



## Press Release

### **RedHill Biopharma Initiates Promotion of Esomeprazole Strontium Delayed-Release Capsules 49.3 mg in the U.S.**

- **Esomeprazole Strontium Delayed-Release (DR) Capsules 49.3 mg is an FDA-approved, proprietary, prescription proton pump inhibitor (PPI) indicated for adults for the treatment of gastroesophageal reflux disease (GERD) and other gastrointestinal (GI) conditions**
- **PPIs are one of the most commonly prescribed classes of medications in the U.S., with an estimated market value exceeding \$20 billion in 2016**
- **RedHill's GI-focused sales force, headquartered in Raleigh, NC, promotes three GI-specialty products in the U.S., Donnatal<sup>®</sup>, EnteraGam<sup>®</sup> and Esomeprazole Strontium DR Capsules 49.3 mg**

**TEL-AVIV, Israel / RALEIGH, NC, September 13, 2017** RedHill Biopharma Ltd. (NASDAQ: RDHL) (Tel-Aviv Stock Exchange: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company primarily focused on late clinical-stage development and commercialization of proprietary, orally-administered, small molecule drugs for gastrointestinal and inflammatory diseases and cancer, today announced that it has initiated promotion of Esomeprazole Strontium Delayed-Release (DR) Capsules 49.3 mg<sup>1</sup> in the U.S.

RedHill's U.S. commercial operations, headquartered in Raleigh, NC, includes a gastrointestinal-focused sales force of approximately 40 sales representatives promoting three gastrointestinal (GI)-specialty products, Donnatal<sup>®</sup> (Phenobarbital, Hyoscyamine Sulfate,

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<sup>1</sup> Esomeprazole Strontium Delayed-Release (DR) Capsules 49.3 mg is an FDA-approved, proprietary, prescription proton pump inhibitor, indicated for adults for the treatment of gastroesophageal reflux disease (GERD) and other gastrointestinal (GI) conditions. For more information, please see the prescribing information: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=53240ab5-98e7-4050-b640-e09c1271899a&type=display>

Atropine Sulfate, Scopolamine Hydrobromide)<sup>2</sup>, EnteraGam® (serum-derived bovine immunoglobulin/protein isolate, SBI)<sup>3</sup> and Esomeprazole Strontium DR Capsules 49.3 mg in select U.S. territories. RedHill's U.S. commercial operations are expected to pave the way for the potential future launch of RedHill's late clinical-stage GI products, if approved by the U.S. Food and Drug Administration (FDA).

Esomeprazole Strontium DR Capsules 49.3 mg is a prescription proton pump inhibitor (PPI) drug product indicated for adults for the treatment of gastroesophageal reflux disease (GERD), risk reduction of NSAID-associated gastric ulcer, *H. pylori* eradication to reduce the risk of duodenal ulcer recurrence and for pathological hypersecretory conditions, including Zollinger-Ellison syndrome<sup>4</sup>. Esomeprazole Strontium DR Capsules 49.3 mg is a proprietary prescription drug approved by the FDA under a New Drug Application (NDA).

PPIs are one of the most commonly prescribed classes of medications in the U.S., with an estimated market value exceeding \$20 billion in 2016<sup>5</sup>.

**Valerie Graceffa, RedHill's VP, U.S. Sales and Marketing, said:** "We are excited to initiate the promotion of a third GI-specialty product. Esomeprazole Strontium DR Capsules 49.3 mg was selected as a strategic fit for RedHill's growing GI-focused product portfolio, which our sales force has been actively promoting in select U.S. territories since June 2017. Our sales team has been well trained and is eager to consult gastroenterologists on the new product and provide patients with an additional therapeutic option."

RedHill has a commercialization agreement with ParaPRO LLC ("ParaPRO"), an Indiana-based specialty pharmaceutical company, granting RedHill the exclusive rights to promote Esomeprazole Strontium DR Capsules to gastroenterologists in certain U.S. territories. Under the terms of the agreement, RedHill was not required to make any upfront, nor future milestone payments, and the parties will share the revenues generated from the promotion of Esomeprazole Strontium DR Capsules 49.3 mg by RedHill based on an agreed upon split between them. The initial term of the commercialization agreement is for four years. ParaPRO has also initiated its promotion of Esomeprazole Strontium DR Capsules 49.3 mg.

Donnatal® is a prescription oral drug used with other drugs for the treatment of irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis (inflammation

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<sup>2</sup> Donnatal® (Phenobarbital, Hyoscyamine Sulfate, Atropine Sulfate, Scopolamine Hydrobromide) is a prescription drug, classified as possibly effective as an adjunctive therapy in the treatment of irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis. For more information, please see the prescribing information: <http://www.donnatal.com/wp-content/uploads/2015/02/2015-02-18-Risk-Benefit-information-DTC-REV.-SE.pdf>.

<sup>3</sup> EnteraGam® (serum-derived bovine immunoglobulin/protein isolate, SBI) is a commercially-available medical food, intended for the dietary management of chronic diarrhea and loose stools due to specific intestinal disorders, which must be administered under medical supervision.

<sup>4</sup> For more information, please see the prescribing information: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=53240ab5-98e7-4050-b640-e09c1271899a&type=display>

<sup>5</sup> Symphony Health (accessed August, 2017)

of the small bowel). RedHill has an exclusive co-promotion agreement with Concordia Pharmaceuticals Inc., a subsidiary of Concordia International Corp. (NASDAQ: CXRX) (TSX: CXR) (“Concordia”), granting RedHill certain U.S. promotion rights for Donnatal®. Under the terms of the agreement, RedHill and Concordia will share the revenues generated from the promotion of Donnatal® by RedHill, based on an agreed upon split.

EnteraGam® is a medical food intended for the dietary management of chronic diarrhea and loose stools which must be administered under medical supervision. RedHill has a license agreement with Entera Health Inc. (“Entera Health”), granting RedHill the exclusive U.S. rights to EnteraGam® for the term of the agreement. Under the terms of the agreement, RedHill will pay Entera Health royalties based on net sales generated from the sale of EnteraGam® by RedHill.

### **About Esomeprazole Strontium Delayed-Release Capsules 49.3 mg<sup>6</sup>:**

Esomeprazole Strontium Delayed-Release Capsules 49.3 mg is indicated for adults:

- for the short-term treatment (4-8 weeks) of heartburn and other symptoms associated with gastroesophageal reflux disease (GERD) and/or in healing and symptomatic resolution of erosive esophagitis (EE).
- to reduce the risk of stomach ulcers in some people taking non-steroidal anti-inflammatory drugs (NSAIDs) (controlled studies did not extend beyond 6 months).
- in combination with amoxicillin 1000 mg and clarithromycin 500 mg is indicated for the treatment of patients with a stomach infection (*Helicobacter pylori*) and duodenal ulcer disease.
- is indicated for the long-term treatment of pathological hypersecretory conditions, including Zollinger-Ellison Syndrome.

### **Important Safety Information about Esomeprazole Strontium Delayed-Release Capsules 49.3 mg:**

- Esomeprazole strontium is contraindicated in patients with known hypersensitivity to proton pump inhibitors. For information about contraindications of antibacterial agents (clarithromycin and amoxicillin) indicated in combination with esomeprazole strontium, refer to the contraindications section of their package inserts.
- Symptomatic response to therapy does not rule out the presence of gastric malignancy. Consider additional follow-up and diagnostic testing in adult patients who have a suboptimal response or an early symptomatic relapse after completing treatment with a proton pump inhibitor (PPI). In older patients, also consider an endoscopy.
- Acute interstitial nephritis has been observed in patients taking PPIs. Discontinue esomeprazole strontium if acute interstitial nephritis develop.
- PPI therapy may be associated with increased risk of *Clostridium difficile*-associated diarrhea. This diagnosis should be considered for diarrhea that does not improve.

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<sup>6</sup> Esomeprazole Strontium Delayed-Release Capsules is also available in a 24.65 mg dose. RedHill promotes the Esomeprazole Strontium Delayed-Release Capsules 49.3 mg formulation only.

- PPI therapy may be associated with an increased risk of osteoporosis-related fractures of the hip, wrist, or spine. The risk of fracture was increased in patients who received high-dose (multiple daily doses) and long-term (a year or longer) therapy.
- Cutaneous lupus erythematosus (CLE) and systemic lupus erythematosus (SLE) have been reported in patients taking PPIs, including esomeprazole. These events included both new onset and exacerbations. If signs or symptoms consistent with CLE or SLE are noted with esomeprazole strontium, discontinue and refer the patient to a specialist. Most patients improve with discontinuation of the PPI alone in 4 to 12 weeks.
- Avoid concomitant use of esomeprazole strontium with clopidogrel, due to a reduction in plasma concentrations of the active metabolite of clopidogrel. When using esomeprazole strontium consider alternative anti-platelet therapy.
- Daily treatment with any acid-suppressing medications over a long period of time (e.g., longer than 3 years) may lead to malabsorption of cyanocobalamin (vitamin B12). Rare reports of cyanocobalamin deficiency occurring with acid-suppressing therapy have been reported in the literature.
- Hypomagnesemia has been reported rarely with prolonged treatment with PPI therapy and may require discontinuing PPI therapy.
- Concomitant use of esomeprazole strontium and St. John's wort or rifampin can substantially decrease esomeprazole strontium concentrations. Avoid concomitant use.
- Literature suggests that concomitant use of PPIs with methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration, a temporary withdrawal of the PPI may be considered in some patients.
- Concomitant use of esomeprazole strontium and atazanavir or nelfinavir is not recommended. esomeprazole strontium is expected to increase the plasma levels of saquinavir. Consider dose reduction of saquinavir.
- Patients treated with PPIs and warfarin concomitantly may need to be monitored for increases in INR and prothrombin time. Esomeprazole may interfere with the absorption of drugs for which gastric pH affects bioavailability (e.g., ketoconazole, iron salts, erlotinib, digoxin and mycophenolate mofetil).
- Esomeprazole strontium may increase systemic exposure of cilostazol and one of its active metabolites. Consider dose reduction of cilostazol.
- In adults, adverse reactions (ARs) reported at a frequency of 1% or greater with esomeprazole strontium include headache, diarrhea, nausea, flatulence, abdominal pain, constipation, and dry mouth.
- Safety and effectiveness of esomeprazole strontium have not been established in pediatric patients. Not recommended for use in pediatric patients.
- Safety of esomeprazole strontium have not been studied in patients with severe renal impairment. Not recommended for use in patients with severe renal impairment.

Talk to your doctor or healthcare professional. Please see Prescribing information including Medication Guide for Esomeprazole Strontium Delayed-Release Capsules at <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=53240ab5-98e7-4050-b640-e09c1271899a&type=display>

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or call 1-800-FDA-1088.

#### **About Donnatal®:**

Donnatal® (Phenobarbital, Hyoscyamine Sulfate, Atropine Sulfate, Scopolamine Hydrobromide), a prescription drug, is classified as possibly effective as an adjunctive therapy in the treatment of irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis. Donnatal® slows the natural movements of the gut by relaxing the muscles in the stomach and intestines. Donnatal® comes in two formulations: immediate release Donnatal® Tablets and immediate release Donnatal® Elixir, a fast-acting liquid.

#### **Important Safety Information about Donnatal®:**

Donnatal® is contraindicated in patients who have glaucoma, obstructive uropathy, obstructive disease of the gastrointestinal tract, paralytic ileus, unstable cardiovascular status, severe ulcerative colitis, myasthenia gravis, hiatal hernia with reflux esophagitis, or known hypersensitivity to any of the ingredients. Patients who are pregnant or breastfeeding or who have autonomic neuropathy, hepatic or renal disease, hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, tachycardia or hypertension should notify their doctor before taking Donnatal®. Side effects may include: dryness of the mouth, urinary retention, blurred vision, dilation of pupils, rapid heartbeat, loss of sense of taste, headache, nervousness, drowsiness, weakness, dizziness, insomnia, nausea, vomiting and allergic reactions which may be severe.

Further information, including prescribing information, can be found on [www.donnatal.com](http://www.donnatal.com).

Please see the following website for complete important safety information about Donnatal®: <http://www.donnatal.com/professionals/important-safety-information/>

To report suspected adverse reactions, contact Concordia Pharmaceuticals Inc. at 1-877-370-1142 or email: [medicalinformation@concordiarx.com](mailto:medicalinformation@concordiarx.com), or the FDA at 1-800-FDA-1088 (1-800-332-1088) or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

#### **About EnteraGam®:**

EnteraGam® (serum-derived bovine immunoglobulin/protein isolate, SBI) is a medical food product intended for the dietary management of chronic diarrhea and loose stools. EnteraGam® must be administered under medical supervision. EnteraGam® binds microbial components<sup>7</sup>, such as toxic substances released by bacteria, that upset the intestinal

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<sup>7</sup> Horgan A, Maas K, Henderson A, Detzel C, Weaver E. Serum-derived bovine immunoglobulin/protein isolate binds to pathogen-associated molecular patterns. Poster presented at: Federation of American Societies for Experimental Biology; April 26-30, 2014; San Diego, CA.

environment. This helps prevent them from penetrating the lining of the intestine, which may contribute to chronic diarrhea and loose stools in people who have specific intestinal disorders<sup>8</sup>.

#### **Safety Information about EnteraGam®:**

EnteraGam® contains beef protein; therefore, patients who have an allergy to beef or any other component of EnteraGam® should not take this product. EnteraGam® has not been studied in pregnant women, in women during labor and delivery, or in nursing mothers. The choice to administer EnteraGam® during pregnancy, labor and delivery, or to nursing mothers is at the clinical discretion of the prescribing physician.

EnteraGam® does not contain any milk-derived ingredients such as lactose, casein or whey. EnteraGam® is gluten-free, dye-free and soy-free.

Please see full [Product Information](#).

To report suspected adverse reactions, contact Entera Health, Inc. at 1-855-4ENTERA (1-855-436-8372), or the FDA at 1-800-FDA-1088 (1-800-332-1088) or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

#### **About ParaPRO LLC:**

ParaPRO is a Specialty Pharmaceutical Company created in 2002 to acquire, develop, and commercialize proprietary products in focused high potential markets. ParaPRO is a wholly owned subsidiary of SePRO Corporation, a management owned life-sciences business. Started in 1994, SePRO Corporation is a research-based life sciences company providing innovative products and services for specialty environmental and human health markets worldwide. SePRO is recognized as a preeminent leader in the aquatics industry and as a vital player in professional turf, horticulture and landscape markets.

#### **About RedHill Biopharma Ltd.:**

RedHill Biopharma Ltd. (NASDAQ: RDHL) (Tel-Aviv Stock Exchange: RDHL) is a specialty biopharmaceutical company headquartered in Israel, primarily focused on the development and commercialization of late clinical-stage, proprietary, orally-administered, small molecule drugs for the treatment of gastrointestinal and inflammatory diseases and cancer. RedHill promotes three gastrointestinal products in the U.S. - **Donnatal®**, a prescription oral adjunctive drug used in the treatment of IBS and acute enterocolitis, and **EnteraGam®**, a medical food intended for the dietary management, under medical supervision, of chronic diarrhea and loose stools, and **Esomeprazole Strontium Delayed-Release Capsules 49.3 mg**, a prescription proton pump inhibitor indicated for adults for the treatment of gastroesophageal reflux disease (GERD) and other gastrointestinal conditions. RedHill's clinical-stage pipeline includes: (i) **TALICIA™ (RHB-105)** - an oral combination therapy for the treatment of *Helicobacter pylori* infection with successful results from a first Phase III study and an ongoing confirmatory Phase

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<sup>8</sup> Petschow BW, Burnett B, Shaw AL, Weaver EM, Klein GL. Serum-derived bovine immunoglobulin/protein isolate: postulated mechanism of action for management of enteropathy. Clin Exp Gastroenterol. 2014;7:181-190. Gasbarrini A, Lauritano EC, Garcovich M, Sparano L, Gasbarrini G. New insights into the pathophysiology of IBS: intestinal microflora, gas production and gut motility. Eur Rev Med Pharmacol Sci. 2008;12 Suppl 1:111-117.

III study; (ii) **RHB-104** - an oral combination therapy for the treatment of Crohn's disease with an ongoing first Phase III study, a completed proof-of-concept Phase IIa study for multiple sclerosis, and a planned pivotal Phase III study for nontuberculous mycobacteria (NTM) infections; (iii) **BEKINDA® (RHB-102)** - a once-daily oral pill formulation of ondansetron with successful top-line results in a Phase III study for acute gastroenteritis and gastritis and an ongoing Phase II study for IBS-D; (iv) **RHB-106** - an encapsulated bowel preparation licensed to Salix Pharmaceuticals, Ltd.; (v) **YELIVA® (ABC294640)** - a Phase II-stage, orally-administered, first-in-class SK2 selective inhibitor targeting multiple oncology, inflammatory and gastrointestinal indications; (vi) **MESUPRON** - a Phase II-stage first-in-class, orally-administered protease inhibitor, targeting pancreatic cancer and other solid tumors and (vii) **RIZAPORT® (RHB-103)** - an oral thin film formulation of rizatriptan for acute migraines, with a U.S. NDA currently under discussion with the FDA and marketing authorization received in two EU member states under the European Decentralized Procedure (DCP). More information about the Company is available at: [www.redhillbio.com](http://www.redhillbio.com).

*This press release contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements may be preceded by the words “intends,” “may,” “will,” “plans,” “expects,” “anticipates,” “projects,” “predicts,” “estimates,” “aims,” “believes,” “hopes,” “potential” or similar words. Forward-looking statements are based on certain assumptions and are subject to various known and unknown risks and uncertainties, many of which are beyond the Company’s control, and cannot be predicted or quantified and consequently, actual results may differ materially from those expressed or implied by such forward-looking statements. Such risks and uncertainties include, without limitation, risks and uncertainties associated with (i) the initiation, timing, progress and results of the Company’s research, manufacturing, preclinical studies, clinical trials, and other therapeutic candidate development efforts; (ii) the Company’s ability to advance its therapeutic candidates into clinical trials or to successfully complete its preclinical studies or clinical trials; (iii) the extent and number of additional studies that the Company may be required to conduct and the Company’s receipt of regulatory approvals for its therapeutic candidates, and the timing of other regulatory filings, approvals and feedback; (iv) the manufacturing, clinical development, commercialization, and market acceptance of the Company’s therapeutic candidates; (v) the Company’s ability to successfully market Donnatal® and EnteraGam®, (vi) the Company’s ability to establish and maintain corporate collaborations; (vii) the Company’s ability to acquire products approved for marketing in the U.S. that achieve commercial success and build its own marketing and commercialization capabilities; (viii) the interpretation of the properties and characteristics of the Company’s therapeutic candidates and of the results obtained with its therapeutic candidates in research, preclinical studies or clinical trials; (ix) the implementation of the Company’s business model, strategic plans for its business and therapeutic candidates; (x) the scope of protection the Company is able to establish and maintain for intellectual property rights covering its therapeutic candidates and its ability to operate its business without infringing the intellectual property rights of others; (xi) parties from whom the Company licenses its intellectual property defaulting in their obligations to the Company; and (xii) estimates of the Company’s expenses, future revenues capital requirements and the Company’s needs for additional financing; (xiii) the Company’s Expanded Access Program, which allows patients with life-threatening diseases*

*potential access, subject to regulatory and other approvals, to RedHill's investigational new drugs that have not yet received regulatory marketing approval, if a patient suffers an adverse experience using such investigative drug, potentially adversely affecting the clinical development program of that investigational product or the Company generally; (xiv) competitive companies and technologies within the Company's industry. More detailed information about the Company and the risk factors that may affect the realization of forward-looking statements is set forth in the Company's filings with the Securities and Exchange Commission (SEC), including the Company's Annual Report on Form 20-F filed with the SEC on February 23, 2017. All forward-looking statements included in this Press Release are made only as of the date of this Press Release. We assume no obligation to update any written or oral forward-looking statement unless required by law.*

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