# Press Release

## RedHill Biopharma Announces FDA Acceptance of New Drug Application for Talicia®

- **U.S. FDA accepts NDA for priority review**
- **PDUFA date set for November 2, 2019**
- ***H. pylori* infection affects approximately 35% of the U.S. population and is the strongest risk factor for the development of gastric cancer and a major risk factor for peptic ulcer disease and MALT lymphoma**

**TEL-AVIV, Israel and RALEIGH, N.C., July 3, 2019** RedHill Biopharma Ltd. (Nasdaq: RDHL) (Tel-Aviv Stock Exchange: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company primarily focused on gastrointestinal diseases, announced today that the U.S. Food and Drug Administration (FDA) has accepted for review the New Drug Application (NDA) for Talicia® (RHB-105)[1] for *H. pylori* infection. The NDA for Talicia has also been granted Priority Review designation and was assigned a target Prescription Drug User Act (PDUFA) action date by the FDA of November 2, 2019.

Priority Review is a designation granted by the FDA to prioritize the review process for drugs that, if approved, would be significant improvements in the safety or effectiveness of the treatment of serious conditions when compared to standard applications.

Commercial launch of Talicia with RedHill's existing U.S. sales force is planned shortly following potential FDA approval.

If approved, Talicia would be eligible for a total of eight years of U.S. market exclusivity.

[1] Talicia® (RHB-105) is an investigational new drug, not available for commercial distribution.

*H. pylori* bacterial infection affects more than 50% of the population worldwide[2] and approximately 35% of the U.S. population[3]. It is classified as a Group I carcinogen and is the strongest risk factor for the development of gastric cancer[2] and a major risk factor for peptic ulcer disease[4] and gastric mucosa-associated lymphoid tissue (MALT) lymphoma[5]. *H. pylori*-infected persons have a 6-fold increased risk of developing non-cardia gastric cancer and mucosa-associated lymphoid tissue (MALT) lymphoma[4].

"The efficacy of current standard-of-care therapies for *H. pylori* bacterial infection continues to decline due to the high and steadily increasing prevalence of antibiotic-resistant strains. This public health concern is widely recognized by the U.S. government and other leading health agencies, including the World Health Organization, which classified *H. pylori* as a Group I carcinogen and highlighted the urgent need for new treatments for *H. pylori* eradication," **said Dror Ben-Asher, Chief Executive Officer of RedHill Biopharma**. "The acceptance for review of the NDA for Talicia and the Priority Review designation are encouraging steps as we continue our intensive preparations for a potential U.S. commercial launch of Talicia as a new first-line, standard-of-care therapy for *H. pylori*. We continue to work closely with the FDA, with the aim of bringing this important new therapy to patients."

"We have been diligently implementing our commercial strategy for Talicia with a target of commercial launch shortly following potential FDA approval. Leading this effort is our established sales force and commercial management team, which we have strengthened through several key new hires over the past few months," **concluded Rick D. Scruggs, Chief Operating Officer, U.S. Operations.**

**About Talicia® (RHB-105)**

Talicia® (RHB-105) is a novel and proprietary fixed-dose, all-in-one oral capsule combination of two antibiotics, rifabutin, and amoxicillin, and a proton pump inhibitor (PPI), omeprazole. Talicia is designed to address the increasing resistance of *H. pylori* bacteria to the antibiotics commonly used in current standard-of-care therapies and the imperative need for new treatments[6]. RedHill is pursuing for Talicia an indication of treatment and eradication of *H. pylori* infection. This is a significantly broader indication than most current standard treatments for *H. pylori* infection, which typically require diagnosis of an ulcer or history of ulcers. Talicia has been investigated in two positive Phase 3 studies in the U.S. for the treatment of *H. pylori*: the ERADICATE Hp2 confirmatory Phase 3 study met its primary endpoint, with results demonstrating 84% eradication of *H. pylori* infection with Talicia ($p<0.0001$). The ERADICATE Hp first Phase 3 study met its primary endpoint, demonstrating 89.4% efficacy in eradicating *H. pylori* infection with Talicia ($p<0.001$). No resistance to rifabutin, a key

[2] Lamb A et al. Role of the *Helicobacter pylori*-induced inflammatory response in the development of gastric cancer. J Cell Biochem 2013;114.3:491-497.

[3] Hooi JKY et al. Global prevalence of Helicobacter pylori infection: systematic review and meta-analysis.Gastroenterology 2017; 153:420-429.

[4] NIH – *Helicobacter pylori* and Cancer, September 2013.

[5] Hu Q et al. Gastric mucosa-associated lymphoid tissue lymphoma and *Helicobacter pylori* infection: a review of current diagnosis and management. Biomarker research 2016;4.1:15.

[6] World Health Organzation, Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics, February 2017.

component of Talicia, was detected in culture results taken throughout the ERADICATE Hp2 study from patients across 20 U.S. states.

Talicia was granted Qualified Infectious Disease Product (QIDP) designation by the FDA, allowing for Fast-Track and Priority Review designations. If approved, Talicia would be eligible for an additional five years of U.S. market exclusivity on top of the standard exclusivity period, for a total of eight years of U.S. market exclusivity. Talicia is also covered by U.S. patents, extending patent protection until at least 2034, with additional patents and applications pending in various territories worldwide.

**About *H. pylori***

*H. pylori* bacterial infection affects over 50% of the population worldwide[2] and approximately 35%, or over 100 million people, in the U.S, with an estimated 2.5 million patients treated annually in the U.S.[7] *H. pylori* is classified as a Group I carcinogen by the International Agency for Research on Cancer. It is the strongest risk factor for the development of gastric cancer[2] and a major risk factor for peptic ulcer disease[4] and gastric mucosa-associated lymphoid tissue (MALT) lymphoma[5], with infected persons having a 6-fold increased risk of developing non-cardia gastric cancer and MALT lymphoma[4]. Eradication of *H. pylori* is becoming increasingly difficult; current standard-of-care therapies fail in approximately 30-40% of patients who remain *H. pylori* positive due to growing resistance of *H. pylori* to clarithromycin and metronidazole, antibiotics commonly used in standard combination therapies[8]. Clarithromycin-resistant *H. pylori* was formally categorized by the World Health Organization (WHO) as a pathogen for which there is a high priority need to develop new treatments[6]. The 2018 potential market for *H. pylori* eradication therapies was estimated at approximately $4.8 billion worldwide and $1.4 billion from the U.S.[7]

The ERADICATE Hp2 and ERADICATE Hp Phase 3 studies with Talicia (RHB-105) are registered on www.ClinicalTrials.gov, a web-based service of the U.S. National Institutes of Health (NIH), which provides access to information on publicly and privately supported clinical studies.

**About RedHill Biopharma Ltd.**

RedHill Biopharma Ltd. is a specialty biopharmaceutical company, primarily focused on the development and commercialization of clinical late-stage, proprietary drugs for the treatment of gastrointestinal diseases. RedHill commercializes and promotes several gastrointestinal products in the U.S.: **Donnatal®** - a prescription oral adjunctive drug used in the treatment of IBS and acute enterocolitis; **EnteraGam®** - a medical food intended for the dietary management, under medical supervision, of chronic diarrhea and loose stools and **Mytesi®** - an anti-diarrheal drug indicated for the symptomatic relief of non-infectious diarrhea in adult

[7] Foster Rosenblatt market analysis, October 2018.

[8] Fallone CA et al. The Toronto Consensus for the Treatment of *Helicobacter pylori* Infection in Adults. Gastroenterology 2016;151:51–69; Malfertheiner P. et al. Management of *Helicobacter pylori* infection - the Maastricht IV/ Florence Consensus Report, Gut 2012;61:646-664; Graham DY et al. New concepts of resistance in the treatment of *Helicobacter pylori* infections. Nat Clin Pract Gastroenterol Hepatol. 2008 Jun;5(6):321-31 and Graham DY et al. *Helicobacter pylori* treatment in the era of increasing antibiotic resistance. Gut 2010;59:1143-1153.

patients with HIV/AIDS on anti-retroviral therapy. RedHill's key clinical late-stage development programs include: (i) **Talicia® (RHB-105)** for the treatment of *Helicobacter pylori* infection with a U.S. NDA submitted and accepted for priority review; (ii) **RHB-104,** with positive top-line results from a first Phase 3 study for Crohn's disease; (iii) **RHB-204,** with a planned pivotal Phase 3 study for pulmonary nontuberculous mycobacteria (NTM) infections; (iv) **BEKINDA® (RHB-102),** with positive results from a Phase 3 study for acute gastroenteritis and gastritis and positive results from a Phase 2 study for IBS-D; (v) **YELIVA® (ABC294640),** a first-in-class SK2 selective inhibitor, targeting multiple oncology, inflammatory and gastrointestinal indications, with an ongoing Phase 2a study for cholangiocarcinoma; (vi) **RHB-106,** an encapsulated bowel preparation licensed to Salix Pharmaceuticals, Ltd. and (vii) **RHB-107,** a Phase 2-stage first-in-class, serine protease inhibitor, targeting cancer and inflammatory gastrointestinal diseases.

*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, the approval of the NDA for Talicia® by the FDA and such approval's timing, the initiation and timing of the commercial launch of Talicia®, as well as 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, and the timing of the commercial launch of its therapeutic candidates; (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 commercialize and promote Donnatal®, EnteraGam®, Mytesi® and Esomeprazole Strontium Delayed-Release Capsules 49.3 mg; (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 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; (xii) estimates of the Company's expenses, future revenues, capital requirements and needs for additional financing; (xiii) the effect of patients suffering adverse experiences using investigative drugs*

*under the Company's Expanded Access Program; (xiv) competition from other companies and technologies within the Company's industry; and (xv) the hiring and employment commencement date of executive managers. 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 26, 2019 , as amended on May 15, 2019. All forward-looking statements included in this press release are made only as of the date of this press release. The Company assumes no obligation to update any written or oral forward-looking statement, whether as a result of new information, future events or otherwise, unless required by law.*


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