



## Press Release

### **RedHill Biopharma Announces Positive Top-Line Results from Phase II Study of BEKINDA<sup>®</sup> in Patients with Diarrhea-Predominant Irritable Bowel Syndrome (IBS-D)**

- BEKINDA<sup>®i</sup> 12 mg Phase II study successfully met its primary endpoint, improving primary efficacy outcome of stool consistency by an absolute difference of 19.4% vs. placebo and comparing favorably with previously reported outcomes from studies of Xifaxan<sup>®</sup> (rifaximin) and Viberzi<sup>®</sup> (eluxadoline)<sup>ii</sup>
- IBS is one of the most common gastrointestinal disorders, affecting an estimated 30 million Americans, of which over 50% are cases of IBS-D; The U.S. market of IBS-D therapies grew by approximately 550% between 2013-2016
- RedHill intends to pursue Phase III studies with BEKINDA<sup>®</sup> 12 mg and plans to meet with the FDA by early 2018 to discuss the path towards potential U.S. marketing approval
- Top-line results remain subject to completion of the independent review and analysis of the Clinical Study Report (CSR)
- In addition, following a successful first Phase III study and a positive guidance meeting with the FDA, RedHill is designing a confirmatory Phase III study to support a New Drug Application (NDA) for BEKINDA<sup>®</sup> 24 mg for acute gastroenteritis and gastritis
- RedHill will host a conference call and webcast today, Tuesday, October 3, 2017, at 9:00 am EDT, to discuss the top-line results from the BEKINDA<sup>®</sup> 12 mg Phase II study, dial-in details can be found below and on the Company's website: <http://ir.redhillbio.com/events.cfm>

**TEL-AVIV, Israel / RALEIGH, NC, October 3, 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 positive top-line results from the Phase II clinical study of BEKINDA<sup>®</sup> (RHB-102) 12 mg for the treatment of diarrhea-predominant irritable bowel syndrome (IBS-D).

The randomized, double-blind, placebo-controlled Phase II study evaluated the efficacy and safety of BEKINDA<sup>®</sup> 12 mg in 126 subjects over 18 years old at 16 clinical sites in the U.S. Subjects were randomized 60:40 to receive either BEKINDA<sup>®</sup> 12 mg or placebo, once daily, for a period of eight weeks.

BEKINDA<sup>®</sup> 12 mg Phase II study successfully met its primary endpoint, improving the primary efficacy outcome of stool consistency response (per FDA guidance definition) by an absolute difference of 19.4%, with 54.7% responders of subjects treated with BEKINDA<sup>®</sup> (n=75) vs. 35.3% responders of the placebo subjects (n=51) (p = 0.05). These top-line results compare favorably with previously reported efficacy outcome values for stool consistency response from two Phase III studies of Xifaxan<sup>®</sup> (rifaximin) 550 mg (averaged absolute difference from Trial 1 and Trial 2 of 10.5%) and two Phase III studies of Viberzi<sup>®</sup> 100 mg (eluxadoline) (averaged absolute difference of 13.5%)<sup>ii</sup>.

BEKINDA<sup>®</sup> 12 mg was also shown to be safe and well tolerated. No serious adverse events, new or unexpected safety issues were noted in the study, suggesting the potential of BEKINDA<sup>®</sup> 12 mg, if approved, to become a first-line standard of care treatment for IBS-D.

**Terry F. Plasse, MD, RedHill’s Medical Director, said:** “We are greatly encouraged by the top-line results from the Phase II study which demonstrated that BEKINDA<sup>®</sup> 12 mg could be an effective treatment for patients suffering from IBS-D, and we look forward to discussing the path towards potential marketing approval in the U.S. with the FDA. Despite recent new drug approvals for IBS-D, there is still a clear unmet medical need for safe and effective new therapies in this indication. I would like to thank the patients and physicians who took part in our study. We will continue to work diligently to bring BEKINDA<sup>®</sup> 12 mg to the market as quickly as possible.”

**June S. Almenoff, MD, PhD, a member of RedHill’s Advisory Board and former President and Chief Medical Officer of Furiex Pharmaceuticals, added:** “BEKINDA<sup>®</sup> 12 mg demonstrated a very good safety profile in this study as well as impressive efficacy. If both the safety and efficacy results are reproduced in the planned pivotal studies, possibly powered to win on pain as well, BEKINDA<sup>®</sup> 12 mg has the potential, if approved, to become an important new therapy and standard-of-care for IBS-D.”

While not powered for statistical significance of the secondary efficacy endpoints, the study suggested clinically meaningful improvement in both secondary efficacy endpoints of abdominal pain response and overall response (combined stool consistency and abdominal

pain response). The secondary efficacy endpoints results also compared favorably to the absolute difference observed for these endpoints in reported studies of Xifaxan<sup>®</sup> and Viberzi<sup>®ii</sup>: Top-line results from the Phase II study demonstrated that BEKINDA<sup>®</sup> 12 mg improved the overall worst abdominal pain response rate by 11.5% vs. placebo (50.7% with BEKINDA<sup>®</sup> 12 mg (n=75) vs. 39.2% with placebo (n=51); (p=0.28)), which compares favorably with previously reported efficacy outcome values for abdominal pain response from two Phase III studies of Xifaxan<sup>®</sup> 550 mg (averaged absolute difference from Trial 1 and Trial 2 of 9.0%) and from two Phase III studies of Viberzi<sup>®</sup> 100 mg (averaged absolute difference of 5.0%)<sup>ii</sup>. Furthermore, the overall response rate (composite measure of stool consistency and abdominal pain response) in the BEKINDA<sup>®</sup> 12 mg Phase II study demonstrated an absolute difference of 15.8% in favor of the BEKINDA<sup>®</sup> 12 mg arm (41.3% with BEKINDA<sup>®</sup> 12 mg (n=75) vs. 25.5% with placebo (n=51); (p=0.10)), also comparing favorably with previously reported efficacy outcome values for overall response from two Phase III studies of Xifaxan<sup>®</sup> 550 mg (averaged absolute difference from Trial 1 and Trial 2 of 9.5%) and from two Phase III studies of Viberzi<sup>®</sup> 100 mg (averaged absolute difference of 10.5%)<sup>ii</sup>.

The theoretical comparison between the BEKINDA<sup>®</sup> 12 mg Phase II study results and published data from studies of IBS-D-approved therapies Xifaxan<sup>®</sup> and Viberzi<sup>®</sup> serves as a general benchmark for the effect size observed with BEKINDA<sup>®</sup> 12 mg and should not be construed as a direct and/or equal comparison given that the studies were not identical in design, patient population and treatment duration and were not conducted head-to-head in the same patient population<sup>ii</sup>.

RedHill will continue to analyze the data from the Phase II study with BEKINDA<sup>®</sup> 12 mg, including all secondary endpoints. RedHill is also analyzing drug allocation and pharmacokinetics in the study, including some aberrant findings which are not expected to have a material impact on the final results. 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), expected in the first quarter of 2018. Detailed results from the Phase II study will be submitted for presentation at upcoming scientific conferences.

IBS is one of the most common gastrointestinal disorders<sup>iii</sup>. It is estimated that up to 30 million Americans suffer from IBS<sup>iv</sup>, of which over 50% are cases of IBS-D<sup>v</sup>. The U.S. market for IBS-D therapies grew by approximately 550% between 2013-2016, to an estimated \$473 million in 2016, and is expected to continue to grow with a compound annual growth rate (CAGR) of 14% (2016 – 2022)<sup>vi</sup>.

BEKINDA<sup>®</sup> is a proprietary, bimodal extended-release, once-daily, oral pill formulation of the antiemetic drug ondansetron, targeting several gastrointestinal indications. 5-HT<sub>3</sub> antagonists such as ondansetron, the active pharmaceutical ingredient in BEKINDA<sup>®</sup>, have been shown to slow intestinal transit time in humans<sup>vii</sup>. Alosetron (Lotronex<sup>®</sup>), a different 5-HT<sub>3</sub> antagonist of the same class of drugs as ondansetron, has been approved by the FDA for

the treatment of women with severe chronic IBS-D, but is under a restricted prescribing (REMS) program due to potential severe side effects<sup>viii</sup>. Other products, including Xifaxan<sup>®</sup> and Viberzi<sup>®</sup>, have been approved for IBS-D, but many patients do not benefit from these treatments. RedHill believes that BEKINDA<sup>®</sup> 12 mg, if approved, has the potential to be a preferred once-daily treatment for a broad segment of patients suffering from IBS-D.

In addition to the BEKINDA<sup>®</sup> 12 mg Phase II IBS-D program, RedHill announced in June 2017 positive top-line results from the Phase III GUARD study with BEKINDA<sup>®</sup> 24 mg. The Phase III GUARD study successfully met its primary endpoint of efficacy in the treatment of acute gastroenteritis and gastritis, and BEKINDA<sup>®</sup> 24 mg was found to be safe and well tolerated in this indication. RedHill recently met with the FDA to discuss the results of the Phase III GUARD study and the clinical and regulatory path towards potential marketing approval of BEKINDA<sup>®</sup> 24 mg in the U.S. Following the positive guidance meeting, the Company is currently working with the FDA to design the confirmatory Phase III study to support a New Drug Application (NDA) with BEKINDA<sup>®</sup> 24 mg for acute gastroenteritis and gastritis.

**The Company will host a conference call and webcast today, October 3, 2017, at 9:00 a.m. EDT to discuss the top-line results from the BEKINDA<sup>®</sup> Phase II study for IBS-D.**

**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: +1-877-280-2342; International: +1-646-254-3365; and Israel: +972-3-763-0146. The access code for the call is 7238671.**

**About BEKINDA<sup>®</sup> (RHB-102):**

BEKINDA<sup>®</sup> is a proprietary, bimodal extended-release (24 hours) oral pill formulation of ondansetron, covered by several issued and pending patents. Positive top-line results from a Phase III clinical study of BEKINDA<sup>®</sup> 24 mg in the U.S. for acute gastroenteritis and gastritis (the GUARD study) were announced in June 2017. Positive top-line results from a Phase II study with BEKINDA<sup>®</sup> 12 mg for the treatment of diarrhea-predominant irritable bowel syndrome (IBS-D) were announced in October 2017.

**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 in acute gastroenteritis and gastritis and from a Phase II study in 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**<sup>®</sup> (**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) 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; (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 market Donnatal<sup>®</sup> and EnteraGam<sup>®</sup>, (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 of 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; and (xii) estimates of the Company's expenses, future revenues capital requirements and the Company's needs for additional financing; (xiii) 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; (xiv) 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.*

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<sup>i</sup> BEKINDA<sup>®</sup> is an investigational new drug, not available for commercial distribution.

<sup>ii</sup> Xifaxan<sup>®</sup> (rifaximin) prescribing information: [www.accessdata.fda.gov/drugsatfda\\_docs/label/2010/022554lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022554lbl.pdf); Viberzi<sup>®</sup> (eluxadoline) prescribing information: [www.accessdata.fda.gov/drugsatfda\\_docs/label/2015/206940s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/206940s000lbl.pdf) ; Average absolute difference from reported phase III studies; The theoretical comparison between the BEKINDA<sup>®</sup> Phase II study results and reported data from studies of IBS-D approved therapies serves as a general benchmark for the effect size observed with BEKINDA<sup>®</sup> and should not be construed as a direct and/or equal comparison given that the studies were not identical in design, patient population and treatment period. For example, in the Xifaxan<sup>®</sup> Phase III studies, the referenced efficacy endpoints were evaluated over a period of 4 weeks after 2 weeks drug administration, and in the Viberzi<sup>®</sup> Phase III studies the referenced efficacy endpoints were evaluated after drug was administered and evaluated for 12 weeks. The studies were not conducted head-to head in the same patient population.

<sup>iii</sup> GlobalData PharmaPoint: Irritable Bowel Syndrome – Global Drug Forecast and Market Analysis to 2023.

<sup>iv</sup> Lovell RM, Ford AC, Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis, Clin Gastroenterol Hepatol (2012), 10(7)712-721; Saito YA et al, The epidemiology of irritable bowel syndrome in North America: a systemic review, Am J Gastroenterol (2002), 97(8): 1910-5.

<sup>v</sup> GlobalData PharmaPoint: Irritable Bowel Syndrome – Global Drug Forecast and Market Analysis to 2023.

<sup>vi</sup> EvaluatePharma – USA sales by indication (IBS-D) (July 2017).

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- <sup>vii</sup> Garsed K. et al, A randomised trial of ondansetron for the treatment of irritable bowel syndrome with diarrhea, *Gut* (2014), 63(10): 1617-25.
- <sup>viii</sup> [www.fda.gov](http://www.fda.gov), post market drug safety information for patients and providers.