



NEWS RELEASE

RedHill Announces New H. pylori and COVID-19 Data Publication and Presentations at Leading Upcoming Scientific Conferences

7/12/2022

Talicia® - World Gastro 2022 congress (August 17-18) : RedHill invited to give prestigious oral presentation of important data detailing high eradication rates across body mass index (BMI) groups with Talicia, the U.S.'s leading brand for Helicobacter pylori (H. pylori) eradication treatment - invitation sent to researchers with significant recently published clinical findings

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Opaganib for COVID-19 – Suggested host-directed mechanism of action described in **Drug Design, Development and Therapy** journal: Multi-faceted potential to: Inhibit spike protein-ACE2 binding, Akt signaling and endocytosis, induce autophagy and apoptosis, and disrupt the viral replication-transcription complex (RTC) through simultaneous inhibition of three sphingolipid-metabolizing enzymes in human cells (SK2, DES1 and GCS) - supports hypothesis of broad antiviral effect and attenuation of multi-organ dysfunction in COVID-19 patients

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Opaganib for COVID-19 - 2nd ARDS Drug Development Summit (July 13-15) : Presenting new COVID-19 biomarker methodology utilizing baseline Fraction of Inspired Oxygen (FiO2) as a new disease severity classification

paradigm - Phase 2/3 data demonstrating a 62% reduction in mortality in opaganib-treated patients requiring FiO2 up to 60% to be presented

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Opaganib and RHB-107 (upamostat) for COVID-19 - International Conference on Emerging Infectious Diseases (ICEID, August 7-10) : Presenting promising efficacy and safety data for RedHill's novel, oral, variant-agnostic investigational COVID-19 therapies, at ICEID, the premier infectious disease conference hosted by the CDC and the Global Task Force for Health

RALEIGH, N.C. and TEL AVIV, Israel, July 12, 2022 /PRNewswire/ -- **RedHill Biopharma Ltd.** (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, announced the upcoming presentation of new Talicia® H. pylori eradication data as well as publication and presentation of data from the opaganib and RHB-107 (upamostat) late clinical-stage COVID-19 programs at important medical congresses in July and August, 2022.

Talicia^[1]: Publication of a study entitled "Helicobacter pylori Eradication by Low-Dose Rifabutin Triple Therapy (Talicia®) is Unaffected by High Body Mass Index" in the journal GastroHep has been selected by reviewers for oral presentation at the World Gastro 2022 congress, August 17-18. Such invitations to present are reserved for researchers with significant clinical findings published over the previous year. This post hoc analysis of 269 patients from the ERADICATE Hp and ERADICATE Hp2 Phase 3 clinical trials, demonstrated that Talicia is highly effective in eradicating H. pylori irrespective of patient BMI, including in obese and severely obese patients, compared to the active comparator (P<0.0001). Patients with a BMI between 30-40 kg/m² and those with BMI >40kg/m² treated with Talicia achieved eradication rates of approximately 90% (88.1% and 90.9% respectively) versus active comparator rates of 62.9% and 31.8% respectively - an approximately 50% lower eradication rate in the severely obese group for the active comparator. Talicia is the leading U.S. branded prescription medicine for H. pylori eradication.

Dr. June Almenoff, MD, Ph.D., RedHill's Chief Medical Officer, said: "Because more than 70% of Americans are either overweight or obese^[2], and because increased BMI has been linked to reduced eradication outcomes of many commonly used H. pylori therapies, this important work supports Talicia as a rational first line option regardless of patient BMI."

RedHill's novel, oral, variant-agnostic late clinical-stage COVID-19 drug candidates, opaganib and RHB-107, have had data selected for publication or presentation as follows:

Opaganib^[3]: Suggested host-directed mechanism of action described in a manuscript entitled "Recent Progress in the Development of Opaganib for the Treatment of COVID-19" accepted for publication in the journal **Drug Design, Development and Therapy**: The paper outlines opaganib's multi-faceted potential to: inhibit spike protein-ACE2 binding, Akt signaling and endocytosis, induce autophagy and apoptosis, and disrupt the viral RTC (replication-transcription complex) through simultaneous inhibition of three sphingolipid-metabolizing enzymes in human cells (SK2, DES1 and GCS). These mechanisms support the hypothesis of broad antiviral effect and attenuation of multi-organ dysfunction in COVID-19 patients. Moreover, because of this tripartite targeting, viral resistance to opaganib is unlikely to be encountered through adaptive mutation during therapy or random mutation to generate additional viral variants.

2nd ARDS Drug Development Summit, Boston, July 13-15: Data to be presented from the opaganib Phase 2/3 study showing the potential for a new methodology for selecting COVID-19 patients for treatment with opaganib, based on a new paradigm for classification of disease severity utilizing baseline Fraction of Inspired Oxygen (FiO₂), in which opaganib demonstrated a 62% reduction in mortality in patients requiring FiO₂ up to 60%.

Opaganib and RHB-107 (upamostat)^[4]: International Conference on Emerging Infectious Diseases (ICEID), Atlanta, August 7-10: Data to be presented at ICEID, the premier infectious disease conference hosted by the CDC and the Global Task Force for Health, will include: Prespecified analyses from opaganib's Phase 2/3 study (NCT04467840), showing improved viral RNA clearance, faster time to recovery and reduced mortality in key subpopulations of opaganib treated moderate to severe hospitalized patients with COVID-19. Data for RHB-107, from Part A of its two-part Phase 2/3 study in a non-hospitalized setting, includes demonstration of a 100% reduction in hospitalization due to COVID-19 and an approximately 88% reduction in reported new severe COVID-19 symptoms after treatment initiation.

Dr. Mark Levitt, RedHill's Chief Scientific Officer said: "Acceptance for publication and presentation of these important data is testament to the quality and strength of RedHill's R&D capability. Oral opaganib and oral RHB-107, both of which have novel host-targeting antiviral mechanisms, have shown effect across multiple variants and virus models, and could serve as important tools in responding to the current and future pandemic waves, whether caused by SARS-CoV-2 variants or by other viruses, and of particular concern, as Fall/Winter approach, is the specter of both COVID-19 and influenza circulating in abundance. We are seeing a shift in focus of government funding sources, public health experts, institutions and industry towards looking for broad host-directed antiviral mechanisms of action that will not be subject to resistance by viral mutation and that could address emerging new variants of SARS-CoV-2 and also combat other viruses that might create future pandemic waves - a more

sustainable long-term approach than having to rediscover and reinvent very specific antiviral therapeutics which quickly become obsolete in the face of rapidly mutating viruses."

About H. pylori infection

H. pylori is a bacterial infection that affects approximately 35%^[5] 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^[11].

About Talicia

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.

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^[12] to their therapy had response rates of 90.3% in the Talicia arm vs. 64.7% in the active comparator arm^[13].

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 Opaganib (ABC294640)

Opaganib, a new chemical entity, is a proprietary, first-in-class, orally-administered, investigational sphingosine kinase-2 (SK2) selective inhibitor, with suggested dual anti-inflammatory and antiviral activity. Opaganib is host-targeted and, based on data accumulated to date, is expected to maintain effect against emerging viral variants,

having already shown in vitro inhibition against variants of concern, including Omicron and Delta. Opaganib has also shown anticancer activity and positive preclinical results in renal fibrosis, and has the potential to target multiple oncology, viral, inflammatory, and gastrointestinal indications.

In prespecified analyses of Phase 2/3 clinical data, oral opaganib has demonstrated improved viral RNA clearance, faster time to recovery and significant mortality reduction in key patient subpopulations versus placebo on top of standard of care. Data from the opaganib global Phase 2/3 study has been submitted for peer review and recently published in **medRxiv**. Opaganib previously delivered promising U.S. Phase 2 data in patients with moderate to severe COVID-19, published in **Open Forum Infectious Diseases**.

Opaganib has also received Orphan Drug designation from the U.S. FDA for the treatment of cholangiocarcinoma and is being evaluated in a Phase 2a study in advanced cholangiocarcinoma and in a Phase 2 study in prostate cancer. Patient accrual, treatment and analysis in the prostate cancer study are ongoing.

Opaganib demonstrated potent antiviral activity against SARS-CoV-2, the virus that causes COVID-19, inhibiting viral replication of the original SARS-CoV-2 and variants tested to date in an in vitro model of human lung bronchial tissue. Additionally, preclinical in vivo studies have demonstrated opaganib's potential to decrease renal fibrosis, have shown decreased fatality rates from influenza virus infection, and amelioration of bacteria-induced pneumonia lung injury with reduced levels of IL-6 and TNF-alpha in bronchoalveolar lavage fluids^[14].

The ongoing clinical studies with opaganib are registered on **www.ClinicalTrials.gov**, a web-based service by the U.S. National Institute of Health, which provides public access to information on publicly and privately supported clinical studies.

About RHB-107 (upamostat)

RHB-107 is a proprietary, first-in-class, once-daily orally-administered investigational antiviral, that targets human serine proteases involved in preparing the spike protein for viral entry into target cells. Because it is host-cell targeted, RHB-107 is expected to also be effective against emerging viral variants with mutations in the spike protein. RHB-107 is being evaluated in a Phase 2/3 study for treatment of patients with symptomatic COVID-19 who do not require inpatient care. In addition, RHB-107 inhibits several proteases targeting cancer and inflammatory gastrointestinal disease. RHB-107 has undergone several Phase 1 studies and two Phase 2 studies, demonstrating its clinical safety profile in approximately 200 patients. RedHill acquired the exclusive worldwide rights to RHB-107, excluding China, Hong Kong, Taiwan and Macao, from Germany's Heidelberg Pharmaceuticals (FSE: HPHA) (formerly WILEX AG) for all indications.

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^[15], **Talicia®** for the treatment of *Helicobacter pylori* (*H. pylori*) infection in adults, and **Aemcolo®** for the treatment of travelers' diarrhea in adults^[16]. 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 3-stage 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 ($\geq 1\%$) 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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Category: R&D

^[1] Talicia® (omeprazole magnesium, amoxicillin and rifabutin) is approved in the U.S. and indicated for the

treatment of H. pylori infection in adults. For full prescribing information see: www.Talicia.com

[2] Adult Obesity Facts. Atlanta, GA: Centers for Disease Control and Prevention (CDC); 2020.

<https://www.cdc.gov/obesity/data/adult.html>.

[3] Opaganib is an investigational new drug, not available for commercial distribution.

[4] RHB-107 is an investigational new drug, not available for commercial distribution.

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

[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] 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.

[12] 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.

[13] 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).

[14] Xia C. et al. Transient inhibition of sphingosine kinases confers protection to influenza A virus infected mice. Antiviral Res. 2018 Oct; 158:171-177. Ebenezer DL et al. Pseudomonas aeruginosa stimulates nuclear sphingosine-1-

phosphate generation and epigenetic regulation of lung inflammatory injury. Thorax. 2019 Jun;74(6):579-591.

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

[16] 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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