Press Release

RedHill Biopharma Announces New European and Japanese Patents for Talicia®

- **The European and Japanese patent applications have been accepted and, once granted, are expected to be valid until 2034**
- **U.S. NDA for Talicia® on track for potential submission in H1/2019 and U.S. commercial launch in Q4/2019**
- **Talicia® was granted QIDP designation, including eligibility for six-month priority FDA review and a total of eight years of U.S. market exclusivity**

TEL-AVIV, Israel and RALEIGH, N.C., March 4, 2019 -- RedHill Biopharma Ltd. (Nasdaq: RDHL) (Tel-Aviv Stock Exchange: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company primarily focused on gastrointestinal (GI) diseases, today announced that both the European Patent Office (EPO) and the Japan Patent Office (JPO) have accepted pending patent applications covering Talicia® (RHB-105)[1] for *H. pylori* infection. Once granted, the new patents are expected to be valid until 2034. RedHill's U.S. and worldwide intellectual property portfolio covering Talicia® includes nine issued patents and approximately 20 pending patent applications.

RedHill's vice president of intellectual property and research, Danielle Abramson, Ph.D., said; "The allowance of these two new patents in Japan and Europe, together with the existing U.S. patent portfolio expected to be valid until 2034, is an important achievement as we continue to execute our intellectual property strategy and grow our robust worldwide patent protection for Talicia®. We expect to continue to strengthen and expand the breadth of our intellectual property towards the planned U.S. NDA submission for Talicia® in the first half of 2019."

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

Talicia® 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, that is being developed for the eradication of *H. pylori* infection. Talicia® is expected to address the increasing resistance of *H. pylori* bacteria to the antibiotics commonly used in current standard-of-care therapies and the urgent need for new treatments, as defined by the World Health Organization[2]. Talicia® could potentially be positioned as the new standard-of-care, best-in-class, first-line therapy for the eradication of *H. pylori* infection, regardless of ulcer status, potentially providing improved convenience and compliance with a favorable safety profile.

Following the recently announced positive results from the two-arm, randomized, double-blind, active comparator-controlled confirmatory Phase 3 study for *H. pylori* infection (ERADICATE Hp2 study), RedHill is preparing to submit a U.S. New Drug Application (NDA) in the first half of 2019 and is planning for the U.S. commercial launch of Talicia® with RedHill's existing sales force in the fourth quarter of 2019, subject to FDA approval.

The ERADICATE Hp2 study successfully met its primary endpoint with a high degree of statistical significance ($p<0.0001$), demonstrating 84% eradication of *H. pylori* infection with Talicia® versus 58% in the active comparator arm in the intent-to-treat (ITT) population. No safety issues were reported in the study and Talicia® was found to be well tolerated.

Talicia® was granted QIDP designation by the FDA, including Fast-Track development, eligibility for six-month priority review and a total of eight years of U.S. market exclusivity.

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 for the treatment of *H. pylori*: The ERADICATE Hp2 confirmatory Phase 3 study met its primary endpoint, with top-line results demonstrating 84% eradication of *H. pylori* infection ($p<0.0001$). The ERADICATE Hp first Phase 3 study met its primary endpoint, demonstrating 89.4% efficacy in eradicating *H. pylori* infection with Talicia® ($p<0.001$). Talicia® was granted Qualified 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 the ERADICATE Hp2 study

The ERADICATE Hp2 confirmatory Phase 3 study is a two-arm, randomized, double-blind, active comparator-controlled, Phase 3 study which compared Talicia® against a dual therapy, amoxicillin and omeprazole, regimen at equivalent doses. The study investigated 455 dyspepsia

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

patients with confirmed *H. pylori* infection at 55 clinical sites across the U.S. Subjects were randomized 1:1 to receive four capsules, three times daily, of either Talicia® or the active comparator, for a period of 14 days. Subjects were assessed for the study's primary endpoint of eradication of *H. pylori* infection at least 43 days after initiation of treatment. The study was 90% powered to detect a 13% treatment effect (active arm 83% vs. control arm 70%). Patients in the study who remained *H. pylori*-positive after completing treatment in either arm were offered treatment with standard-of-care therapies that included clarithromycin and/or metronidazole-based triple therapy or quadruple therapy, in an open-label setting.

About *H. pylori*

H. pylori bacterial infection affects over 50% of the adult population worldwide[3] and over 30%, or over 100 million people, in the U.S.[4], with an estimated 2.5 million patients treated annually in the U.S.[5] *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[6] and a major risk factor for peptic ulcer disease[7], and gastric mucosa-associated lymphoid tissues (MALT) lymphoma[8]. Eradication of *H. pylori* is becoming more 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[9]. Clarithromycin-resistant *H. pylori* was formally categorized by the World Health Organization as a pathogen for which there is a high priority need to develop new treatments[10]. The 2018 global market for *H. pylori* eradication therapies is estimated at approximately $4.8 billion, of which $1.4 billion is from the U.S.[11]

The ERADICATE Hp2 confirmatory Phase 3 study with Talicia® (RHB-105) is 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

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[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, J. K., Lai, W. Y., Ng, W. K., Suen, M. M., Underwood, F. E., Tanyingoh, D., ... & Chan, F. K. (2017). Global prevalence of Helicobacter pylori infection: systematic review and meta-analysis. *Gastroenterology*, *153*(2), 420-429.

[5] Foster Rosenblatt market analysis, October 2018.

[6] 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.

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

[8] 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.

[9] Savoldi A et al. *Prevalence of antibiotic resistance in Helicobacter pylori: a systematic review and meta-analysis in World Health Organization regions*. Gastroenterology 2018;155:1372-1382; Malfertheiner, P., et al. *Management of Helicobacter pylori infection—the Maastricht V/Florence consensus report*. *Gut* 2017;66.1:6-30.

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

[11] Foster Rosenblatt market analysis, October 2018.

biopharmaceutical company, primarily focused on the development and commercialization of late-stage clinical, proprietary drugs for the treatment of gastrointestinal diseases. RedHill commercializes and promotes four 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; **Mytesi® -** an anti-diarrheal drug indicated for the symptomatic relief of non-infectious diarrhea in adult patients with HIV/AIDS on anti-retroviral therapy, 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 key clinical-stage development programs include: (i) **Talicia® (RHB-105)** for the treatment of *Helicobacter pylori* infection with two positive Phase 3 studies; (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 (formerly MESUPRON),** 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.

Company contact:
Adi Frish
Senior VP Business Development & Licensing
RedHill Biopharma
+972-54-6543-112
adi@redhillbio.com

IR contact (U.S.):
Timothy McCarthy, CFA, MBA
Managing Director, Relationship Manager
LifeSci Advisors, LLC
+1-212-915-2564
tim@lifesciadvisors.com