



## RedHill Biopharma Announces FDA Approval of Talicia® for Treatment of *H. pylori* in Adults

November 4, 2019

- RedHill plans to launch Talicia®<sup>1</sup> in the U.S. in Q1/2020 for the treatment of *H. pylori* infection in adults, targeting more than two million patients estimated to be treated for *H. pylori* infection annually
- Talicia® is the first and only FDA approved rifabutin-based *H. pylori* therapy and is designed to address the high and growing bacterial resistance and diminished efficacy of clarithromycin-based standard-of-care therapy
- *H. pylori* affects approximately 35% of U.S. adult population; it is classified as a Group I carcinogen and is the strongest risk factor for the development of peptic ulcer disease, gastritis and non-cardia gastric cancer
- Talicia® is eligible for 8 years of U.S. market exclusivity under QIDP designation, in addition to patent protection extending until 2034
- Debt-free balance sheet with approximately \$59 million in cash and short-term investments following a recent strategic investment by Cosmo Pharmaceuticals
- RedHill will host Investor and Analyst day and live webcast on November 22, 2019 to present its planned commercial launch of Talicia® and Aemcolo®

TEL-AVIV, Israel and RALEIGH, N.C., Nov. 04, 2019 (GLOBE NEWSWIRE) -- [RedHill Biopharma Ltd.](#) (Nasdaq: [RDHL](#)) (Tel-Aviv Stock Exchange: [RDHL](#)) ("RedHill" or the "Company"), a specialty biopharmaceutical company primarily focused on the development and commercialization of proprietary drugs for the treatment of gastrointestinal diseases, today announced that the U.S. Food and Drug Administration (FDA) has approved Talicia® (omeprazole magnesium, amoxicillin and rifabutin) delayed-release capsules 10 mg<sup>1</sup>/250 mg/12.5 mg for the treatment of *Helicobacter pylori* (*H. pylori*) infection in adults. RedHill expects to launch Talicia in the U.S. in the first quarter of 2020 with its dedicated sales force.

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 current clarithromycin-based standard-of-care therapies. It is estimated that *H. pylori* resistance to clarithromycin more than doubled between 2009-2013<sup>2</sup>.

**Professor David Y. Graham, MD, MACG, Professor of Medicine, Molecular Virology and Microbiology at Baylor College of Medicine, Houston and Lead Investigator of the Talicia Phase 3 studies, said:** "Talicia offers patients a much-needed new treatment option for *H. pylori* with an excellent safety and efficacy profile that is not compromised by clarithromycin or metronidazole resistance. The clinical studies for Talicia demonstrated high efficacy in eradication of *H. pylori*. Studies with Talicia found zero resistance to rifabutin and showed 17% resistance to clarithromycin, a current standard-of-care macrolide antibiotic, consistent with current data showing that clarithromycin-containing therapies fail in approximately 25-40% of cases."

**Colin W. Howden, MD, AGAF, FACP, Hyman Professor of Medicine & Chief of the Division of Gastroenterology, University of Tennessee Health Science Center, added:** "*H. pylori* is a major cause of peptic ulcer and gastritis. It is also carcinogenic and is the leading cause of gastric cancer. Treatment of *H. pylori* infection has become increasingly difficult due to growing bacterial resistance and the lack of advances in treatment options over the past decade. Talicia offers a new effective treatment option to overcome bacterial resistance and provide optimal efficacy and I believe it could become a recommended first-line standard-of-care treatment for *H. pylori* infection."

"The FDA's approval of Talicia demonstrates our unwavering dedication to patients suffering from gastrointestinal diseases. We thank the patients, researchers and clinical staff who participated in the studies of Talicia and the RedHill team and vendors for this important milestone achieved by their commitment and hard work," **said Dror Ben-Asher, Chief Executive Officer of RedHill Biopharma.** "We are working to expand our sales force to approximately 140 representatives who will promote Talicia, Aemcolo and other gastrointestinal-focused products in our basket."

RedHill will host an Investor and Analyst day on November 22, 2019 in New York to review launch plans for Aemcolo® and Talicia® and provide an overview of the Company's commercial operations. A live webcast of the event, including the slide presentation, will be available on the Company's website: <https://ir.redhillbio.com/events>. Additional information will be made available on the Company's website.

### About Talicia®

Talicia® (omeprazole magnesium, amoxicillin and rifabutin) delayed-release capsules 10 mg<sup>1</sup>/250 mg/12.5 mg 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. 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 designed to address the increasing resistance of *H. pylori* bacteria to the antibiotics commonly used in current standard-of-care therapies and the

imperative need for new treatments.<sup>5</sup> Talicia's approval is based, in part, on the results of two positive Phase 3 studies in the U.S. for the treatment of *H. pylori*-positive adult patients complaining of epigastric pain and/or discomfort. The confirmatory Phase 3 study of Talicia demonstrated 84% eradication of *H. pylori* infection with Talicia vs. 58% in the active comparator arm ( $p < 0.0001$ ). Further, in an analysis of data from this study, it was observed that subjects with measurable blood levels of drug at Day 13 had response rates of 90.3% in the Talicia arm vs. 64.7% in the active comparator arm<sup>3</sup>. No resistance to rifabutin, a key component of Talicia, was detected in the study. Treatment discontinuation due to an adverse reaction occurred in 1% of patients (4/305) receiving Talicia. The adverse reactions leading to the patients' discontinuation of Talicia were nausea and vomiting, nausea, nasal congestion, and nasopharyngitis, respectively. Talicia is eligible for a total of eight years of U.S. market exclusivity under its Qualified Infectious Disease Product (QIDP) designation, in addition to patent protection extending until at least 2034.

#### **About *H. pylori***

*H. pylori* bacterial infection affects over 50% of the population worldwide<sup>4</sup> and approximately 35%, or over 100 million people, in the U.S., with an estimated 2.5 million patients treated annually in the U.S.<sup>5</sup> *H. pylori* is classified as a Group I carcinogen by the International Agency for Research on Cancer. It is the strongest risk factor for the development of gastric cancer<sup>6</sup> and a major risk factor for peptic ulcer disease<sup>7</sup> and gastric mucosa-associated lymphoid tissue (MALT) lymphoma<sup>8</sup>, with infected persons having a 6-fold increased risk of developing non-cardia gastric cancer and MALT lymphoma<sup>9</sup>. Eradication of *H. pylori* is becoming increasingly difficult; current standard-of-care therapies fail in approximately 25-40% of patients who remain *H. pylori* positive due to growing resistance of *H. pylori* to clarithromycin and metronidazole, antibiotics commonly used in standard combination therapies<sup>10</sup>. Clarithromycin-resistant *H. pylori* was formally categorized by the World Health Organization (WHO) as a pathogen for which there is a high priority need to develop new treatments<sup>11</sup>.

#### **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 CONTRAINDICATIONS**

- Known hypersensitivity to omeprazole, amoxicillin or any other beta-lactam antibacterial drugs, rifabutin or any other rifamycin, or any component of TALICIA.
- Rilpivirine-containing products.
- Delavirdine.
- Voriconazole.

#### **WARNINGS AND PRECAUTIONS**

- Hypersensitivity Reactions: Serious and occasionally fatal reactions (e.g., anaphylaxis) have been reported with components of TALICIA. If hypersensitivity reactions occur, discontinue TALICIA and institute immediate therapy (e.g., anaphylaxis management).
- *Clostridioides difficile*-Associated Diarrhea (CDAD): Evaluate if diarrhea occurs.
- Reduction in the Efficacy of Hormonal Contraceptives: Additional non-hormonal highly effective methods of contraception should be used while taking TALICIA.
- Acute Interstitial Nephritis (AIN): Observed in patients taking Proton Pump Inhibitors (PPIs) and penicillins. Discontinue TALICIA if AIN develops.
- Cutaneous and Systemic Lupus Erythematosus: Mostly cutaneous; new onset or exacerbation of existing disease; discontinue TALICIA and evaluate.

#### **ADVERSE REACTIONS**

Most common adverse reactions ( $\geq 1\%$ ) were diarrhea, headache, nausea, abdominal pain, chromaturia, rash, dyspepsia, oropharyngeal pain, vomiting, and vulvovaginal candidiasis.

#### **DRUG INTERACTIONS**

Components of TALICIA have the potential for clinically important drug interactions. See full prescribing information for important drug interactions with TALICIA.

#### **USE IN SPECIFIC POPULATIONS**

- TALICIA may cause fetal harm.
- Renal Impairment: Avoid use in severe renal impairment.
- Hepatic Impairment: Avoid use.

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](http://www.fda.gov/medwatch).

Please also see [full Prescribing Information](#).

#### **About RedHill Biopharma Ltd.**

RedHill Biopharma Ltd. (Nasdaq: [RDHL](#)) (Tel-Aviv Stock Exchange: [RDHL](#)) is a specialty biopharmaceutical company, primarily focused on the development and commercialization of proprietary drugs for the treatment of gastrointestinal diseases. RedHill commercializes and promotes several

gastrointestinal products in the U.S., **Donnatal**<sup>®</sup>, **EnteraGam**<sup>®</sup> and **Mytesi**<sup>®</sup>, and is planning to launch **Aemcolo**<sup>®</sup> and **Talicia**<sup>®</sup> in the U.S.<sup>12</sup> In November 2019, the FDA approved Talicia<sup>®</sup> for marketing in the U.S. for the treatment and of *Helicobacter pylori* (*H. pylori*) infection in adults. 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)**<sup>®</sup>, 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) **ABC294640 (Yeliva)**<sup>®</sup>, a first-in-class SK2 selective inhibitor, targeting multiple oncology, inflammatory and gastrointestinal indications, with an ongoing Phase 2a study for cholangiocarcinoma; (v) **RHB-106**, an encapsulated bowel preparation licensed to Salix Pharmaceuticals, Ltd. 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](http://www.redhillbio.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 include, without limitation, risks related to the timing of our launch of Talicia<sup>®</sup> and Aemcolo<sup>®</sup>, as well as risks and uncertainties associated with (i) the initiation, timing, progress and results of the Company's research, manufacturing, preclinical studies, clinical trials, and other therapeutic candidate development efforts, and the timing of the commercial launch of its therapeutic candidates; (ii) the Company's ability to advance its therapeutic candidates into clinical trials or to successfully complete its preclinical studies or clinical trials or the development of a commercial companion diagnostic for the detection of MAP; (iii) the extent and number 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<sup>®</sup>; (v) the Company's ability to successfully commercialize and promote Talicia<sup>®</sup>, Aemcolo<sup>®</sup>, Donnatal<sup>®</sup>, EnteraGam<sup>®</sup> and Mytesi<sup>®</sup>; (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, preclinical 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 February 26, 2019, as amended on May 15, 2019. 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.*

**Company contact:**

Adi Frish  
Senior VP of Business Development & Licensing  
RedHill Biopharma  
+972-54-6543-112  
[adi@redhillbio.com](mailto:adi@redhillbio.com)

**IR contact (U.S.):**

Timothy McCarthy, CFA, MBA  
Managing Director, Relationship Manager  
LifeSci Advisors, LLC  
+1-212-915-2564  
[tim@lifesciadvisors.com](mailto:tim@lifesciadvisors.com)

<sup>1</sup> Each delayed-release capsule contains omeprazole 10 mg (equivalent to 10.3 mg omeprazole magnesium), amoxicillin 250 mg, and rifabutin 12.5 mg.

<sup>2</sup> Shiota S, Reddy R, Alsarraj A, et al. Antibiotic resistance of *Helicobacter pylori* among male United States veterans. *Clin Gastroenterol Hepatol*. 2015;13:1616-1624.

<sup>3</sup> This PK population 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.

<sup>4</sup> 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.

<sup>5</sup> Foster Rosenblatt market analysis, October 2018.

<sup>6</sup> 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.

<sup>7</sup> NIH – *Helicobacter pylori* and Cancer, September 2013.

<sup>8</sup> 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.

<sup>9</sup> NIH – *Helicobacter pylori* and Cancer, September 2013.

<sup>10</sup> Fallone CA et al. The Toronto Consensus for the Treatment of *Helicobacter pylori* Infection in Adults. *Gastroenterology* 2016;151:51–69; Malfertheiner P. et al. Management of *Helicobacter pylori* infection - the Maastricht IV/ Florence Consensus Report, *Gut* 2012;61:646-664; Graham DY et al. New concepts of resistance in the treatment of *Helicobacter pylori* infections. *Nat Clin Pract Gastroenterol Hepatol*. 2008 Jun;5(6):321-31 and Graham DY et al. *Helicobacter pylori* treatment in the era of increasing antibiotic resistance. *Gut* 2010;59:1143-1153.

<sup>11</sup> World Health Organization, Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics, February 2017.

<sup>12</sup> For full prescribing information see: Aemcolo<sup>®</sup>: [www.Aemcolo.com](http://www.Aemcolo.com); Mytesi<sup>®</sup>: [www.Mytesi.com](http://www.Mytesi.com); EnteraGam<sup>®</sup> <https://bit.ly/2N3q7DW>; Talicia<sup>®</sup>:

[w.accessdata.fda.gov](http://w.accessdata.fda.gov)



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