RedHill Biopharma Announces Positive Top-Line Results from Phase III Study of RHB-104 in Crohn's Disease

July 30, 2018

- **Primary endpoint successfully achieved - superior remission rate at week 26 in patients treated with RHB-104 (p= 0.013)**
- **Key secondary endpoints also met, demonstrating consistent benefit to Crohn's disease patients treated with RHB-104**
- **RedHill to host conference call and live webcast today, Monday, July 30, at 8:30 am ET**

TEL-AVIV, Israel and RALEIGH, N.C., July 30, 2018 (GLOBE NEWSWIRE) -- 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, today announced positive top-line safety and efficacy results from the first Phase III study with RHB-104 for Crohn's disease (the MAP US study). The study successfully met its primary endpoint and key secondary endpoints.

Top-line results in the intent-to-treat (ITT) population demonstrated superiority of RHB-104 over placebo in achieving remission at week 26, defined as Crohn's Disease Active Index (CDAI) value of less than 150, the primary endpoint of the study. The proportion of patients meeting the primary endpoint was significantly greater in the RHB-104 group compared to placebo (37% vs. 23%, p= 0.013).

Ira Kalfus, M.D., RedHill's medical director, said: "The robust results of this study demonstrate that RHB-104 could become a leading therapeutic option in Crohn's disease and bring hope to patients worldwide."

The study also successfully met key secondary endpoints, demonstrating consistent benefit to Crohn's disease patients treated with RHB-104.

Patients treated with RHB-104 also achieved a statistically significant greater response at week 26 (defined as a decrease of ≥100 in CDAI from baseline) compared to placebo (44% vs. 31%, p= 0.028).

Patients treated with RHB-104 also experienced a statistically significant benefit in achieving early remission defined as remission at week 16 (42% vs. 29%, p= 0.019).

Patients receiving RHB-104 also experienced a statistically significant benefit in durable remission over weeks 16-52, defined as continuous remission throughout the period, (18% vs. 9%, p= 0.038), demonstrating an improvement of 100% over placebo[1].

At 52 weeks of treatment, remission in the RHB-104 arm continued to be favorable to placebo (27% vs. 20%, p= 0.155).

An analysis of maintenance of remission at week 52 in subjects noted to be in remission at week 16 also demonstrated statistically significant benefit with RHB-104 over placebo (25% vs. 12%, p= 0.007).

RHB-104 was found to be generally safe and well tolerated. Top-line results demonstrated that the active and placebo treatment groups experienced similarly low rates of serious adverse events and treatment emergent adverse events leading to study drug discontinuation, indicating a positive safety profile for RHB-104.

The company will continue to assess additional exploratory endpoints as data becomes available, including mucosal healing, MAP status, quality of life assessment, sub-population analyses and pharmacokinetics. Additional data is expected in the comings months.

Dr. Kalfus added: "This is the first global, double-blind, placebo-controlled study that demonstrates the efficacy of anti-MAP therapy in Crohn's disease. The availability of antibiotic therapy for treating Crohn's disease could be transformative. The results from the MAP US study are excellent, successfully meeting the primary endpoint at week 26 and demonstrating that treatment with RHB-104 also has an early benefit at week 16, which is persistent though week 52. The study results compare favorably to existing standard-of-care therapies[2]. RHB-104 appeared to be safe and well tolerated in the study. We continue to analyze the study data and plan to meet with key opinion leaders and the FDA to present the data package and discuss the development path to potential approval of RHB-104."

Professor David Graham, M.D., M.A.C.G., lead investigator of the RHB-104 MAP US Phase III study, added: "I am impressed and extremely pleased with the results of the study, which indicate that RHB-104 could lead to a paradigm shift in the treatment of Crohn's disease, a chronic and debilitating and currently incurable condition with a strong unmet medical need. Many patients with Crohn's disease do not achieve remission on current standard-of-care therapies, which are accompanied with poor side effects. RHB-104 appears to have the potential to become a promising, new, orally-administered therapy for this important debilitating disease."

Dror Ben-Asher, RedHill's CEO, said: "The compelling top-line results with RHB-104, our potential ground-breaking therapy, are a remarkable accomplishment. We thank the patients who participated in this global study, as well as the physicians and clinical staff who supported them. We also want to extend our deep gratitude to the lead investigator of the study, Professor David Graham, to the RedHill team and to the experts and vendors

for their commitment throughout the study. We look forward to discussing the path to approval with the FDA and to accelerating discussions with potential pharma partners."

The MAP US randomized, double-blind, placebo-controlled first Phase III study of RHB-104 enrolled 331 subjects with moderately to severely active Crohn's disease (defined as CDAI between 220 and 450) in the U.S., Canada, Europe, Australia, New Zealand and Israel. Subjects were randomized 1:1 to receive RHB-104 or placebo, on-top of baseline background medication including of 5-ASAs, corticosteroids, immunomodulators or anti-TNFα agents.

In addition, an open-label extension Phase III study (MAP US2 study) is ongoing to evaluate the safety and efficacy of RHB-104 in subjects who remain with active Crohn's disease (CDAI ≥ 150) after 26 weeks of blinded study therapy in the Phase III MAP US study.

Additional clinical studies are most likely to be required to support a U.S. New Drug Application (NDA) for RHB-104, if filed. RedHill will meet with key opinion leaders and the U.S. Food and Drug Administration (FDA) to present the data package and discuss the development path to potential approval and will continue discussions with potential partners for RHB-104.

As of 2017, approximately 1.5 million people worldwide had been diagnosed with Crohn's disease. Global sales of Crohn's disease therapies are estimated to exceed $10 billion in 2018[3].

The 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 (CSR). Detailed results from the Phase III study will be submitted for presentation at upcoming scientific conferences.

RedHill will host a conference call today, Monday, July 30, 2018, at 8:30 a.m. ET, to discuss the MAP US study results.

The webcast, including a slide presentation, will be broadcasted live and available for replay on the Company's website, http://ir.redhillbio.com/events, for 30 days. Please access the website at least 15 minutes ahead of the conference call to register, download, and install any necessary audio software.

Participants who wish to ask questions during the live Q&A can do so by telephone. To access the event by telephone, please dial one of the following numbers 5-10 minutes prior to the start of the call: **United States: +1-888-204-4368; International: +1-929-477-0402; and Israel: +972-3-376-1315. The access code for the call is 9535837.**

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

About RHB-104:
RHB-104 is a potentially ground-breaking, proprietary, orally-administered antibiotic combination therapy, with potent intracellular, antimycobacterial and anti-inflammatory properties, with positive top-line results in a first Phase III study. RHB-104 is 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, if filed. RHB-104 is covered by several issued and pending patents. RedHill also completed a Phase IIa, proof-of-concept clinical study evaluating RHB-104 as an add-on therapy to interferon beta-1a in subjects treated for relapsing-remitting multiple sclerosis (CEASE MS study), supporting additional 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 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. More information about the Company is available at: www.redhillbio.com.

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, 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 Company's reliance on third parties to conduct key portions of its clinical trials, including data management services, and the potential for those third parties to not perform satisfactorily; (iv) 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; (v) the manufacturing, clinical development, commercialization, and market acceptance of the Company's therapeutic candidates; (vi) the Company's ability to successfully promote Donnatal ® and Esomeprazole Strontium Delayed-Release Capsules 49.3 mgand commercialize EnteraGam®; (vii) 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; (ix) 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; (x) the implementation of the Company's business model, strategic plans for its business and therapeutic candidates; (xi) 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; (xii) parties from whom the Company licenses its intellectual property defaulting in their obligations to the Company; (xiii) estimates of the Company's expenses, future revenues, capital requirements and needs for additional financing; (iv) 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] 12 patients have yet to complete 52 weeks of treatment.

[2] The comparison to standard-of-care should not be construed as a direct and/or equal comparison given that studies were not identical in design, patient population and treatment period and were not conducted head-to-head.

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

Primary Logo

Source: RedHill Biopharma Ltd.