RedHill Biopharma Presents New Data from Talicia®'s Phase 3 Studies at ACG 2020 Focused on Achieving Successful First-Line Treatment in H. pylori Eradication

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H. pylori eradication rates with clarithromycin-based triple therapy were found to be predictably low in the Phase 3 trial, with antibiotic resistance a contributing factor. Despite declining efficacy, physicians are still prescribing these regimens counter to ACG guidelines, which advocate for using first-line regimens that provide the highest likelihood of eradication success

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Talicia's efficacy in the Phase 3 study was unaffected by patient body mass index (BMI), while published data suggest that BMI may be associated with the failure of clarithromycin-based H. pylori treatments, further supporting the use of Talicia as a first-line therapy in all populations

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Talicia is the first and only FDA-approved rifabutin-based therapy for the treatment of H. pylori infection, designed as a first-line option to address the high and growing resistance of H. pylori to commonly used antibiotics

TEL AVIV, Israel and RALEIGH, N.C., Oct. 26, 2020 (GLOBE NEWSWIRE) -- RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced that new data supporting the use of Talicia®[1] as a first-line therapy for eradication of *H. pylori* in adults was presented at the American College of Gastroenterology (ACG) 2020 Virtual Annual Scientific Meeting. The Company also presented data highlighting the emerging patterns of *H. pylori* resistance to antibiotics used in current standard-of-care therapies.

A key objective of the new U.S. Government "National Action Plan for Combating Antibiotic-Resistant Bacteria, 2020-2025"[2] is lowering the annual rate of inappropriate outpatient antibiotic prescribing. Efficacy of treatments for *H. pylori*, one of the most prevalent infections in the U.S. and the leading cause of gastric cancer, has been steadily declining due to increasing levels of antibiotic resistance[3]. In tackling this problem, it is important to ensure successful first-line eradication of *H. pylori* infection. The analyses presented by RedHill at the ACG annual meeting aim to provide insights that may help avoid the risk of antibiotic resistance in the eradication of *H. pylori*.

Poster 1: **Persistent *H. pylori* infection following participation in two randomized controlled trials: Outcomes of patients receiving physician-directed standard-of-care therapy**[4].
This analysis of data from the Talicia Phase 3 studies looked at the cure rates of physician-directed standard-of-care therapy for persistent *H. pylori* infection. The analysis found that eradication rates with empiric clarithromycin-based triple therapy were predictably low, and that despite declining efficacy of clarithromycin-containing therapies, physicians are still prescribing these regimens.

"Despite the ACG treatment guideline recommendations for avoiding clarithromycin-containing triple therapy in patients with prior macrolide use and as salvage treatment, as well as other recommended restrictions based on resistance, clarithromycin-based therapies unfortunately remain an all too often prescribed treatment for *H. pylori*," **said Dr. Colin W. Howden, MD, AGAF, FACG, Hyman Professor of Medicine & Chief of the Division of Gastroenterology, University of Tennessee Health Science Center.** "Because *H. pylori* treatment is largely empiric, it is important that physicians prescribe a first-line regimen with the highest probability of successful eradication. A treatment regimen that does not contain clarithromycin, such as low dose rifabutin-based therapy, is a good first-line option to consider for *H. pylori* eradication."

Poster 2: **Efficacy of *H. pylori* eradication by low-dose rifabutin triple therapy (RHB-105) is unaffected by BMI: Post-hoc analysis from two Phase 3 trials**[5].
Winner of the ACG "Outstanding Poster Presenter" Award.
With rising rates of obesity in the U.S., and published data suggesting that Body Mass Index (BMI) may be associated with the failure of clarithromycin-based *H. pylori* treatments[6], it is imperative to study the influence of patient BMI on treatment success. This post-hoc analysis assessed the impact of BMI on eradication rates of *H. pylori* in patients with a BMI of both above and below 40, with results demonstrating that eradication rates with Talicia remained within the same high range, irrespective of patient BMI status. This maintenance of Talicia efficacy compares to an almost 50% reduction of eradication rates in amoxicillin/omeprazole-comparator-treated patients with BMI ≥40.

"Antibiotic treatment failure in obese populations with *H. pylori* is a significant concern and may be linked to elevations in BMI," **said Dr. June Almenoff, MD, Ph.D., RedHill's Chief Scientific Officer** . "Given the trends of increasing BMI and growing antibiotic resistance in the U.S., it is critical to work towards first-line *H. pylori* eradication success in all patients irrespective of BMI. These data demonstrate that Talicia's efficacy rates were similarly high across patient sub-groups by BMI."

About Talicia (omeprazole magnesium, amoxicillin and rifabutin)
Talicia is the only rifabutin-based therapy approved for the treatment of *H. pylori* infection and is designed to address the high resistance of *H. pylori* bacteria to commonly used clarithromycin-based therapies. The high rates of *H. pylori* resistance to clarithromycin have led to significant rates of treatment failure with clarithromycin-based therapy and are a strong public health concern, as highlighted by the FDA and the World Health Organization (WHO) in recent years.

Talicia is a novel, fixed-dose, all-in-one oral capsule combination of two antibiotics (amoxicillin and rifabutin) and a proton pump inhibitor (PPI) (omeprazole). In November 2019, Talicia was approved by the U.S. FDA for the treatment of *H. pylori* infection in adults. In the pivotal Phase 3 study, Talicia demonstrated 84% eradication of *H. pylori* infection in the intent-to-treat (ITT) group vs. 58% in the active comparator arm ($p<0.0001$). Minimal to zero resistance to rifabutin, a key component of Talicia, was detected in RedHill's pivotal Phase 3 study. Further, in an analysis of data from this

study, it was observed that subjects who were confirmed adherent[7] to their therapy had eradication rates of 90.3% in the Talicia arm vs. 64.7% in the active comparator arm[8].

Talicia is eligible for a total of eight years of U.S. market exclusivity under its Qualified Infectious Disease Product (QIDP) designation and is also covered by U.S. patents which extend patent protection until 2034 with additional patents and applications pending and granted in various territories worldwide.

About *H. pylori*

H. pylori is a bacterial infection that affects approximately 35%[9] of the U.S. population, with an estimated two million patients treated annually[10]. Worldwide, more than 50% of the population has *H. pylori* infection, which is classified by the WHO as a Group 1 carcinogen. It remains the strongest known risk factor for gastric cancer[11] and a major risk factor for peptic ulcer disease[12] and gastric mucosa-associated lymphoid tissue (MALT) lymphoma[13]. More than 27,000 Americans are diagnosed with gastric cancer annually[14]. Eradication of H. pylori is becoming increasingly difficult, with current therapies failing in approximately 25-40% of patients who remain H. pylori-positive due to high resistance of H. pylori to antibiotics commonly used in standard combination therapies[15].

About RedHill Biopharma

RedHill Biopharma Ltd. (Nasdaq: RDHL) is a specialty biopharmaceutical company primarily focused on gastrointestinal and infectious diseases. RedHill promotes the gastrointestinal drugs, **Movantik®** for opioid-induced constipation in adults with non-cancer pain[16], **Talicia®** for the treatment of *Helicobacter pylori (H. pylori)* infection in adults[17], and **Aemcolo®** for the treatment of travelers' diarrhea in adults [18]. RedHill's key clinical late-stage investigational development programs include: (i) **RHB-204**, with a planned 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 Phase 2 studies for prostate cancer and cholangiocarcinoma ongoing; (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-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 and (vi) **RHB-106**, an encapsulated bowel preparation. More information about the Company is available at www.redhillbio.com.

TALICIA: INDICATION AND USAGE

Talicia is a three-drug combination of omeprazole, a proton pump inhibitor, amoxicillin, a penicillin-class antibacterial, and rifabutin, a rifamycin antibacterial, indicated for the treatment of *Helicobacter pylori* infection in adults.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Talicia and other antibacterial drugs, Talicia should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

IMPORTANT SAFETY INFORMATION

Talicia contains omeprazole, a proton pump inhibitor (PPI), amoxicillin, a penicillin-class antibacterial and rifabutin, a rifamycin antibacterial. It is contraindicated in patients with known hypersensitivity to any of these medications, any other components of the formulation, any other beta-lactams or any other rifamycin.

Talicia is contraindicated in patients receiving rilpivirine-containing products.

Talicia is contraindicated in patients receiving delavirdine or voriconazole.

Serious and occasionally fatal hypersensitivity reactions have been reported with omeprazole, amoxicillin and rifabutin.

Clostridioides difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents and may range from mild diarrhea to fatal colitis. Talicia may cause fetal harm. Talicia is not recommended for use in pregnancy.

Talicia may reduce the efficacy of hormonal contraceptives. An additional non-hormonal method of contraception is recommended when taking Talicia.

Talicia should not be used in patients with hepatic impairment or severe renal impairment.

Acute Interstitial Nephritis has been observed in patients taking PPIs and penicillins.

Cutaneous lupus erythematosus (CLE) and systemic lupus erythematosus (SLE) have been reported in patients taking PPIs. These events have occurred as both new onset and exacerbation of existing autoimmune disease.

The most common adverse reactions (≥1%) were diarrhea, headache, nausea, abdominal pain, chromaturia, rash, dyspepsia, oropharyngeal pain, vomiting, and vulvovaginal candidiasis.

To report SUSPECTED ADVERSE REACTIONS, contact RedHill Biopharma INC. at 1-833-ADRHILL (1-833-237-4455) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Full prescribing information for Talicia is available at www.Talicia.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 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 commercial products; (v) the Company's ability to successfully commercialize and promote Talicia®, and Aemcolo® and Movantik®; *(vi) the Company's ability to est ablish 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 commercial products 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 maintaining employment 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.*

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[1] Omeprazole magnesium, amoxicillin and rifabutin delayed release capsules. Also referred to as RHB-105

[2] https://aspe.hhs.gov/pdf-report/carb-plan-2020-2025

[3] Prevalence of Antibiotic Resistance in *Helicobacter pylori*: A Systematic Review and Meta-analysis in World Health Organization Regions. Alessia Savoldi et al. Gastroenterology 2018;155:1372–1382.

[4] Persistent *H. pylori* infection following participation in two randomized controlled trials: Outcomes of patients receiving physician-directed standard-of-care therapy. Colin W. Howden, Raymond M. Panas, June S. Almenoff, and Willian D. Chey.

[5] Efficacy of *H. pylori* eradication by low-dose rifabutin triple therapy (rhb-105) is unaffected by BMI: Post-hoc analysis from two Phase 3 trials. Kely L. Sheldon, Steven F. Moss, Mohd Amer Alsamman, Elliot Offman, Raymond M. Panas, and June S. Almenoff.

[6] Cerqueira, R. M., Correia, M. R., Fernandes, C. D., et al. (2013). Cumulative *Helicobacter pylori* eradication therapy in obese patients undergoing gastric bypass surgery. Obes Surg, 23(2), 145-149. doi:10.1007/s11695-012-0747-4.

[7] Defined as the PK population which included those subjects in the ITT population who had demonstrated presence of any component of investigational drug at visit 3 (approx. day 13) or had undetected levels drawn >250 hours after the last dose.

[8] The pivotal Phase 3 study with Talicia® demonstrated 84% eradication of *H. pylori* infection with Talicia® vs. 58% in the active comparator arm (ITT analysis, p<0.0001).

[9] Hooi JKY et al. Global Prevalence of *Helicobacter pylori* Infection: Systematic Review and Meta-Analysis. Gastroenterology 2017; 153:420-429.

[10] IQVIA Custom Study for RedHill Biopharma, 2019

[11] Lamb A et al. Role of the *Helicobacter pylori*-Induced inflammatory response in the development of gastric cancer. J Cell Biochem 2013;114.3:491-497.

[12] NIH – *Helicobacter pylori* and Cancer, September 2013.

[13] Hu Q et al. Gastric mucosa-associated lymphoid tissue lymphoma and *Helicobacter pylori* infection: a review of current diagnosis and management. Biomarker research 2016;4.1:15.

[14] National Cancer Institute, Surveillance, Epidemiology, and End Results Program (SEER).

[15] Malfertheiner P. et al. Management of *Helicobacter pylori* infection - the Maastricht IV/ Florence Consensus Report, Gut 2012;61:646-664; O'Connor A. et al. Treatment of *Helicobacter pylori* Infection 2015, Helicobacter 20 (S1) 54-61; Venerito M. et al. Meta-analysis of bismuth quadruple therapy versus clarithromycin triple therapy for empiric primary treatment of *Helicobacter pylori* infection. Digestion 2013;88(1):33-45.

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

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

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

Source: RedHill Biopharma Ltd.