NEWS RELEASE

RedHill Biopharma Announces EU Orphan Drug Designation for RHB-204 for NTM Infections

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Developed as the first stand-alone standard of care first-line therapy for NTM disease caused by Mycobacterium avium complex (MAC) infection, RHB-204 is currently undergoing a Phase 3 study in the U.S.

EMA Orphan Drug Designation provides eligibility for 10 years post-approval EU market exclusivity. U.S. FDA Fast Track, Orphan and QIDP priority designations, previously granted to RHB-204, extend U.S. post-approval market exclusivity to a total of 12 years

The Company is advancing discussions with prospective partners for RHB-204 across multiple territories

TEL AVIV, Israel and RALEIGH, N.C., Aug. 17, 2022 /PRNewswire/ -- **RedHill Biopharma Ltd.** (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced that the European Commission has granted Orphan Drug Designation to RHB-204[1] for the treatment of nontuberculous mycobacteria (NTM) disease, following a positive opinion recommendation by the European Medicines Agency's (EMA) Committee for Orphan Medicinal Products (COMP).

The EMA grants Orphan status to treatments of a life-threatening or chronically debilitating condition that is rare (affecting not more than five in 10,000 people in the European Union)[2]. Orphan Designation provides for free protocol assistance (scientific advice from the EMA), potential reductions in fees, and eligibility for 10 years post-launch market exclusivity.

"NTM infections are increasing across the world and they are notoriously difficult to treat. There are no approved first-line stand-alone therapies in the U.S, EU, and Japan, highlighting the significant need for new options to treat this challenging and debilitating infectious disease," **said Patricia Anderson, RedHill's SVP Regulatory Affairs**. "The granting of EU Orphan Designation is important and brings significant developmental benefits, in addition to the provision for a potential 10 years of EU post-approval market exclusivity, which adds to the strong exclusivity secured in the U.S."

A U.S. Phase 3 study is ongoing to evaluate the efficacy and safety of RHB-204 in adults with pulmonary NTM disease caused by Mycobacterium avium complex (MAC) infection (NCT04616924). The study protocol provides for 6 months co-primary endpoint of sputum culture conversion (SCC) and clinical outcome (patient-reported outcomes - PRO) in a randomized placebo-controlled design, followed by open label active treatment with RHB-204 for 12 months from conversion.

The Company is advancing discussions with prospective partners for RHB-204 across multiple territories.

About Pulmonary Nontuberculous Mycobacteria (NTM) Infections

Pulmonary nontuberculous mycobacteria (NTM) disease is a chronic and debilitating lung disease caused by ubiquitous environmental bacteria, found in soil as well as natural and engineered water systems. The most common NTM symptoms include persistent cough, fever, weight loss, chest pain, and blood in sputum[3]. NTM infections can lead to recurring cases of bronchitis and pneumonia and can, in some cases, lead to respiratory failure[4]. Although rare, the incidence and prevalence of pulmonary NTM disease are increasing in many areas of the world[5]. There were an estimated 110,000 pulmonary NTM disease patients in the U.S. in 2017[6] and an estimated 28,000 in the EU. Pulmonary manifestations account for 80-90% of all NTM-associated diseases[7], and approximately 80% of pulmonary NTM infections are caused by Mycobacterium avium complex (MAC)[8].

Treatment of NTM infection can be difficult with guidelines recommending that MAC infection be treated with a multi-drug regimen for treatment, with at least three antimicrobials, for at least 12 months[9]. There is no FDA- or EMA-approved first-line standard-of-care combination therapy. Many patients fail current therapy, and more than half will have either recurring disease or a new infection after completing treatment[10]. Thus, new treatment options for NTM are needed.

About RHB-204

RHB-204 is a proprietary, fixed-dose oral capsule containing a combination of clarithromycin, rifabutin and clofazimine, developed for the treatment of pulmonary NTM infections caused by Mycobacterium avium Complex (MAC). RHB-204 was granted FDA Fast Track and Orphan Drug Designation, in addition to QIDP Designation under the Generating Antibiotic Incentives Now Act (GAIN Act), extending U.S. post-approval U.S. market exclusivity to a

potential total of 12 years. RHB-204 has additionally been granted EU Orphan Designation, providing eligibility for 10 years EU post-approval market exclusivity. RHB-204 is also covered by U.S. patents which extend patent protection until 2029 and a pending U.S. patent application which, if allowed, could extend RHB-204 patent protection until 2041.

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[11], **Talicia®**for the treatment of Helicobacter pylori (H. pylori) infection in adults, and **Aemcolo®** for the treatment of travelers' diarrhea in adults[12]. 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; and (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. 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 include, without limitation, the risk that the Company will not initiate the Phase 3 clinical study in all or part of the sites in the U.S. or will be delayed; the risk that the U.S. Phase 3 clinical study evaluating RHB-204 will not be successful or, if successful, will not suffice for regulatory marketing approval without the need for additional clinical and/or other studies; 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®, Movantik® 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 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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[1] RHB-204 is an investigational new drug, not available for commercial distribution.

[2] https://www.ema.europa.eu/en/human-regulatory/overview/orphan-designation-overview

[3] Kim RD, et al. Pulmonary Nontuberculous Mycobacterial Disease. Prospective Study of a Distinct Preexisting Syndrome Am J Respir Crit Care Med. 2008; 178(10):1066–74.

[4] The American Lung Association, 2020.

[5] Winthrop KL, et al. Incidence and Prevalence of Nontuberculous Mycobacterial Lung Disease in a Large U.S. Managed Care Health Plan, 2008-2015. Ann Am Thorac Soc. 2020 Feb;17(2):178-185.

[6] Foster|Rosenblatt, 2017

[7] Griffith DE, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases Am J Respir Crit Care Med. 2007;175(4):367-416.

[8] Prevots DR et al. Nontuberculous mycobacterial lung disease prevalence at four integrated health care delivery systems. Am J Respir Crit Care Med 2010; 182:970-76; Winthrop KL, et al. Pulmonary nontuberculous mycobacterial disease prevalence and clinical features: an emerging public health disease. Am J Respir Crit Care Med 2010; 182: 977-82

[9] Daley CL, et al. Treatment of Nontuberculous Mycobacterial Pulmonary Disease: An Official ATS/ERS/ESCMID/IDSA Clinical Practice Guideline: Executive Summary. Clinical Infectious Diseases. Ciaa241, **https://doi.org/10.1093/cid/ciaa241**.

[10] Henkle E, et al. Patient-Centered Research Priorities for Pulmonary Nontuberculous Mycobacteria (NTM) Infection. An NTM Research Consortium Workshop Report Annals of the American Thoracic Society 2016; S379-84.

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

[12] 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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