



## Press Release

### **RedHill Biopharma Accelerates RHB-104 Phase III Study in Crohn's Disease with Top-Line Results Expected Mid-2018**

- **RedHill has curtailed the target sample size in the ongoing first Phase III study with RHB-104 for Crohn's disease (MAP US) from 410 to approximately 325 subjects, of which 322 have been enrolled to date, while maintaining statistical power of over 80% with a treatment effect of 15%**
- **A review of the blended efficacy rate of the current blinded data, as well as additional input from experts, including statisticians and key opinion leaders, suggests that the total number of treatment successes is consistent with predefined expected treatment outcomes and that the study has sufficient enrollment to potentially demonstrate efficacy**
- **Development program will be shortened by approximately one year, with enrollment expected to be completed by November 2017 and top-line results expected in mid-2018**
- **Estimated cost saving is approximately \$14 million**
- **RedHill will host a conference call and webcast today, Monday, October 2, 2017, at 9:00 am EDT**

**TEL-AVIV, Israel / RALEIGH, NC, October 2, 2017** RedHill Biopharma Ltd. (NASDAQ: RDHL) (Tel-Aviv Stock Exchange: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company primarily focused on late clinical-stage development and commercialization of proprietary, orally-administered, small molecule drugs for gastrointestinal and inflammatory diseases and cancer, today announced that the Company has accelerated the timelines for the ongoing first Phase III study with RHB-104 for Crohn's disease (MAP US) by curtailing the number of subjects planned to be enrolled in the study from 410 to approximately 325 subjects.

Given that 322 subjects have been enrolled in the MAP US Phase III study to date, the Company expects to complete enrollment by November 2017 and to announce top-line results in mid-2018. RedHill remains blinded to the ongoing data from the study. The protocol amendment implementing the curtailment strategy has been filed with the FDA and healthcare regulators in other relevant countries.

The MAP US study is a randomized, double-blind, placebo-controlled first Phase III study evaluating the safety and efficacy of RHB-104 in subjects with moderately to severely active Crohn's disease (defined as Crohn's Disease Active Index (CDAI) between 220 and 450). The primary endpoint of the MAP US study is disease remission, defined as a reduction in CDAI to less than 150 at week 26. The MAP US study is being conducted in up to 150 clinical sites in the U.S, Canada, Europe, Israel, Australia and New Zealand.

**Ira Kalfus, MD, Medical Director at RedHill, commented:** “We believe that curtailment to a target sample size of approximately 325 subjects is the preferred approach in our effort to bring this potentially groundbreaking new therapy to the market as soon as possible. A review of the blended efficacy rate of the current blinded data suggests that the total number of treatment successes at this point in the study is consistent with the predefined expected treatment outcome. Upon discussion with internal and external experts, we have concluded that the study has sufficient enrollment to potentially demonstrate efficacy within the protocol-defined 15% treatment effect (RHB-104 36% vs. placebo 21%). The blended remission rate of the currently blinded data has been consistently within or superior to our pre-specified protocol defined assumptions, indicating potential study success at the curtailed sample size of approximately 325 subjects, assuming the placebo and RHB-104 remission rates in our study are in line with trial assumptions. Placebo remission rates in similar, but not identical, pivotal studies in Crohn's disease range from approximately 7% to approximately 25%<sup>1</sup> with the two most recently approved therapies at 7% (Entyvio® (vedolizumab))<sup>2</sup> and 20% (Stelara® (ustekinumab))<sup>3</sup>. The Company remains blinded to the data and has no visibility into the actual treatment effect. We are excited about the significant progress achieved with RHB-104 and look forward to top-line results from the MAP US Phase III study, expected in mid-2018.”

**Professor David Graham, MD, M.A.C.G., renowned researcher and physician at the Baylor College of Medicine and the lead investigator of the RHB-104 MAP US Phase III study, added:** “After reviewing the blinded, blended data from the patients enrolled in the Phase III MAP US study, we found that we could curtail the study and complete it earlier while still maintaining power and treatment effect. If the RHB-104 MAP US Phase III study

---

<sup>1</sup> Remicade® ((infliximab) package insert:

[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2013/103772s5359lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/103772s5359lbl.pdf)

<sup>2</sup> Entyvio® (vedolizumab) package insert:

[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2014/125476s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/125476s000lbl.pdf)

<sup>3</sup> Stelara® (ustekinumab) package insert:

[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2016/761044lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/761044lbl.pdf)

is successful and if the drug is approved after completion of the required regulatory path, this curtailment may allow the treatment to be available earlier than initially planned, potentially changing the treatment paradigm for patients suffering from Crohn's disease.”

The curtailment in the number of subjects planned to be enrolled in the MAP US study reflects input from internal and external experts, including statisticians who concluded that curtailment to a target sample size of approximately 325 subjects would maintain statistical power of over 80% with a treatment effect of 15%. Final statistical analysis remains unchanged and will be carried out using a two-sided p-value of 0.049 significance level using the O'Brien-Fleming method, as described in the protocol.

RedHill estimates that the development program will be shortened by approximately one year and the Company will benefit from cost savings of approximately \$14 million.

RHB-104 is a proprietary, orally-administered, potentially ground-breaking, antibiotic combination therapy with potent intracellular, antimycobacterial and anti-inflammatory properties, targeting a suspected underlying bacterial infectious cause of Crohn's disease, *Mycobacterium avium subspecies paratuberculosis* (MAP).

Additional clinical studies are likely to be required to support a U.S. New Drug Application (NDA) for RHB-104. If the MAP US Phase III study results are positive, RedHill will meet with the FDA and key opinion leaders to present the data package and discuss the preferred development path.

Two pre-planned independent DSMB meetings were held to review data from the MAP US study in which unanimous recommendations to continue the study without any changes to the protocol, investigator's brochure, study conduct or informed consent form were given. At the first DSMB meeting, held in December 2016, safety data from the study was reviewed. At the second DSMB meeting, held in July 2017, safety and efficacy data from the first 222 subjects who had completed week 26 assessments of the study was reviewed.

In addition, an open-label extension Phase III study (the MAP US2 study) continues to evaluate the safety and efficacy of RHB-104 in subjects who remain with active Crohn's disease (CDAI  $\geq$  150) after 26 weeks of blinded study therapy in the ongoing Phase III MAP US study. These subjects have the opportunity to receive treatment with RHB-104 for a 52-week period in the open-label MAP US2 extension study. The data collected in the MAP US2 study will be supplemental to the MAP US study data. The MAP US2 study's primary endpoint is disease remission at week 16, defined as CDAI of less than 150. The MAP US2 study is planned to enroll approximately 50-70 subjects in up to 150 clinical sites in the U.S., Canada, Europe, Israel and New Zealand. Additional open-label studies with RHB-104 for Crohn's disease are being planned to provide further supportive clinical data for potential future marketing applications.

RedHill has conducted several supportive studies with the current formulation of RHB-104 and a long-term population pharmacokinetic (pop-PK) study is ongoing as part of the Phase III MAP US study. RHB-104 is covered by several issued and pending patents.

RedHill also continues to advance the development program for a commercial companion diagnostic for the detection of MAP bacteria in Crohn's disease patients, in collaboration with several U.S. universities and with Q<sup>2</sup> Solutions. The Company held a pre-submission meeting with the FDA regarding the diagnostic test in 2015. The development of the commercial companion diagnostic is an extension of RedHill's RHB-104 Phase III development program.

There is currently no validated, FDA-approved, commercially-available method of detecting the presence or absence of MAP in patients suffering from Crohn's disease or other diseases. The development of a commercial companion diagnostic is expected to contribute to the understanding of the role of MAP infection in Crohn's disease and potentially other inflammatory diseases.

The clinical studies with RHB-104 are registered on [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov), a web-based service of the U.S. National Institutes of Health, which provides access to information on publicly and privately-supported clinical studies.

RedHill remains blinded to the data from the ongoing MAP US Phase III study and cannot ascertain the potential impact of the curtailed number of subjects on the study's final outcome.

**RedHill will host a conference call and webcast call today, October 2, 2017, at 9:00 a.m. EDT, to review the RHB-104 development program and the changes to the MAP US Phase III study.**

**The conference call, including a slide presentation, will be broadcasted live and available for replay on the Company's website, <http://ir.redhillbio.com/events.cfm>, for 30 days. Please access the Company's 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 event can do so by telephone. To participate in the conference call, please dial the following numbers 5-10 minutes prior to the start of the call: United States: +1-877-280-1254; International: +1-646-254-3367; and Israel: +972-3-763-0145. The access code for the call is 2719928**

**About RHB-104:**

Currently in a first Phase III study for the treatment of Crohn's disease (the MAP US study), RHB-104 is a proprietary, orally-administered, potentially ground-breaking oral antibiotic combination therapy, with potent intracellular, antimycobacterial and anti-inflammatory properties. RHB-104 is based on increasing evidence supporting the hypothesis

that Crohn's disease is related to *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. Clinical trials conducted with earlier formulations of RHB-104 include an Australian Phase III study conducted by Pharmacia/Pfizer. RedHill has conducted several supportive studies with the current formulation of RHB-104 and a long-term population pharmacokinetic (pop-PK) study is ongoing as part of the Phase III MAP US study. Additionally, an open-label extension Phase III study (the 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  $\geq$  150) at week 26. RHB-104 is covered by several issued and pending patents. RHB-104 was granted Qualified Infectious Disease Product (QIDP) designation by the U.S. FDA for the treatment of nontuberculous mycobacteria (NTM) infections, providing a Fast-Track development pathway, as well as NDA Priority Review and an additional five years of U.S. market exclusivity, if approved. A pivotal Phase III study with RHB-104 for NTM infections is planned to be initiated in the first quarter of 2018. 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 (the CEASE MS study), with top-line final results suggesting meaningful positive safety and clinical signals upon 24 weeks of treatment with RHB-104 as an add-on therapy, thereby supporting further clinical development.

#### **About RedHill Biopharma Ltd.:**

RedHill Biopharma Ltd. (NASDAQ: RDHL) (Tel-Aviv Stock Exchange: RDHL) is a specialty biopharmaceutical company headquartered in Israel, primarily focused on the development and commercialization of late clinical-stage, proprietary, orally-administered, small molecule drugs for the treatment of gastrointestinal and inflammatory diseases and cancer. RedHill promotes three gastrointestinal products in the U.S. - **Donnatal**<sup>®</sup>, a prescription oral adjunctive drug used in the treatment of IBS and acute enterocolitis, **EnteraGam**<sup>®</sup>, a medical food intended for the dietary management, under medical supervision, of chronic diarrhea and loose stools, 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 clinical-stage pipeline includes: (i) **TALICIA**<sup>™</sup> (**RHB-105**) - an oral combination therapy for the treatment of *Helicobacter pylori* infection with successful results from a first Phase III study and an ongoing confirmatory Phase III study; (ii) **RHB-104** - an oral combination therapy for the treatment of Crohn's disease with an ongoing first Phase III study, a completed proof-of-concept Phase IIa study for multiple sclerosis, and a planned pivotal Phase III study for nontuberculous mycobacteria (NTM) infections; (iii) **BEKINDA**<sup>®</sup> (**RHB-102**) - a once-daily oral pill formulation of ondansetron with successful top-line results from a Phase III study for acute gastroenteritis and gastritis and an ongoing Phase II study for IBS-D; (iv) **RHB-106** - an encapsulated bowel preparation licensed to Salix Pharmaceuticals, Ltd.; (v) **YELIVA**<sup>®</sup> (**ABC294640**) - a Phase II-stage, orally-administered, first-in-class SK2 selective inhibitor targeting multiple oncology, inflammatory and gastrointestinal indications; (vi) **MESUPRON** - a Phase II-stage first-in-class, orally-administered protease inhibitor,

targeting pancreatic cancer and other solid tumors and (vii) **RIZAPORT® (RHB-103)** - an oral thin film formulation of rizatriptan for acute migraines, with a U.S. NDA currently under discussion with the FDA and marketing authorization received in two EU member states under the European Decentralized Procedure (DCP). More information about the Company is available at: [www.redhillbio.com](http://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, without limitation, risks and uncertainties associated with (i) changes in the outcomes of our clinical trials resulting from changes in the size of the trials, and the accuracy of projected cost savings from changes to clinical trials; (ii) the initiation, timing, progress and results of the Company’s research, manufacturing, preclinical studies, clinical trials, and other therapeutic candidate development efforts and projected cost savings from any changes to these trials; (iii) the Company’s ability to advance its therapeutic candidates into clinical trials or to successfully complete its preclinical studies or clinical trials; (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 market Donnatal® and EnteraGam®, (vii) the Company’s ability to establish and maintain corporate collaborations; (viii) 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 of 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; and (xiii) estimates of the Company’s expenses, future revenues capital requirements and the Company’s needs for additional financing; (xiv) the Company’s Expanded Access Program, which allows patients with life-threatening diseases potential access, subject to regulatory and other approvals, to RedHill’s investigational new drugs that have not yet received regulatory marketing approval, if a patient suffers an adverse experience using such investigative drug, potentially adversely affecting the clinical development program of that investigational product or the Company generally; (xv) competitive 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 23, 2017. All forward-looking statements included in this Press Release are made only as of the date of this Press Release. We assume no obligation to update any written or oral forward-looking statement unless required by law.*

**Company contact:**

Adi Frish  
Senior VP Business Development & Licensing  
RedHill Biopharma  
+972-54-6543-112  
[adi@redhillbio.com](mailto:adi@redhillbio.com)

**IR contact (U.S.):**

Marcy Nanus  
Senior Vice President  
The Trout Group  
+1-646-378-2927  
[Mnanus@troutgroup.com](mailto:Mnanus@troutgroup.com)