NEWS RELEASE

RedHill Publishes New Talicia® Data on Generic Non-Bioequivalence in AP&T and Presents New Dosing Data at Digestive Disease Week

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New Talicia PBPK modeling data, published in AP&T Journal, showed that generically substituted regimens are non-bioequivalent to Talicia

Separately, new Talicia PBPK modeling data, presented at DDW, supports bioequivalence between TID and Q8H dosing regimens for H. pylori eradication therapy; TID dosing is thought to promote patient adherence without impacting efficacy

These new data support Talicia's place as the leading prescribed branded H. pylori therapy by U.S. gastroenterologists [1], and as an empiric first-line therapy for eradication of H. pylori, a bacterial infection that affects approximately 35% of the U.S. adult population [2]

RALEIGH, N.C. and TEL-AVIV, Israel, May 9, 2023 /PRNewswire/ -- **RedHill Biopharma Ltd.** (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, announced two distinct sets of new Talicia[3] data focused on generic non-bioequivalence and on dosing regimens. The first new dataset, published in the **Journal Alimentary Pharmacology and Therapeutics** (AP&T) showed that generically substituted regimens are non-bioequivalent to Talicia. The second set of data, presented at Digestive Disease Week (DDW), supports bioequivalence between Talicia TID (three times daily) and Q8H (every eight hours) dosing regimens for H. pylori

eradication therapy.

In eradicating H. pylori, previous work has shown the importance of antibiotic exposure at the site of the infection[4]. The recently published data in AP&T[5], entitled 'Physiologically based pharmacokinetic (PBPK) modelling to predict intragastric rifabutin concentrations in the treatment of Helicobacter pylori infection', showed that Talicia 50 mg, three times daily, had higher intragastric exposure times than 150 mg once daily or twice daily, or 300 mg once daily generic rifabutin, achieving significantly longer times with intragastric concentration above MIC90 (22.3 ± 1.1 h) than 150 mg once daily (8.3 ± 1.7 h), 150 mg twice daily (16.3 ± 2.3 h), or 300 mg once daily (8.5 ± 1.9 h) - while also providing the lowest mean maximal plasma concentration and mean area under the plasma concentration–time curve of all regimens studied.

Dr. Colin W. Howden, MD, Professor Emeritus, University of Tennessee Health Science Center, said: "This is one of those occasions where it is important to recognize that generic options are not equivalent to the original. In our study we showed that intragastric exposure times with Talicia, when given three times daily, were consistently higher than the generic options, and that Talicia provided the highest potential for H. pylori eradication based on gastric exposure, since the stomach is the site of H. pylori infection. Given the potential for antibiotic resistance and treatment failure, the non-equivalence of generics shown by these data should be kept front of mind when prescribing first-line therapy for H. pylori eradication."

The data presented at DDW confirm, using PBPK modeling, the bioequivalence of Talicia TID and Q8H dosing for the eradication of H. pylori, with a 90% overlap of intragastric AUC312-336h between TID and Q8H for 14 days. Talicia is currently indicated for Q8H administration.

Dr Nimish Vakil, MD, Clinical Adjunct Professor Gastroenterology & Hepatology, University of Wisconsin School of Medicine and Public Health said: "The PBPK modeling data we have presented supports bioequivalence between Talicia TID and Q8H dosing regimens for H. pylori eradication therapy showing that the overall exposures are comparable for all three Talicia-containing drugs, amoxicillin, rifabutin, and omeprazole. Therapy adherence is one of the most important factors for H. pylori eradication, and as treatment complexity is an established contributing factor to adherence, it is to be expected that the more optimal the treatment regimen, the better the adherence will be, and, subsequently, the better the treatment outcome."

About H. pylori infection

H. pylori is a bacterial infection that affects approximately 35%[2] of the U.S. population, with an estimated two-million patients treated annually[6]. 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[7] and a major risk factor for peptic ulcer disease[8] and gastric mucosa-associated lymphoid tissue (MALT) lymphoma[9]. More than 27,000 Americans are diagnosed with gastric cancer annually[10]. 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[2].

About Talicia

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), approved by the U.S. FDA for the treatment of H. pylori infection in adults.

Talicia is the only low-dose rifabutin-based therapy approved for the treatment of H. pylori infection and is designed to address H. pylori's high resistance to 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.

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 the key components 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[11] to their therapy had response rates of 90.3% in the Talicia arm vs. 64.7% in the active comparator arm[12]. 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.

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.

TALICIA: IMPORTANT SAFETY INFORMATION

Tell your healthcare provider about all of the medicines you take, including prescription or non-prescription medications or herbal supplements before starting Talicia. Talicia may affect the way other medicines work, and other medicines may affect the way Talicia works. Do not start any new medications while taking Talicia without first speaking with your healthcare provider.

- You should not take Talicia if you are known to be sensitive to any of the components of Talicia (omeprazole,

amoxicillin, rifabutin), penicillins, proton pump inhibitors or rifamycins.
- You should not take Talicia if you are taking rilpivirine-containing products, delavirdine or voriconazole.

Before you take Talicia, tell your healthcare provider about all of your medical conditions, including if you:

- Are pregnant or plan to become pregnant. Talicia may harm your unborn baby. Tell your healthcare provider if you become pregnant or think you may be pregnant during your treatment with Talicia.
- Have severe kidney disease or liver disease.

When taking Talicia, do not crush or chew capsules. Do not take Talicia with alcohol.

Call your healthcare provider immediately if while taking Talicia you develop:

- New rash or other skin changes, muscle or joint pains, swelling of any area of the body, severe flu-like symptoms, difficulty breathing, fever, blood in your urine, increased or decreased urination, drowsiness, confusion, nausea, vomiting, ongoing stomach pain, bloody diarrhea, or if diarrhea continues after therapy is completed, weight gain or changes in your eyesight.

What are the common side effects of Talicia?

- The most common side effects of Talicia are diarrhea, headache, nausea, stomach pain, rash, indigestion, mouth or throat pain, vomiting, and vaginal yeast infection. Call your healthcare professional for medical advice about side effects.
- Tell your healthcare provider if you experience tiredness, weakness, achiness, headaches, dizziness, depression, increased sensitivity to light, or pain when taking a deep breath.
- Talicia may reduce the effectiveness of oral or other forms of hormonal birth-control. You should use an additional non-hormonal highly effective method of birth control while taking Talicia.
- You may experience a brown-orange discoloration of your urine or tears while taking Talicia.
- The information here is not comprehensive. Talk to your healthcare provider to learn more.

APPROVED USE FOR TALICIA

TALICIA is a prescription medicine for the treatment of a bacteria, Helicobacter pylori (H. pylori), in the stomach of adults.

Click here for the full Prescribing Information for TALICIA.

You are encouraged to report Adverse Reactions to RedHill Biopharma Inc. at 1-833-ADRHILL (1-833-237-4455) or the FDA at 1-800-FDA-1088 or **www.fda.gov/medwatch.**

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, **Talicia®** for the treatment of Helicobacter pylori (H. pylori) infection in adults[1], and **Aemcolo®** for the treatment of travelers' diarrhea in adults[13]. 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 broad-acting, host-directed, SK2 selective inhibitor targeting multiple indications, including for pandemic preparedness, with a Phase 2/3 program for hospitalized COVID-19 and a Phase 2 program in oncology and a radiation protection program ongoing; (iii) **RHB-107** (**upamostat**), an oral broad-acting, host-directed serine protease inhibitor with potential for pandemic preparedness, is in late-stage development for treatment of non-hospitalized symptomatic COVID-19, and is targeting multiple other cancer and inflammatory gastrointestinal diseases; (iv) **RHB-104**, with positive results from a first Phase 3 study for Crohn's disease; and (v) **RHB-102**, with expected UK submission for chemotherapy and radiotherapy induced nausea and vomiting, positive results from a Phase 3 study for acute gastroenteritis and gastritis and positive results from a Phase 2 study for IBS-D. More information about the Company is available at **www.redhillbio.com**/ **twitter.com/RedHillBio**.

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 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® and Aemcolo®; (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 April 28, 2023. 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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Category: Commercial

[1] IQVIA XPO Data on file

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

[3] 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**.

[4] K. Satoh et al. Treatment of Helicobacter pylori infection by topical administration of antimicrobial agents. Scand J Gastroenterol Suppl 1996 Vol. 214 Pages 56; discussion 57-60. Accession Number: 8722409.
https://www.ncbi.nlm.nih.gov/pubmed/8722409

[5] Howden CW et al. Physiologically based pharmacokinetic modelling to predict intragastric rifabutin concentrations in the treatment of Helicobacter pylori infection. Alimentary Pharmacology and Therapeutics, 20 April 2023. **https://doi.org/10.1111/apt.17526**

[6] IQVIA Custom Study for RedHill Biopharma, 2019

[7] 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.

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

[9] 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.

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

[11] 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.

[12] 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).

[13] 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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