



June 14, 2017

## RedHill Biopharma Announces Successful Phase III Top-Line Results with BEKINDA® for Acute Gastroenteritis

- | **The positive Phase III top-line results indicate that the study successfully met its primary endpoint and BEKINDA® 24 mg was shown to be effective, safe and well tolerated in patients with acute gastroenteritis and gastritis**
- | **RedHill will host a conference call and webcast to discuss the top-line results from the BEKINDA® Phase III study on Wednesday, June 21, 2017, at 8:00 am EDT; Please visit the Company's website for dial-in information and webcast access: <http://ir.redhillbio.com/events.cfm>**

TEL-AVIV, Israel and RALEIGH, N.C., June 14, 2017 (GLOBE NEWSWIRE) -- 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 III GUARD study with BEKINDA® (RHB-102)<sup>1</sup> 24 mg for acute gastroenteritis and gastritis. The study successfully met its primary endpoint of efficacy in treatment of acute gastroenteritis. BEKINDA® was found to be safe and well tolerated in this indication.

The randomized, double-blind, placebo-controlled Phase III GUARD study evaluated the efficacy and safety of BEKINDA® 24 mg in treating acute gastroenteritis and gastritis. 321 adults and children over the age of 12 were enrolled at 21 clinical sites in the U.S. and randomized in a 60:40 ratio to receive either BEKINDA® 24 mg or placebo, respectively. The primary endpoint of the study was the proportion of patients without further vomiting, without rescue medication, and who were not given intravenous hydration from 30 minutes post first dose of the study drug until 24 hours post dose, compared to placebo.

Top-line results indicated that the Phase III GUARD study successfully met its primary endpoint in the Intent to Treat (ITT) population ( $p = 0.04$ ), despite high positive outcome rate in the placebo arm. BEKINDA® improved the efficacy outcome by 21%; 65.6% of BEKINDA® treated patients as compared to 54.3% of placebo patients ( $p = 0.04$ ;  $n=192$  in the BEKINDA® group and  $n=129$  in the placebo group). Correcting for a randomization error, the difference in effect is greater with 65.8% vs. 53.9% favoring BEKINDA® vs. placebo in reaching the primary endpoint of the study ( $p = 0.03$ ). In per-protocol (PP) analysis of patients who met all protocol entry criteria and for which the diagnosis of gastroenteritis was confirmed ( $n=177$  in the BEKINDA® group and  $n=122$  in the placebo group), BEKINDA® improved the efficacy outcome by 27%; 69.5% of patients in the BEKINDA® group vs. 54.9% in the placebo group ( $p = 0.01$ ). BEKINDA® 24 mg was also shown to be safe and well-tolerated. Importantly, electrocardiogram results showed no adverse changes with treatment.

**Robert A. Silverman, MD, MS, Emergency Medicine specialist at Northwell Health and Lead Investigator of the BEKINDA® Phase III GUARD study, said:** "The positive results of the Phase III GUARD study demonstrate that BEKINDA® 24 mg is beneficial in the treatment of acute gastroenteritis and gastritis and can provide patients with 24 hours of relief. Gastroenteritis is a very common illness in the U.S., with approximately 179 million cases annually. If approved by FDA, BEKINDA® may become the new standard of care helping us treat patients quickly and effectively in both the emergency and outpatient settings."

**Terry F. Plasse, MD, RedHill's Medical Director, added:** "We are excited about the positive outcome of the Phase III GUARD study, which met its efficacy primary endpoint and demonstrated the safety and tolerability of BEKINDA® 24 mg. Notably, when looking at results by initial severity of nausea, we see a treatment effect even in patients with very severe nausea at baseline, suggesting that the drug works regardless of the initial severity of gastroenteritis. We continue to analyze the data, with the final clinical study report expected in the third quarter of 2017. We look forward to presenting the data to the FDA and discussing the potential path for marketing approval of BEKINDA® 24 mg in the U.S. and whether additional clinical studies are required prior to NDA filing. We are also expecting top-line Phase II results from the clinical study of BEKINDA® 12 mg in diarrhea-predominant irritable bowel syndrome (IBS-D) in September 2017. I would like to thank the patients, investigators, clinical staff and service providers who participated in the GUARD study and commend the RedHill team for achieving this important milestone."

BEKINDA® is a proprietary, bimodal extended-release, once-daily oral pill formulation of the antiemetic drug ondansetron, targeting several gastrointestinal indications. BEKINDA® 24 mg is intended to provide patients with relief from nausea and vomiting symptoms for a full 24-hour period with a single oral tablet. If approved for marketing by the FDA, BEKINDA® 24 mg

could become the first 5-HT3 antiemetic drug in the U.S. indicated for the treatment of acute gastroenteritis and gastritis.

RedHill will continue to analyze the GUARD Phase III study top-line data, including secondary endpoints, and plans to meet with the FDA to present the data and discuss the clinical and regulatory path towards potential marketing approval of BEKINDA® 24 mg in the U.S. Additional clinical studies may be required prior to potential submission of a New Drug Application (NDA).

The top-line results from the GUARD Phase III study 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 third quarter of 2017.

Acute gastroenteritis and gastritis are inflammations of the mucus membranes of the gastrointestinal tract leading to a combination of symptoms which include nausea, vomiting, diarrhea or abdominal pain. Acute gastroenteritis is a common infectious disease, with approximately 179 million cases annually in the U.S.<sup>2</sup> It is caused by many different infectious agents, most commonly by viral infections, accounting for up to 70% of cases<sup>3</sup>. Noroviruses cause the most outbreaks of non-bacterial acute gastroenteritis in all age groups and often occur in epidemic outbreaks in schools, nursing homes and other group settings<sup>3</sup>. Gastroenteritis and gastritis are major causes of emergency room visits, with up to 474,000 estimated hospitalizations annually in the U.S. alone<sup>2</sup>. Oral rehydration is the preferred therapy in mild to moderate dehydration, whereas intravenous fluids are recommended in more severe cases<sup>4</sup>. Adding ondansetron, the active ingredient in BEKINDA®, to the standard intravenous rehydration therapy has shown to significantly reduce the amount of vomiting in children with gastroenteritis<sup>5</sup>; however, to the best of RedHill's knowledge, its efficacy in adult gastroenteritis patients has not been shown beneficial in a randomized clinical trial in the U.S.

Ondansetron is approved as an antiemetic in patients suffering from chemotherapy and radiotherapy-induced nausea and vomiting and from postoperative nausea and vomiting<sup>6</sup>. BEKINDA® may decrease the frequency of vomiting, improve the success and compliance of oral rehydration therapy and decrease the rate of intravenous therapy in patients suffering from gastroenteritis. BEKINDA® is targeting a potential worldwide market estimated to exceed \$650 million annually<sup>3</sup>. For additional information on acute gastroenteritis and BEKINDA®, please see presentation and webcast from the R&D Day held by RedHill on April 27, 2017: <http://ir.redhillbio.com/events.cfm>.

**RedHill will host a conference call and webcast call on Wednesday June 21, 2017 at 8:00 a.m. EDT, to review the Phase III GUARD study top-line results. Please visit the Company's website for dial-in information and webcast access: <http://ir.redhillbio.com/events.cfm>**

BEKINDA® is being studied for an additional indication. A randomized, double-blind, placebo-controlled Phase II study with BEKINDA® 12 mg is currently ongoing in the U.S. for the treatment of diarrhea-predominant irritable bowel syndrome (IBS-D). Enrollment of patients for the Phase II study has been completed, with top-line results expected in September 2017.

The Phase II study and the Phase III GUARD study with BEKINDA® 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.

The top-line results from the Company's GUARD study are preliminary in nature, as they are based solely on top-line information provided to the Company by an independent third-party contractor. The Company intends to examine the data from this study in greater detail, along with all the information gathered during this study, including all safety and other secondary objectives. Such analysis may result in findings inconsistent with the top-line data disclosed in this release. As such, investors should not rely on the top-line results reported in this release as the final definitive results of the GUARD study. Once the Company has fully analyzed the results of the GUARD study, including the CSR, it will announce the definitive findings.

#### **About BEKINDA® (RHB-102):**

BEKINDA® is a proprietary, bimodal extended-release (24 hours) oral pill formulation of ondansetron, covered by several issued and pending patents. Successful top-line results from a Phase III clinical study of BEKINDA® 24 mg in the U.S. for acute gastroenteritis and gastritis (the GUARD study) were announced in June 2017. A Phase II study with BEKINDA® 12 mg is ongoing in the U.S. for the treatment of diarrhea-predominant irritable bowel syndrome (IBS-D), with patient enrollment completed and top-line results expected in the third quarter of 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 two gastrointestinal products in the U.S. - **Donnatal**<sup>®</sup>, a prescription oral adjunctive drug used in the treatment of IBS and acute enterocolitis, and **EnteraGam**<sup>®</sup>, a medical food intended for the dietary management, under medical supervision, of chronic diarrhea and loose stools. RedHill's clinical-stage pipeline includes: (i) **RHB-105** - an oral combination therapy for the treatment of *Helicobacter pylori* infection with successful results from a first 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 QIDP status for nontuberculous mycobacteria (NTM) infections; (iii) **BEKINDA**<sup>®</sup> (**RHB-102**) - a once-daily oral pill formulation of ondansetron with successful top-line results in 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**<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).

<sup>1</sup> BEKINDA<sup>®</sup> is an investigational new drug, not available for commercial distribution.

<sup>2</sup> Scallan E, Griffin PM, Angulo FJ, Tauxe RV, Hoekstra RM, *Foodborne Illness Acquired in the United States - Unspecified Agents*, Emerg Infect Dis. 2011;17(1):16-22.

<sup>3</sup> Graves S. Nancy, *Acute Gastroenteritis*, Prim Care Clin Office Pract 40 (2013) 727-741.

<sup>4</sup> Reeves JJ, Shannon MW, Fleisher GR, *Ondansetron decreases vomiting associated with acute gastroenteritis: a randomized, controlled trial*, Pediatrics. 2002;109(4):e62.

<sup>5</sup> Elliott, Elizabeth Jane, *Acute Gastroenteritis in Children*, BMJ, 334.7583 (2007): 35-40. PMC. Web. 8 Feb. 2017.

<sup>6</sup> Ondansetron prescribing information.

*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 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) 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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