RedHill Biopharma Presents a New Travelers' Diarrhea Clinical Severity Classification Tool and its Use in Aemcolo Efficacy Analysis at DDW 2021

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- **New Travelers' Diarrhea (TD) severity classification tool, developed with the University of Texas Houston School of Public Health, provides clear separation of clinical severity categories and prognostic information for TD resolution with potential utility in clinical practice**
- **The data presented include a new efficacy assessment of Aemcolo® (rifamycin) for the treatment of TD, demonstrating high levels of efficacy across both moderate and severe patient groups**
- **Aemcolo (rifamycin) is a non-systemic antibiotic whose delivery is targeted to the site of non-invasive Escherichia Coli (E. coli) infection in the distal small bowel and colon, approved by the FDA for the treatment of TD**

TEL AVIV, Israel and RALEIGH, N.C., May 21, 2021 /PRNewswire/ -- RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced presentation (poster number: Fr244) at Digestive Disease Week 2021 of a new Travelers' Diarrhea (TD) severity classification tool providing clear separation of clinical severity categories and prognostic information for TD resolution, with potential utility in clinical practice. The new tool was developed with the Center for Infectious Diseases, University of Texas Houston School of Public Health.

The new classification tool was used to assess the efficacy of Aemcolo® (rifamycin) for the treatment of TD caused by non-invasive strains of *E. coli* in adults[1], reconfirming high levels of efficacy across both moderate and severe patient groups.

"Antibiotics are the mainstay of treating bacterial TD; due to growing resistance, they should be reserved for use in more severe cases of the disease," **said Professor Herbert L. DuPont, Director of the Center for Infectious Diseases, University of Texas Houston School of Public Health**. "In order to help direct treatment to the most appropriate patients, we developed a new severity classification tool able to support accurate prognosis of disease course and resolution, based on extensive patient data from two Phase 3 trials in Travelers' Diarrhea, providing significant potential clinical utility. We then used the new classifications to assess the efficacy of rifamycin, reconfirming highly statistically significant efficacy across both newly reclassified moderate and severe patient groups."

"Outcomes-focused clinical tools to assess the prognosis in TD have been lacking, and the development of this new Travelers' Diarrhea severity classification tool provides prognostic information that may help guide clinical practice," **said June Almenoff, M.D., Ph.D., FACP, RedHill's Chief Medical Officer**. "As the world returns to normal post-COVID pandemic, many Americans will likely want to resume travelling to countries where they are at high risk of infection with TD and will want to avoid the risk of ruining their trip by planning ahead for potential cases of TD."

Aemcolo, containing 194 mg of rifamycin as delayed-release tablets, is an orally-administered, non-systemic antibiotic employing MMX® technology, a proprietary drug delivery system that distributes rifamycin in a controlled manner to the lower intestine. Due to its non-systemic delivery, Aemcolo is associated with limited side effects and minimal potential for interactions with other medications.

Aemcolo is listed as an acute diarrhea antibiotic treatment recommendation in the Centers for Disease Control and Prevention (CDC) Yellow Book[2]. The recommended dosage of Aemcolo is 388 mg (two tablets) orally, twice daily for three days.

About Traveler's Diarrhea
Travelers' Diarrhea (TD) is the most common travel-related illness, affecting an estimated 10% to 40% of travelers annually[iii]. Each year, approximately 70 million Americans travel abroad[iv]. Attack rates of TD range up to 70% of travelers, depending on the destination and season of travel[v]. TD may often result in short-term morbidity adversely impacting travel plans. Untreated diarrhea can also lead to an underappreciated risk of

chronic complications, including functional bowel disorders[vi].

About Aemcolo® (rifamycin)

Aemcolo® (rifamycin) is an orally-administered, delayed-release, non-systemic antibiotic approved for the treatment of travelers' diarrhea caused by non-invasive strains of *Escherichia coli* (*E. coli*) in adults. Aemcolo® is the first antibiotic engineered with Cosmo Pharmaceuticals' Multi Matrix Technology (MMX®). MMX technology is designed to deliver the active pharmaceutical ingredients in a delayed and controlled manner directly to the lower intestine.

INDICATION AND IMPORTANT SAFETY INFORMATION

Aemcolo® is indicated for the treatment of travelers' diarrhea caused by noninvasive strains of *Escherichia coli* (*E. coli*) in adults.

Limitations of Use

Aemcolo® is not indicated in patients with diarrhea complicated by fever or bloody stool or due to pathogens other than noninvasive strains of *E. coli*.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Aemcolo® and other antibacterial drugs, Aemcolo® should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

CONTRAINDICATION

Aemcolo® is contraindicated in patients with a known hypersensitivity to rifamycin, any of the other rifamycin class antimicrobial agents, or any of the components in Aemcolo®.

WARNINGS AND PRECAUTIONS

Risk of Persistent or Worsening Diarrhea Complicated by Fever and/or Bloody Stool

Aemcolo® was not shown to be effective in patients with diarrhea complicated by fever and/or bloody stool or diarrhea caused by pathogens other than *E. coli* and is not recommended for use in such patients.

Discontinue Aemcolo® if diarrhea gets worse or persists more than 48 hours and consider alternative antibacterial therapy.

***Clostridium difficile*-Associated Diarrhea (CDAD)**

CDAD has been reported with use of nearly all antibacterial agents and may range in severity from mild diarrhea to fatal colitis.

Consider CDAD in all patients who present with diarrhea following antibacterial drug use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

Development of Drug-Resistant Bacteria

Prescribing Aemcolo® in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

ADVERSE REACTIONS

Discontinuation of Aemcolo® due to adverse reactions occurred in 1% of patients. The most frequent adverse reactions were abdominal pain (0.5%) and pyrexia (0.3%).

Adverse reactions that occurred in at least 2% of Aemcolo®-treated patients and with a higher incidence than in the placebo or ciprofloxacin groups were constipation 3.5% and headache 3.3%, respectively.

USE IN SPECIFIC POPULATIONS

Pregnancy

There are no available data on AEMCOLO use in pregnant women to inform any drug-associated risks for major birth defects, miscarriage, or adverse maternal or fetal outcomes.

Lactation

There is no information regarding the presence of AEMCOLO in human milk, the effects on the breastfed infant, or the effects on milk production.

Pediatric Use

The safety and effectiveness of AEMCOLO has not been established in pediatric patients <18 years of age.

Click here for full Aemcolo® prescribing information

To submit adverse event reports or product complaint reports, contact RedHill Biopharma, Inc. at 1(833)-ADR-HILL. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088 (1-800-332-1088).

Aemcolo is a registered trademark of Cosmo Technologies Ltd. Aemcolo is manufactured by Cosmo S.p.A. for RedHill Biopharma Inc.

About RedHill Biopharma Ltd.

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[vii], **Talicia®** for the treatment of *Helicobacter pylori (H. pylori)* infection in adults[viii], and **Aemcolo®** for the treatment of travelers' diarrhea in adults[ix]. 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 (Yeliva®, ABC294640)**, a first-in-class SK2 selective inhibitor targeting multiple indications with positive Phase 2 COVID-19 data and an ongoing Phase 2/3 program for COVID-19 and Phase 2 studies for prostate cancer and cholangiocarcinoma ongoing; (iii) **RHB-107 (upamostat)**, a serine protease inhibitor in a U.S. Phase 2/3 study as treatment for 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 (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; and (vi) **RHB-106**, an encapsulated bowel preparation. More information about the Company is available at www.redhillbio.com / https://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 include, without limitation; the risk that the Company will not successfully commercialize its products; 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 18, 2021. 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] See full prescribing information: www.aemcolo.com

[2] https://wwwnc.cdc.gov/travel/yellowbook/2020/preparing-international-travelers/travelers-diarrhea

[iii] FDA. https://www.fda.gov/news-events/press-announcements/fda-approves-new-drug-treat-travelers-diarrhea

[iv] Cosmo Pharmaceuticals Investor Presentation July 2019

[v] CDC Yellow Book

[vi] Steffen R, et al. *JAMA*. 2015;313(1):71-80.

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

[viii] Full prescribing information for Talicia® (omeprazole magnesium, amoxicillin and rifabutin) is available at: www.Talicia.com.

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

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