RedHill Biopharma Publishes Positive IBS-D Phase 2 Study Data in The American Journal of Gastroenterology

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Publication of the Phase 2 U.S. study data show that RHB-102 (Bekinda®) 12mg delivers a clinically meaningful improvement in overall stool consistency response versus placebo in patients with diarrhea-predominant irritable bowel syndrome (IBS-D), meeting the study's primary endpoint

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In addition, the publication highlights that elevated baseline C-reactive protein (CRP) may be used to identify treatment responders in this complex disease, which lacks reliable predictive markers

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The 126-patient study was conducted in 16 sites across the U.S.

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RHB-102, a novel, proprietary, once-daily bimodal release formulation of ondansetron that allows for both immediate relief and 24-hour maintenance of effect, is also in Phase 3 development for acute gastroenteritis and gastritis

TEL AVIV, Israel and RALEIGH, N.C., July 28, 2020 (GLOBE NEWSWIRE) -- RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced the publication of data from its previously announced Phase 2 study of RHB-102 (Bekinda®)[1], a novel, proprietary, once-daily, 12mg bimodal-release ondansetron, in diarrhea-predominant irritable bowel syndrome (IBS-D), in *The American Journal of Gastroenterology*.

The peer-reviewed article[2], entitled "Bimodal Release Ondansetron Improves Stool Consistency and Symptomatology in Diarrhea-Predominant Irritable Bowel Syndrome, A Randomized, Double-Blind, Trial," is available online.

"The newly published positive data in patients who received RHB-102 for IBS-D, are a demonstration of RedHill's ongoing ability to successfully execute its R&D programs to meet specified endpoints. The data are particularly encouraging given the need for new treatment options, that demonstrate both effectiveness and tolerability, in this challenging condition that significantly impacts quality of life," **said Terry Plasse, MD, Medical Director at RedHill and lead author of the publication.** "In addition to the positive efficacy data, an important finding reported in the publication was the identification of baseline CRP as a potential predictive marker of RHB-102 treatment response in IBS-D, which could be a major benefit in future trials and commercialization. We intend to continue realizing the potential of RHB-102 for IBS-D patients."

The publication reports that RHB-102 delivered a response rate in stool consistency of 56.0% compared to 35.3% in the placebo group (P = .036). The treatment effect, the difference between response rates in patients receiving RHB-102 compared to those receiving placebo, was greater in patients with baseline CRP levels above the median for this study. This suggests that CRP may be a predictor of response. While not powered to show statistical significance, RHB-102 also demonstrated favorable outcomes in the secondary endpoints of overall pain response (50.7% vs 39.2%) and composite response rates (40.0% vs 25.5%). RHB-102 was well tolerated with similar rates of adverse events reported for both arms of the study.

The Phase 2 study, conducted in 16 sites across the U.S., included 126 male and female patients, aged 18 and older, who met the Rome III criteria for IBS-D and had a Bristol Stool Scale rating of at least six on two or more days weekly. Patients were randomly assigned at a 3:2 ratio to receive either RHB-102 (n = 75) or placebo (n = 51) once daily for eight weeks. The primary outcome measure of the study was overall stool consistency response for at least four of eight weeks.

Results from the study, according to a Company analysis, suggest that outcomes for RHB-102 compare favorably with previously reported efficacy outcome values from studies of Xifaxan® (rifaximin) and Viberzi® (eluxadoline), across all three efficacy endpoints[3].

About Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is a complex and debilitating condition, reported to affect in excess of 10% of Americans[4]. According to the American College of Gastroenterology it is the most common disease diagnosed by gastroenterologists and one of the most common disorders seen by primary care physicians in the U.S.[5]. IBS-D accounts for around 40% of all IBS sufferers[6]. It has a significant impact on quality of life, causing symptoms such as pain and cramping, in addition to urgency and diarrhea.

About RHB-102 (Bekinda®)

RHB-102 is a proprietary investigational bimodal release, once-daily formulation of ondansetron that is unique in its ability to combine immediate release ondansetron, for fast symptom relief, with a slow-release matrix, that maintains therapeutic effect for up to 24 hours.

Following the successful Phase 2 study of RHB-102 (12mg) in IBS-D, RedHill is currently finalizing the design of two pivotal Phase 3 studies for IBS-D.

RedHill is also developing RHB-102 as a (24mg) formulation, for acute gastroenteritis and gastritis. The Phase 3 GUARD study with RHB-102 (24mg) in acute gastroenteritis and gastritis successfully met its primary endpoint of prevention of vomiting for at least 24 hours in adolescent and adult patients with gastroenteritis-related emesis without the use of IV hydration or rescue medication. The Company is currently working towards a confirmatory Phase 3 study to support a potential New Drug Application (NDA) for this indication. RHB-102 is covered by several issued and pending patents.

About RedHill Biopharma

RedHill Biopharma Ltd. (Nasdaq: RDHL) is a specialty biopharmaceutical company primarily focused on gastrointestinal diseases. RedHill promotes the gastrointestinal drugs **Movantik®** for opioid-induced constipation in adults[7], **Talicia®** for the treatment of *Helicobacter pylori (H. pylori)* infection in adults[8] and **Aemcolo®** for the treatment of travelers' diarrhea in adults [9]. RedHill's key clinical late-stage development programs include: (i) **RHB-204**, with a planned pivotal Phase 3 study for pulmonary nontuberculous mycobacteria (NTM) infections; (ii) **opaganib (Yeliva®)**, a first-in-class SK2 selective inhibitor targeting multiple indications with a Phase 2/3 program for COVID-19 and ongoing Phase 2 studies for prostate cancer and cholangiocarcinoma; (iii) **RHB-104**, with positive results from a first Phase 3 study for Crohn's disease; (iv) **RHB-102** (**Bekinda®**), with positive results from a Phase 3 study for acute gastroenteritis and gastritis and positive results from a Phase 2 study for IBS-D; (v) **RHB-106**, an encapsulated bowel preparation, and (vi) **RHB-107**, a Phase 2-stage first-in-class, serine protease inhibitor, targeting cancer and inflammatory gastrointestinal diseases and is also being evaluated for COVID-19. 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, without limitation, the risk that subsequent studies, if conducted at all, will not demonstrate positive data regarding RHB-102 as well as risks and uncertainties associated with (i) the initiation, timing, progress and results of the Company's research, manufacturing, pre-clinical studies, clinical trials, and other therapeutic candidate development efforts, and the timing of the commercial launch of its commercial products and ones it may acquire or develop in the future; (ii) the Company's ability to advance its therapeutic candidates into clinical trials or to successfully complete its pre-clinical studies or clinical trials or the development of a commercial companion diagnostic for the detection of MAP; (iii) the extent and number and type 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 and Talicia®; (v) the Company's ability to successfully commercialize and promote Talicia ®, and Aemcolo® and Movantik®; (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, pre-clinical 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; (xiv) competition from other companies and technologies within the Company's industry; and (xv) the hiring and employment commencement date of executive managers. 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 March 4, 2020. 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.

Company contact:
Adi Frish
Senior VP Business Development & Licensing
RedHill Biopharma
+972-54-654-3112
adi@redhillbio.com

IR contact (U.S.):
Timothy McCarthy, CFA, MBA
Managing Director, Relationship Manager
LifeSci Advisors, LLC
+1-212-915-2564
tim@lifesciadvisors.com

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[1] RHB-102 (Bekinda®) is an investigational new drug, not available for commercial distribution.

[2] Plasse, Terry F. MD et al; Bimodal Release Ondansetron Improves Stool Consistency and Symptomatology in Diarrhea-Predominant Irritable Bowel Syndrome, The American Journal of Gastroenterology: June 24, 2020 - Volume Publish Ahead of Print - Issue - doi: 10.14309/ajg.0000000000000727.

[3] For more details, see RedHill's press releases dated October 3, 2017 and January 16, 2018, and Xifaxan® (rifaximin) prescribing information: www.accessdata.fda.gov/drugsatfda_docs/label/2010/022554lbl.pdf, Viberzi® (eluxadoline) prescribing information: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/206940s003lbl.pdf. Average absolute difference from reported Phase 3 studies; the theoretical comparison between the RHB-102 12 mg Phase 2 study results and reported data from studies of IBS-D-approved therapies serves as a general benchmark for the effect size observed with RHB-102 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 period. For example, in the Xifaxan® 550 mg Phase 3 studies, the referenced efficacy endpoints were evaluated over a period of 4 weeks after 2 weeks drug administration, and in the Viberzi® 100 mg Phase 3 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.

[4] JAMA. 2015;313(9):949-958.

[5] American College of Gastroenterology: https://gi.org/topics/irritable-bowel-syndrome/.

[6] Lovell RM, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. *Clin Gastroenterol Hepatol*. 2012;10(7):712-72 doi: 10.1016/j.cgh.2012.02.029.

[7] Full prescribing information for Movantik® (naloxegol) is available at: www.Movantik.com.

[8] Full prescribing information for Talicia® (omeprazole magnesium, amoxicillin and rifabutin) is available at: www.Talicia.com.

[9] Full prescribing information for Aemcolo® (rifamycin) is available at: www.Aemcolo.com.

Source: RedHill Biopharma Ltd.