof dispersed therein; and (2) a second dosage component comprising: a core comprising a third amount of ondansetron or an equivalent amount of an ondansetron salt thereof, at least one filler, and a lubricant; and a coating surrounding the core, the coating comprising water and a mixture of methacrylic acid- alkyl acrylate copolymers with alkaline groups.

WO 2014/184662 A3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 14/01589

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 31/4178; A61K 9/20; A61K 9/52 (2014.01)
CPC - A61K 31/4178; A61K 9/2004; A61K 9/2031; A61K 9/209; A61K 9/2086
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(8) - A61K 31/4178; A61K 9/20; A61K 9/52 (2014.01)
CPC - A61K 31/4178; A61K 9/2004; A61K 9/2031; A61K 9/209; A61K 9/2086

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Patents and NPL (classification, keyword; search terms below)
USPC - 514/397; 424/465; 424/468; 424/472; 424/475

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatBase (AU BE BR CA CH CN DE DK EP ES FI FR GB IN JP KR SE TH TW US WO), PubWest, Google Web
search terms: Ondansetron Zofran Zophren Zudan Zuplenz sustained extended delayed controlled timely prolonged modified release fast immediate rapid release solid dosage tablet pill capsule seal coating layer filler lubricant Eudragit compressed core

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2008/0200508 A1 (Rariy et al.) 21 August 2008 (21.08.2008) para [0024], [0029]-[0030], [0035], [0063], [0070], [0081], [0083], [0085], [0088], [0089], [0096], [0098], [0104], [0110]-[0111], [0113]-[0114], [0117], [0132], [0135], [0140], [0142], [0152], [0159]; Fig 4.	1-21
Y	US 6,090,411 A (Pillay et al.) 18 July 2000 (18.07.2000) col 1, ln 66 to col 2, ln 27	1-21
Y	US 2005/0131045 A1 (Aronhime et al.) 16 June 2005 (16.06.2005) para [0022], [0065]-[0066]	14-16
Y	US 2008/0299197 A1 (Toneguzzo et al.) 4 December 2008 (04.12.2008) para [0042], [0108]-[0111], [0118], [0124], [0131], [0134], [0152], [0154], [0156], [0159], [0163], [0167], [0171], [0223], [0225], [0228], [0229]; Fig 2-3.	1-13, 17-20
Y	US 2010/0196472 A1 (Hirsh et al.) 5 August 2010 (05.08.2010) para [0024]-[0025], [0040]-[0043, [0045], [0050], [0055], [0059]-[0061], [0063].	1-13, 17-20

☐ Further documents are listed in the continuation of Box C. ☐

* 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
26 November 2014 (26.11.2014)	17 DEC 2014
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)