RedHill Biopharma Announces Additional Data from Positive Phase III Study of RHB-104 in Crohn's Disease at United European Gastroenterology (UEG) Week 2018

October 22, 2018

- **The presentation highlighted enhanced p-values for previously reported outcomes, including the primary endpoint of clinical remission at week 26 (p=0.007) and key secondary and other efficacy endpoints of clinical response at week 26 (p=0.016), early clinical remission at week 16 (p=0.015), clinical remission at weeks 16 and 52 (p=0.003) and durable remission at all visits, weeks 16 through 52 (p=0.018)**

- **The UEGW presentation included new positive week 26 remission data demonstrating consistent treatment effects and meaningful clinical benefit strongly favoring RHB-104 as compared to placebo in subgroups of patients receiving baseline standard-of-care therapies, including immunomodulators (39% vs. 20%), corticosteroids (36% vs. 20%) and anti-TNF agents (36% vs. 17%)**

- **MAP US, a Phase III study of RHB-104 in the treatment of patients with moderate to severe Crohn's disease, successfully met its primary endpoint and key secondary endpoints, demonstrating meaningful, consistent and statistically significant treatment effect of orally-administered RHB-104 as an add-on to standard-of-care treatments**

TEL-AVIV, Israel and RALEIGH, N.C., Oct. 22, 2018 (GLOBE NEWSWIRE) -- RedHill Biopharma Ltd. (Nasdaq: RDHL) (Tel-Aviv Stock Exchange: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company focused on proprietary drugs for gastrointestinal diseases, reported today additional positive data from the MAP US study, its first Phase III study of RHB-104 in the treatment of Crohn's disease. An abstract discussing the study's top-line results, *'A Phase III Randomized, Double Blind, Placebo-Controlled, Multicenter, Parallel Group Study To Assess The Efficacy And Safety Of Add-On Fixed-Dose Anti-Mycobacterial Therapy (RHB-104) In Moderately To Severely Active Crohn's Disease (MAP US)'* was presented as a late-breaking abstract today at the United European Gastroenterology Week (UEG Week 2018) by Dr. David Y. Graham, M.D., Professor of Medicine, Molecular Virology and Microbiology at Baylor College of Medicine, Houston and Lead Investigator of the MAP US study.

MAP US is a randomized, double-blind, placebo-controlled Phase III study of RHB-104. The study enrolled 331 subjects with moderately to severely active Crohn's disease [1] at over 100 investigative sites in the U.S, Europe, Australia, New Zealand and Israel. Subjects were randomized 1:1 to receive orally-administered RHB-104 or placebo as an add-on therapy to baseline standard-of-care (SoC) medications, which included 5-ASAs, corticosteroids, immunomodulators and anti-TNF agents (infliximab/adalimumab).

The MAP US study successfully met its primary endpoint and key secondary endpoints with meaningful and statistically significant treatment effects, including the primary endpoint of clinical remission[2] at week 26 (37% vs. 23%, p=0.007) and key secondary and other efficacy endpoints of clinical response[3] at week 26 (44% vs. 31%, p=0.016), early clinical remission at week 16 (42% vs. 29%, p=0.015), clinical remission at weeks 16 and 52 (25% vs. 12%, p=0.003) and durable clinical remission on all visits, weeks 16 through 52 (18% vs. 9%, p=0.018). These previously reported outcomes[4] were further enhanced when stratified for concomitant anti-TNF agent use as prospectively specified in the statistical analysis plan. The data was provided to RedHill by an independent third party CRO following an independent analysis and remains subject to completion of the Clinical Study Report (CSR).

The UEGW presentation highlighted new positive week 26 remission data showing the impact of RHB-104 as an add-on therapy to a variety of SoC agents. Despite not being prospectively powered, meaningful and statistically significant treatment effects (RHB-104 vs. placebo) were observed in patients using concomitant immunomodulators (39% vs. 20%, p<0.01) and corticosteroids (36% vs. 20%, p=0.045) throughout the trial. Furthermore, despite very small sample sizes of the following subgroups of patients and lack of prospective powering, strong trends in favor of RHB-104 were also observed in patients receiving anti-TNF agents achieving remission at week 26 (36% vs.17%, p=0.08) (total patients analyzed=67) and the proportion of patients achieving corticosteroid-free remission at week 52 (24% vs. 6%, p=0.175) (total patients analyzed=37). Additionally, in a small subset of patients in whom endoscopy was performed, the study also showed statistical significant improvement in endoscopic healing at week 26 (36% vs. 10%, p=0.048) (total patients analyzed=35). This data confirms the broad benefit of RHB-104 as add-on therapy to SoC in Crohn's disease.

RHB-104 was also found to be generally safe and well tolerated with similar treatment-emergent adverse events, serious adverse events and adverse events leading to study drug discontinuation experienced between treatment groups.

Ira Kalfus, M.D., RedHill's medical director, said : "Continued analysis of data collected during the MAP US study has further bolstered the positive top-line results in Crohn's disease initially reported a few months ago. Today's presentation demonstrates RHB-104's potential as a therapy that can improve the outcomes seen with the current standard-of-care treatments across a broad spectrum of Crohn's disease patients. We look forward to discussing the data and development path to approval with the FDA with our goal of making a positive impact on the lives of people suffering from Crohn's disease."

The number of diagnosed prevalent Crohn's disease cases worldwide is estimated to reach over 1.59 million in 2018, with sales of Crohn's disease

therapies estimated to exceed $10 billion[5].

The top-line results and subsequent analyses 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 (CSR).

The clinical studies with RHB-104 are registered on www.ClinicalTrials.gov, a web-based service of the U.S. National Institute of Health, that provides access to information on publicly and privately-supported clinical studies.

About RHB-104:
RHB-104 is a proprietary, orally-administered antibiotic combination therapy, with potent intracellular, antimycobacterial and anti-inflammatory properties, with positive results from a first Phase III study. RHB-104 was developed based on the hypothesis that Crohn's disease is caused by *Mycobacterium avium subspecies paratuberculosis* (MAP) infection in susceptible patients. The development of RHB-104 is consistent with the growing awareness of the possibility that a bacterially-induced dysregulated immune system may contribute to the pathogenesis of various autoimmune diseases of unknown etiology. Positive top-line results from the first Phase III study with RHB-104 in Crohn's disease (the MAP US study) were announced in July 2018. The study successfully met its primary endpoint and key secondary endpoints. RedHill has conducted several supportive studies with the current formulation of RHB-104 and a population pharmacokinetic (pop-PK) study is ongoing as part of the Phase III MAP US study. Additionally, an open-label extension Phase III study (MAP US2 study) is ongoing to assess the safety and efficacy of RHB-104 in subjects who have completed week 26 assessments in the ongoing Phase III MAP US study and remain with active Crohn's disease (CDAI ≥ 150). Additional clinical studies are likely to be required to support a U.S. NDA for RHB-104.

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 an ongoing confirmatory Phase III study and positive results from a first Phase III study; (ii) **RHB-104,** with positive top-line results from a first Phase III study for Crohn's disease; (iii) **RHB-204,** with a planned pivotal Phase III study for nontuberculous mycobacteria (NTM) infections; (iv) **BEKINDA® (RHB-102),** with positive results from a Phase III study for acute gastroenteritis and gastritis and positive results from a Phase II 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 IIa study for cholangiocarcinoma; (vi) **RHB-106,** an encapsulated bowel preparation licensed to Salix Pharmaceuticals, Ltd. and (vii) **RHB-107 (formerly MESUPRON),** a Phase II-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 mgand 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 SECon 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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[1] Defined as CDAI (Crohn's Disease Activity Index) 220 to 450.

[2] Defined as CDAI < 150.

[3] Defined as a decrease of ≥100 in CDAI from baseline.

[4] See also MAP US Phase III study top-line results press release (July 30, 2018); Elaboration on MAP US Phase III study top-line results press release (Aug 1, 2018).

[5] GlobalData PharmaPoint: Crohn's Disease - Global Forecast 2016–2026, September 2017.

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