



RedHill Biopharma Announces Publication of Talicia® Pivotal Phase 3 Study Results in *Annals of Internal Medicine*

May 5, 2020

Talicia® is approved by the U.S. FDA and promoted by RedHill's U.S. sales force

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Abstract discussing Talicia pharmacokinetics and exposure-response presented as ePoster at Digestive Disease Week® (DDW) 2020

TEL-AVIV, Israel and RALEIGH, N.C., May 05, 2020 (GLOBE NEWSWIRE) -- [RedHill Biopharma Ltd.](#) (Nasdaq: [RDHL](#)) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced the publication of the Company's pivotal Phase 3 study results with Talicia® (RHB-105)¹ for *Helicobacter pylori* (*H. pylori*) infection in the *Annals of Internal Medicine*.

The peer-reviewed [article](#)², entitled "Rifabutin-Based Triple Therapy (RHB-105) for *Helicobacter pylori* Eradication: A Double-Blind, Randomized, Controlled Trial", is available online and the print article is scheduled to be published in the journal's June issue.

Talicia was approved by the FDA in November 2019. It is the only rifabutin-containing therapy approved for the treatment of *H. pylori* infection and is designed to address the high and growing resistance of *H. pylori* to the currently widely used clarithromycin-containing regimens.

"RedHill's FDA-approved drug, Talicia, a rifabutin-containing therapy for treating *H. pylori* infection, is designed to address the public health concern of high and growing bacterial resistance to standard-of-care therapies which result in treatment failures of up to 40%. The rifabutin-containing Talicia is the first FDA-approved therapy in more than two decades and was shown to have improved efficacy in treating *H. pylori* infection, whilst adhering to the ACG guidelines that generally recommend against clarithromycin-based triple therapy," said **David Y. Graham, MD, Professor of Medicine, Molecular Virology and Microbiology at Baylor College of Medicine, Houston and the Lead Investigator of the Talicia Phase 3 studies**. "Talicia is effective despite clarithromycin or metronidazole resistance and future guidelines will likely adopt it as first-line empiric therapy for *H. pylori* infections."

The double-blind, randomized, controlled trial compared Talicia (omeprazole magnesium, amoxicillin, and rifabutin) against an equivalent dose dual therapy of amoxicillin and omeprazole in 455 treatment-naïve subjects with confirmed dyspepsia and *H. pylori* infection. Results demonstrated the added rifabutin benefit with 83.8% eradication of *H. pylori* infection with Talicia vs. 57.7% in the active comparator arm (ITT analysis, $p < 0.0001$), showing a 26.1% benefit with Talicia. The subjects who were confirmed adherent³ to their therapy had response rates of 90.3% in the Talicia arm vs. 64.7% in the active comparator arm ($p < 0.0001$)⁴. No resistance to rifabutin, a key component of Talicia, was detected in the study. Efficacy was not reduced by the presence of clarithromycin or metronidazole resistance, which were noted to be 17.4% and 43.6%, respectively. Furthermore, the safety profiles of both Talicia and the active comparator were similar. These findings support the potential for Talicia as a preferred first-line empirical *H. pylori* therapy, addressing an unmet need in the current environment of increasing antibiotic resistance.

In addition, an ePoster⁵ entitled "Pharmacokinetics and Exposure-Response of RHB-105, A Novel Fixed-Dosed Rifabutin-Based Combination (Rifabutin, Amoxicillin, and Omeprazole) Treatment of *Helicobacter Pylori*" (SU1378), was published online on May 3, 2020 as part of Digestive Disease Week® (DDW) 2020 online education portal, following the cancellation of this year's conference. The ePoster and accompanying presentation describe key findings from the pharmacokinetic analysis of the pivotal Phase 3 study with Talicia. The authors conclude that the curative effect of Talicia is sensitive to the exposure of rifabutin, further supporting the clinical results of the study and superiority over the dual therapy.

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). In November 2019, Talicia was approved by the U.S. FDA as the only rifabutin-based therapy approved for the treatment of *H. pylori* infection and is being promoted by RedHill's sales force in the U.S., calling on gastroenterologists, primary care physicians, and other healthcare providers. Talicia is designed to address the high and growing resistance of *H. pylori* bacteria to clarithromycin-based standard-of-care therapies. The high rates of *H. pylori* resistance to current standard-of-care therapies have led to significantly increasing rates of treatment failure.

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*

Worldwide, more than 50% of the population is affected by *H. pylori* infection, which is classified by the World Health Organization (WHO) as a Group 1 carcinogen and remains the strongest known risk factor for gastric cancer⁶. *H. pylori* bacterial infection affects approximately 35%⁷ of the U.S. population, with an estimated two million patients treated annually⁸ and remains a major risk factor for peptic ulcer disease⁹, gastric mucosa-associated lymphoid tissue (MALT) lymphoma¹⁰, and gastric cancer. More than 27,000 Americans are diagnosed with gastric cancer annually¹¹. Eradication of *H. pylori* is becoming increasingly difficult, with current standard-of-care therapies failing in approximately 25-40% of patients who remain *H. pylori*-positive due to growing resistance of *H. pylori* to antibiotics commonly used in standard combination therapies¹².

About the ERADICATE Hp2 study

The ERADICATE Hp2 is a two-arm, randomized, double-blind, active comparator-controlled confirmatory Phase 3 study that compared Talicia[®] against a dual therapy amoxicillin and omeprazole regimen at equivalent doses. The study investigated 455 dyspepsia patients with confirmed *H. pylori* infection at 55 clinical sites across the U.S. Results demonstrated statistically significant eradication of *H. pylori* infection with Talicia, 83.8% vs. 57.7% in the active comparator arm (ITT analysis, $p < 0.0001$), showing a 26.1% benefit for Talicia. Further analysis of study data noted statistically significant eradication rates in subjects who were confirmed adherent¹³ to their therapy with Talicia, 90.3% vs. 64.7% in the active comparator arm ($p < 0.001$)⁴, showing the specific added benefit of rifabutin substantially increased efficacy when added to the dual regimen of omeprazole and amoxicillin. No resistance to rifabutin, a key component of Talicia, was detected in the pivotal Phase 3 study. Further, the safety of both Talicia and the active comparator had no difference in serious adverse events between both subgroups.

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 adults¹⁴, **Talicia[®]** for the treatment of *Helicobacter pylori* (*H. pylori*) infection in adults and **Aemcolo[®]** for the treatment of travelers' diarrhea in adults¹⁵. RedHill's key clinical late-stage development programs include: (i) **RHB-104**, with positive results from a first Phase 3 study for Crohn's disease; (ii) **RHB-204**, with a planned pivotal Phase 3 study for pulmonary nontuberculous mycobacteria (NTM) infections; (iii) **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; (iv) **Opaganib (Yeliva[®])**, a first-in-class SK2 selective inhibitor, targeting multiple oncology, inflammatory and gastrointestinal indications, with an ongoing Phase 1/2a study for cholangiocarcinoma; (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. More information about the Company is available at www.redhillbio.com.

About Talicia[®] (omeprazole magnesium, amoxicillin and rifabutin)

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 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 CONTRAINDICATIONS

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 ($\geq 1\%$) 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 <http://bit.ly/2CozHNN>.

*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 Talicia[®] will not be adopted as the best-in-class, first-line therapy for *H. pylori* infection or included in future medical guidelines 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.

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¹ For more details, see RedHill's press release dated December 3, 2018. Full prescribing information for Talicia (omeprazole magnesium, amoxicillin, and rifabutin) is available at: www.Talicia.com.

² The article was authored by: Prof. David Y. Graham, MD, Baylor College of Medicine; Yamil Canaan, MD, Jesscan Medical Research; James Maher, MD, BI Research Center; Gregory Wiener, MD, GW Research Inc.; Kristina G. Hulten, PhD, Baylor College of Medicine and Ira N. Kalfus, MD, RedHill's Medical Director for the Talicia development program and an independent consultant to pharmaceutical companies. See full text here: <https://annals.org/aim/article-abstract/2765671/rifabutin-based-triple-therapy-rhb-105-helicobacter-pylori-eradication-double>

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

⁴ The Pivotal Phase 3 study of Talicia demonstrated 84% eradication of *H. pylori* infection with Talicia vs. 58% in the active comparator arm (ITT analysis, p<0.0001).

⁵ The abstract was authored by Elliot Offman, PhD, Certara Integrated Drug Development; Nastya Kassir, PharmD, PhD, FCP, Montreal, QC, Canada; Patricia Anderson, RedHill Biopharma, Tel Aviv, Israel; and Ira N. Kalfus, MD, 3M2G Consulting, New York, NY, United States.

⁶ 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.

⁷ Hooi JKY et al. Global Prevalence of *Helicobacter pylori* Infection: Systematic Review and Meta-Analysis. *Gastroenterology* 2017; 153:420-429.

⁸ IQVIA custom study for RedHill Biopharma, 2019

⁹ NIH – *Helicobacter pylori* and Cancer, September 2013.

¹⁰ 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.

¹¹ National Cancer Institute, Surveillance, Epidemiology, and End Results Program (SEER).

¹² 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.

¹³ Defined as the 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.

¹⁴ Full prescribing information for Movantik® (naloxegol) is available at: www.Movantik.com.

¹⁵ Full prescribing information for Aemcolo® (rifamycin) is available at: www.Aemcolo.com.



Source: RedHill Biopharma Ltd.