Press Release

RedHill Biopharma Submits New Drug Application for Talicia® for *H. pylori* Infection

- **The NDA follows a recent positive pre-NDA meeting with the FDA**
- **The NDA for Talicia® is eligible for six-month priority review**
- **Talicia® is eligible for a total of eight years of U.S. market exclusivity, in addition to patent protection until at least 2034**
- **RedHill continues to strengthen its U.S. commercial operations with senior industry executives ahead of the planned commercial launch of Talicia®, as early as Q4/2019**
- ***H. pylori* bacterial infection is the strongest risk factor for developing gastric cancer and affects over 50% of the population worldwide and approximately 35% of the U.S. population**
- **Current standard-of-care therapies fail in approximately 30-40% of patients due to increasing resistance to antibiotics commonly used in standard combination therapies; notably, no resistance to rifabutin, a key component of Talicia®, was detected throughout the Phase 3 ERADICATE Hp2 study**
- **Talicia® has the potential to become the new first-line standard-of-care therapy for *H. pylori* infection, targeting an estimated 2.5 million U.S. patients treated annually**

TEL-AVIV, Israel and RALEIGH, N.C., May 7, 2019 -- RedHill Biopharma Ltd. (Nasdaq: RDHL) (Tel-Aviv Stock Exchange: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company primarily focused on gastrointestinal diseases, today announced that, following a positive pre-NDA meeting held recently with the U.S. Food and Drug

Administration (FDA), it has submitted a New Drug Application (NDA) to the FDA for Talicia® (RHB-105)[1] for the treatment of *H. pylori* infection.

The NDA was submitted under the 505(b)(2) regulatory pathway. Talicia was granted Qualified Infectious Disease Product (QIDP) designation by the FDA and is eligible for six-month priority review of the NDA. If approved, Talicia will receive an additional five years of U.S. market exclusivity on top of the standard exclusivity period, for a total of eight years of market exclusivity. Talicia is also covered by U.S. patents which extend patent protection until at least 2034, with additional patents and applications pending in various territories worldwide.

Gilead Raday, RedHill's chief operating officer, stated: "The NDA submission for Talicia is a transformative milestone for RedHill and a critical step in our efforts to bring this much needed potential new therapy for *H. pylori* infection to the market. Assuming FDA approval, commercial launch is planned for the fourth quarter of 2019 with our established U.S. sales force, led by a highly experienced commercial management team."

The NDA for Talicia is supported by a clinical package including two positive Phase 3 studies in the U.S., along with two pharmacokinetic studies evaluating food effects and the comparative bioavailability of Talicia. The first Phase 3 study with Talicia (ERADICATE Hp) successfully met its primary endpoint of superiority over historical standard-of-care eradication rate of 70%, demonstrating 89.4% efficacy in eradicating *H. pylori* infection with Talicia ($p<0.001$). The confirmatory Phase 3 study (ERADICATE Hp2) also met its primary endpoint, demonstrating 84% eradication of *H. pylori* infection with Talicia vs. 58% in the active comparator arm ($p<0.0001$). Moreover, 90% of subjects with confirmed blood levels of Talicia's actives on day 13 of treatment (an indicator of compliance) achieved confirmed eradication of *H. pylori*. Importantly, low rates of eradication were obtained in patients treated with physician-directed standard-of-care therapies in the open-label parts of these studies (63% and 53%, respectively). These results are consistent with the literature describing the diminished efficacy of standard-of-care therapies. RedHill plans to share the ERADICATE Hp2 data in greater detail at upcoming scientific conferences and publications.

Ira Kalfus, M.D., RedHill's medical director, said: "Talicia demonstrated robust results in its clinical studies for *H. pylori* infection, a common and increasingly resistant and difficult to treat pathogen. Importantly, in our clinical study, no *H. pylori* resistance to rifabutin, one of the key ingredients in Talicia, was identified pre and post treatment. We believe Talicia has the potential to become the new first-line, standard-of-care therapy for *H. pylori* infection and would like to thank the patients, investigators and clinical support staff who were involved in the clinical studies of this important potential new therapy."

RedHill continues to implement its U.S. commercialization strategy in anticipation of the potential launch of Talicia with its dedicated sales force. As part of the ongoing preparations for the potential launch, RedHill continues to strengthen its commercial management team with additional senior industry executives. The Company's sales and marketing teams currently

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

promote several commercial GI products to gastroenterologists, other high-prescribing specialists and primary care physicians across select U.S. territories.

Talicia is a novel, patent-protected and proprietary fixed-dose, all-in-one oral capsule for the treatment of *H. pylori* infection. Talicia is addressing 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, as defined by the World Health Organization (WHO)[2].

It is estimated that *H. pylori* infection affects over 50% of the population worldwide[3] and approximately 35% of the U.S. population[4], with an estimated 2.5 million patients treated annually in the U.S.[5] *H. pylori*, classified as a group I carcinogen, is the strongest risk factor for the development of gastric cancer[3] and a major risk factor for development of peptic ulcer disease[6]. The 2018 potential market for *H. pylori* eradication therapies was estimated at approximately $4.8 billion worldwide and $1.4 billion in the U.S.[7]

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 pursuing an indication of treatment of *H. pylori* infection, regardless of ulcer status, a significantly broader indication than current standard treatments for *H. pylori* infection. 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 ($p<0.001$). 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 increasing resistance of *H. pylori* to antibiotics commonly used in standard combination therapies[8]. No resistance to rifabutin, a key 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

[2]www.who.int/news-room/detail/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed.

[3] 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.

[4] Hooi JKY et al. *Global Prevalence of Helicobacter pylori Infection: Systematic Review and Meta-Analysis.* Gastroenterology 2017; 153:420-429.

[5] Ma JL et al. *Fifteen-year effects of Helicobacter pylori, garlic, and vitamin treatments on gastric cancer incidence and mortality*. Journal of the National Cancer Institute 2012; 104(6):488-492.

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

[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.

Infectious Disease Product (QIDP) designation and Fast-Track development designation by the FDA, including eligibility for six-month priority review and a total of eight years of U.S. market exclusivity. Talicia is also covered by U.S. patents, which extend 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[3] and approximately 35%, or over 100 million people, in the U.S.[4], with an estimated 2.5 million patients treated annually in the U.S.[8] *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[3], a major risk factor for peptic ulcer disease[7] and gastric mucosa-associated lymphoid tissues (MALT) lymphoma[9]. 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[9]. 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[2]. The 2018 potential market for *H. pylori* eradication therapies was estimated at approximately $4.8 billion worldwide and $1.4 billion is from the U.S.[8]

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. (Nasdaq: RDHL) (Tel-Aviv Stock Exchange: RDHL) 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 patients with HIV/AIDS on anti-retroviral therapy. RedHill's key clinical-stage development programs include: (i) **Talicia® (RHB-105)** for the treatment of *Helicobacter pylori* infection with a U.S. NDA submitted; (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

[9] 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.

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, 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; and (xiv) competition from other 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 26, 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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