Press Release

RedHill Biopharma Announces Positive Top-Line Results from Confirmatory Phase 3 Study with TALICIA® for *H. pylori* Infection

- **The ERADICATE Hp2 confirmatory Phase 3 study successfully met its primary endpoint of *H. pylori* eradication (84% vs. 58%) with high degree of statistical significance (p<0.0001)**
- **High resistance to standard-of-care antibiotics observed in the ERADICATE Hp2 study is consistent with the diminishing efficacy of standard-of-care therapies, which has declined to approximately 60%**
- **The Phase 3 study results support potential positioning of TALICIA® as a best-in-class, first-line therapy for treating *H. pylori* infection, with an estimated 2.5 million patients treated annually in the U.S.**
- **Preparations ongoing for potential NDA submission in H1/2019 and commercial U.S. launch with RedHill's existing salesforce in H2/2019**
- **Conference call and live webcast to be held today, Monday, Dec. 3, at 8:30 a.m. EST**

TEL-AVIV, Israel and RALEIGH, N.C., USA, December 3, 2018 -- RedHill Biopharma Ltd. (Nasdaq: RDHL) (Tel-Aviv Stock Exchange: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company primarily focused on proprietary drugs for gastrointestinal (GI) diseases, announced today positive top-line results from the ERADICATE Hp2 study, a two-arm, randomized, double-blind, active comparator-controlled, confirmatory Phase 3 study with TALICIA® (RHB-105)[1] for *H. pylori* infection.

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

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

Dror Ben-Asher, RedHill's CEO, stated: "We are delighted with these excellent top-line results and are preparing for U.S. New Drug Application (NDA) submission, expected in the first half of 2019, subject to FDA feedback. Our established U.S. commercial operations team and GI-focused sales force are well-positioned for the potential U.S. commercial launch of TALICIA®, expected in the second half of 2019, subject to FDA approval."

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. The ERADICATE Hp2 two-arm, randomized, double-blind, active comparator-controlled study investigated 455 dyspepsia 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, a dual therapy amoxicillin and omeprazole regimen at equivalent doses, for a period of 14 days.

The efficacy of current standard-of-care therapies continues to decline and has been reported in literature to be approximately 60%[2] due to high resistance of *H. pylori* bacteria to the antibiotics commonly used in these therapies, primarily clarithromycin and metronidazole.

Preliminary *H. pylori* culture results taken throughout the ERADICATE Hp2 study from patients across 20 U.S. states confirmed the high resistance[3] of *H. pylori* to the antibiotics most commonly used for treatment, clarithromycin (17% resistance) and metronidazole (43% resistance). Importantly, no resistance to rifabutin, a key component in TALICIA®'s unique and proprietary formulation, was detected in the study.

Moreover, consistent with the literature describing the diminished efficacy of standard-of-care therapies, preliminary results[4] from the open-label part of the ERADICATE Hp2 Phase 3 study showed 64% eradication of *H. pylori* with these therapies.

Results from the ERADICATE Hp2 study showed consistent 21-29% treatment benefit of TALICIA® versus the active comparator across all *H. pylori* culture susceptibility and resistance subgroups, including amoxicillin, clarithromycin and metronidazole.

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[2] Fallone CA et al. *The Toronto Consensus for the Treatment of Helicobacter pylori Infection in Adults. Gastroenterology* 2016;151:51–69.

[3] 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.

[4] N=82; Not all patients in the open-label part have completed last visit; therapy in open-label part was determined by the treating physician.

"The growing resistance of *H. pylori* to the antibiotics commonly used in standard-of-care therapies was confirmed in this study, which demonstrated the high resistance of the *Helicobacter* bacteria to clarithromycin and metronidazole. The resulting high failure rates of standard-of-care treatments, estimated at 30-40%, are a major public concern among the medical community worldwide and underscore the urgent need for new *H. pylori* eradication therapies, especially those utilizing antibiotics where resistance is rare such as amoxicillin and rifabutin," **stated Professor David Graham, M.D., M.A.C.G., lead investigator of the ERADICATE Hp2 study.**

The ERADICATE Hp2 Phase 3 top-line results confirm the positive findings demonstrated in RedHill's previously reported first Phase 3 study (ERADICATE Hp) and further support TALICIA®'s potential to become a next generation, best-in-class, first-line therapy for treating *H. pylori* infection. RedHill plans to share ERADICATE Hp2 data in greater detail at upcoming scientific conferences.

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 pending patents and applications in various territories worldwide.

H. pylori bacterial infection affects over 50% of the adult population worldwide[5] and 30-40% of the U.S. population[6], with an estimated 2.5 million patients treated annually in the U.S.[7] *H. pylori* infection is the strongest risk factor for the development of gastric cancer[8] and a major risk factor for development of peptic ulcer disease[9].

Ira Kalfus, M.D. RedHill's medical director, added: "I am thrilled with the study results which support the outstanding efficacy of TALICIA® for treating *H. pylori* infection. The excellent results from both Phase 3 studies could position TALICIA® to become the new standard-of-care, best-in-class, first-line therapy for eradication of *H. pylori*. I look forward to further discussion with FDA about advancing this potential new therapy for *H. pylori* infection towards an NDA submission. I would like to thank all the patients, physicians and clinical staff who were involved in this study, as well as the lead investigator of the study, Professor David Graham and the RedHill team for their commitment to benefiting people infected with *H. pylori*."

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[5] Kakelar HM et al. *Pathogenicity of Helicobacter pylori in cancer development and impacts of vaccination.* Gastric Cancer 2018:1-14.

[6] Chey WD et al. *American College of Gastroenterology guideline on the management of Helicobacter pylori infection.* Am J Gastroenterol 2007;102:1808–1825.

[7] Foster Rosenblatt market analysis, October 2018.

[8] 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.

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

RedHill will continue to analyze the top-line data from the ERADICATE Hp2 study, including antibiotic susceptibility and resistance, and plans to meet with the FDA to present the data and discuss the path towards potential marketing approval of TALICIA® in the U.S.

The ERADICATE Hp2 study top-line results were provided to RedHill by an independent third-party following an independent analysis and remain subject to completion of the independent review and analysis of the underlying data, including all safety, secondary and other outcome measures, and completion of the Clinical Study Report.

Conference call on the ERADICATE Hp2 study results:

RedHill will host a conference call today, Monday, Dec. 3, 2018, at 8:30 a.m. EST, to discuss the ERADICATE Hp2 study results.

The webcast, including a slide presentation, will be broadcast live and available for replay 30 days on the Company's website, http://ir.redhillbio.com/events.

To participate in the conference call, please dial one of the following numbers 15 minutes prior to the start of the call: United States: +1-800-239-9838; International: +1-929-477-0448; and Israel: +972-3-721-9463. The access code for the call is: 2626201.

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 pending patents and applications 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, confirmatory Phase 3 study which compared TALICIA® against a dual therapy amoxicillin and omeprazole regimen at equivalent doses. The study investigated 455 dyspepsia 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[8] and 30-40% of the U.S. population[6], with an estimated 2.5 million patients treated annually in the U.S. *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[8] and a major risk factor for peptic ulcer disease[9], and gastric mucosa-associated lymphoid tissues (MALT) lymphoma[10]. 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[3]. 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[11]. 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.[7]

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 biopharmaceutical company, primarily focused on the development and commercialization of late clinical-stage, 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; **Mytesi®** - an anti-diarrheal drug indicated for the symptomatic relief of non-infectious diarrhea in adult patients with HIV/AIDS on anti-retroviral therapy; **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, and **EnteraGam®** - a medical food intended for the dietary management, under medical supervision, of chronic diarrhea and loose stools. 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)

[10] 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.

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

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; (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 promote Donnatal®, Mytesi® and Esomeprazole Strontium Delayed-Release Capsules 49.3 mg and commercialize 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 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 22, 2018. 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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