NEWS RELEASE

RedHill Presents New Talicia® Data Analyses at DDW 2022

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Talicia's efficacy and safety profile evaluated in patients with H. pylori infection and diabetes mellitus, a large and challenging patient population associated with sub-optimal outcomes with clarithromycin-based H. pylori eradication therapy

Physiologically based pharmacokinetic modeling study of Talicia evaluated intragastric antibiotic exposure, which is critical for successful H. pylori eradication, by comparing low-dose rifabutin 50 mg every 8 hours to the generic formulation of rifabutin 150 mg once a day

Talicia, the leading FDA-approved brand for H. pylori treatment, is intended for empiric first-line eradication of H. pylori, a bacterial infection that affects approximately 35% of the U.S. adult population, representing significant unmet need

RALEIGH, N.C. and TEL AVIV, Israel, May 25, 2022 /PRNewswire/ -- **RedHill Biopharma Ltd.** (NASDAQ: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, announced the presentation of two new data analyses from the Talicia®H. pylori eradication clinical trials program at Digestive Diseases Week (DDW) 2022.

The first analysis evaluated the maintenance of Talicia's efficacy and safety in the treatment of patients with H. pylori infection and diabetes mellitus (DM). DM is associated with higher rates of H. pylori infection and higher rates of treatment failure with clarithromycin-based therapies. Furthermore, clarithromycin interacts with some common

diabetes medications potentially leading to hypoglycemia[1].

The second analysis, a physiologically based pharmacokinetic (PBPK) study, used modeling to compare Talicia's low-dose rifabutin formulation's (rifabutin 50 mg every 8 hours) sustained intragastric antibiotic exposure, a critical component of successful H. pylori eradication, to exposure rates seen with the generic formulation of rifabutin (150 mg taken once daily (QD).

Poster one (poster number: Tu1078): **Low-Dose Rifabutin Triple Therapy (Talicia) Maintains High Helicobacter pylori Eradication Rates and Shows Favorable Safety and Efficacy in Subjects with Diabetes Mellitus**.

Presenting Author: Dr. Colin W. Howden, MD, Professor Emeritus, University of Tennessee Health Science Center

This supplemental analysis of the pooled modified intent-to-treat (mITT) population (n=293) from two Phase 3 clinical trials (ERADICATE Hp, ERADICATE Hp2) assessed the safety and efficacy of Talicia in patients with DM. H. pylori isolates from treatment-naïve patients from study 2 were also tested for antibiotic resistance according to the presence of DM. The 293 patient-analyzable mITT population who received Talicia had pooled eradication rates of 91.7% (n=44) and 84.1% (n=206) in patients with and without DM, respectively (p=0.17). Moreover, no resistance was seen to rifabutin in patients with or without DM. Resistance rates were 4% v 7% for amoxicillin, 45% v 43% for metronidazole, and 21% v 17% resistance to clarithromycin in patients with and without DM, respectively. With the exception of an observed higher rate of diarrhea in patients without diabetes versus those with (13.8% vs 6%), the presence of diabetes did not alter the safety or tolerability of Talicia, and generally matched the safety profile of the total patient population.

"More than 37 million Americans have diabetes, which presents significant issues in the treatment of H. pylori infection. Firstly, we know that the risk of treatment failure with clarithromycin-based therapies is significantly higher in patients with diabetes[2], and secondly, the use of clarithromycin in diabetic patients can impair the management of their diabetes due to drug-drug interactions," said **Dr. Barry Johns, MD, from The Jones Center for Diabetes and Endocrine Wellness, Macon, GA.** "Consequently, it is vital that we know which therapies are most appropriate for first-line H. pylori eradication treatment. Since Talicia maintains high eradication rates and is well tolerated regardless of a patient's diabetes, it represents a rational empiric first-line choice for the treatment of H. pylori infection."

Poster two (poster number: Tu1077): **Low-Dose Rifabutin Triple Therapy Demonstrates High Helicobacter pylori Eradication Rates: Physiologically-Based Pharmacokinetic (PBPK) Modeling Supports Favorable Intragastric Rifabutin Concentrations for 50 mg Q8H Dosing vs. 150 mg QD**

Presenting Author: Dr. Colin W. Howden, MD, Professor Emeritus, University of Tennessee Health Science Center.

Sufficient intragastric antibiotic exposure is critical for eradication of H. pylori. Consequently, understanding the influence of antibiotic dosing on intragastric exposure is imperative. This study used PBPK modeling to compare intragastric rifabutin concentrations with Talicia (low-dose rifabutin 50 mg) administered every 8 hours (Q8H) vs. rifabutin 150 mg (the generically available dose) administered once daily (QD). Intragastric rifabutin concentration time above the mean inhibitory concentration (MIC90 = 0.008 mcg/mL) was calculated over a 24-hour period for each regimen. Low-dose rifabutin 50 mg Q8H, as in Talicia, maintained intragastric rifabutin concentrations at or above the MIC90 for approximately three times longer than rifabutin 150 mg QD. When taken with food (as indicated in the prescribing information), low-dose rifabutin 50 mg Q8H, as in Talicia, provided intragastric concentrations at or above the MIC90 for about 93% of the day, compared to 35% of the day when dosed as 150 mg QD.

"Maintaining high intragastric antibiotic concentrations is necessary for successful H. pylori eradication. Dosing rifabutin at 150 mg QD does not replicate the sustained intragastric concentrations predicted with low-dose rifabutin at 50 mg Q8H. The differences in intragastric exposure seen in this study may potentially explain the lower and less consistent eradication rates seen with generic rifabutin (about 70% eradication) than seen in the Talicia clinical trial program (about 84-90% eradication)," said Dr. Colin W. Howden, MD, Professor Emeritus, University of Tennessee Health Science Center. "Given the need to aim for the most effective empiric first-line eradication therapy, it is important to utilize a therapy with the highest likelihood of H. pylori eradication success, such as Talicia."

"These important new data enhance the body of evidence supporting the use of Talicia as a first line therapy for H. pylori," **said Dr. June Almenoff, MD, Ph.D., RedHill's Chief Medical Officer**. "Talicia consistently shows its ability to maintain high H. pylori eradication rates, even in challenging patient populations, with zero to minimal resistance. This work also demonstrates Talicia's sustained intragastric exposure, providing optimized conditions for eradication of H. pylori at the first treatment attempt."

About H. pylori infection

H. pylori is a bacterial infection that affects approximately 35%[3] of the U.S. population, with an estimated two million patients treated annually[4]. 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[5] and a major risk factor for peptic ulcer disease[6] and gastric mucosa-associated lymphoid tissue (MALT) lymphoma[7]. More than 27,000 Americans are diagnosed with gastric cancer annually[8]. 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 – especially clarithromycin – which is still commonly used in standard combination therapies[9].

About Talicia®

Talicia® is the only low-dose rifabutin-based therapy approved for the treatment of H. pylori infection and is designed to address the high resistance of H. pylori bacteria seen with other antibiotics. The high rates of H. pylori resistance to clarithromycin have led to significant rates of treatment failure with clarithromycin-based therapies and are a strong public health concern, as highlighted by the ACG, 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[10] to their therapy had response rates of 90.3% in the Talicia® arm vs. 64.7% in the active comparator arm[11]. 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 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[12], **Talicia®** for the treatment of Helicobacter pylori (H. pylori) infection in adults[13], and **Aemcolo®** for the treatment of travelers' diarrhea in adults[14]. RedHill's key clinical late-stage development programs include: (i) **RHB-204**, with an ongoing Phase 3 study for pulmonary nontuberculous mycobacteria (NTM) disease; (ii) **opaganib (ABC294640)**, a first-in-class oral SK2 selective inhibitor targeting multiple indications with a Phase 2/3 program for hospitalized COVID-19 and Phase 2 studies for prostate cancer and cholangiocarcinoma ongoing; (iii) **RHB-107** (**upamostat**), an oral serine protease inhibitor in a Phase 2/3 study as treatment for non-hospitalized symptomatic COVID-19, and targeting multiple other cancer and inflammatory gastrointestinal diseases; (iv) **RHB-104**, with positive results from a first Phase 3 study for Crohn's disease; (v) **RHB-102** , with positive results from a Phase 3 study for acute gastroenteritis and gastritis and positive results from a Phase 2 study for IBS-D; and (vi) **RHB-106**, an encapsulated bowel preparation. More information about the Company is available at **www.redhillbio.com**/ **twitter.com/RedHillBio**.

TALICIA: INDICATION AND IMPORTANT SAFETY INFORMATION

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.

Severe cutaneous adverse reactions (SCAR) (e.g., Stevens-Johnson syndrome (SJS), Toxic epidermal necrolysis (TEN)) have been reported with rifabutin, amoxicillin, and omeprazole. Additionally, drug reaction with eosinophilia and systemic symptoms (DRESS) has been reported with rifabutin.

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

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.

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, including without limitation risks regarding the treatment effectiveness of Talicia and the risk that the Company will not succeed to expand Talicia's reach to additional ex-U.S. territories; as well as other risk 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; (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®, 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; and (xiv) competition from other 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 March 17, 2022. 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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[10] 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.

[11] 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, $p<0.0001$).

[12] Movantik® (naloxegol) is indicated for opioid-induced constipation (OIC). Full prescribing information see: **www.movantik.com**.

[13] Talicia® (omeprazole magnesium, amoxicillin and rifabutin) is indicated for the treatment of H. pylori infection in adults. For full prescribing information see: **www.Talicia.com**.

[14] Aemcolo® (rifamycin) is indicated for the treatment of travelers' diarrhea caused by noninvasive strains of Escherichia coli in adults. For full prescribing information see: **www.aemcolo.com**.

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