NEWS RELEASE

RedHill's RHB-204 Demonstrates Comparable MAP Killing Efficacy to RHB-104 - Important Step in RHB-204 Development for MAP-related Crohn's Disease

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RHB-204[1] is a next-generation optimized formulation of RedHill's oral RHB-104[2], designed for enhanced tolerability, safety profile and patient adherence, that employs a groundbreaking Mycobacterium avium subspecies paratuberculosis (MAP)-targeted therapeutic approach for Crohn's disease (CD)

In its positive Phase 3 study, RHB-104 met the primary and key secondary endpoints with statistical significance, showing RHB-104 plus standard of care (SoC) to be 64% more effective than SoC alone, in treating CD compared to the placebo (standard of care only) group ($p = 0.0048$)[3]

New RHB-204 in vitro data, from both spot and phage assays, demonstrated comparable MAP killing to RHB-104[4]. Importantly, MAP killing efficacy was achieved with lower doses of two of the active ingredients compared to RHB-104, indicative of potential for reduced toxicity and side effects

Based on the FDA guidance on path to approval, RedHill's novel Phase 2 RHB-204 study is designed to be the first-ever adequately controlled clinical study in a specifically defined MAP-positive CD patient population - a potentially paradigm changing approach to treatment of Crohn's disease. With discussions ongoing and grant application submitted, funding for this program is planned to be non-dilutive

Expected transferal of RHB-104's FDA pediatric orphan drug designation to RHB-204, potential for breakthrough therapy designation, fast track designation, additional regulatory exclusivity and priority review voucher. RHB-204 is patent protected through 2041, granted FDA Fast Track and Orphan Drug Designation, QIDP Designation under the GAIN Act (extending US market exclusivity to a potential total of 12 years) and EU Orphan Designation (eligibility for 10 years EU market exclusivity) for NTM disease caused by MAC[5]

The multibillion-dollar CD market is expected to grow from $13.6 billion in 2024 to over $19 billion in 2033 in key markets,[6] presenting a significant opportunity for new FDA-approved therapies

RALEIGH, N.C. and TEL AVIV, Israel, April 30, 2026 /PRNewswire/ -- **RedHill Biopharma Ltd.** (NASDAQ: **RDHL**) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced new in vitro testing results demonstrating RHB-204's comparability to RHB-104 in Mycobacterium avium subspecies paratuberculosis (MAP) killing efficacy. Oral RHB-204 is a next-generation optimized formulation of RedHill's RHB-104, designed for enhanced tolerability, safety profile and patient adherence, that employs a groundbreaking MAP-targeted therapeutic approach to the treatment of Crohn's disease (CD).

The comparability results were achieved in both spot and phage assays of several different MAP strains. Importantly, the MAP killing efficacy was achieved with lower doses of two of the active ingredients compared to RHB-104, indicative of the potential for reduced toxicity and side effects.

"As published in the peer-reviewed journal, **Antibiotics**[3], RedHill's RHB-104 had previously delivered positive Phase 3 results showing a statistically significant 64% improvement in efficacy in treating CD using this potentially transformative MAP-targeted approach, achieving the primary endpoint of induction of clinical remission at week 26 ($p = 0.0048$). The demonstration of RHB-204's comparability to RHB-104 is an important step forward in the ongoing development of RHB-204 for MAP-related CD, following the pathway to approval guided by the FDA at our positive meeting," **said Reza Fathi, PhD, Senior VP, R&D at RedHill**. "Up to 40% of CD patients fail to respond to anti-TNF treatment, and over time a similar number of responders lose response and have disease flare-ups[7]. Many existing treatment options are both expensive and intravenously administered, further increasing the cost burden. Moreover, several of these existing therapies have known safety issues, including Black Box Warnings. A safe and effective orally administered therapy would provide a welcome alternative approach."

A planned Phase 2 study of RHB-204 in CD is expected to be the first clinical study in a specifically defined MAP-positive CD patient population. There is a significant body of peer reviewed published research supporting the scientific rationale that MAP may be a root cause of CD[8], however, a major hurdle in previous clinical studies for new therapies directed at MAP has been the ability to rapidly and accurately detect MAP – one of the slowest growing and hard to detect bacteria on the planet. This study, along with RedHill's collaborations with two leading European academic centers for the provision of cutting-edge MAP detection diagnostics, which support the study's

novel design and the potential future commercial application of RHB-204, represents a groundbreaking approach that could potentially make RHB-204, if approved, an exciting new therapy treating both the suspected cause of the disease and its symptoms.

RedHill is actively pursuing partnerships and collaborations for this program, including via an innovation development grant application, which has already been submitted. In addition, RedHill is engaging in ongoing discussions with non-dilutive external funding sources.

The development of RHB-204 is supported by a strong foundation of published clinical efficacy and safety data from the randomized, double-blind, placebo-controlled 331-patient Phase 3 study of RHB-104 in active CD, which successfully met its primary and secondary endpoints, showing RHB-104 plus standard of care (SoC) to be 64% more effective than SoC alone, achieving clinical CD remission at week 26 (the primary endpoint) in 36.7% of the RHB-104-treated group compared to 22.4% in the placebo (standard of care only) group[3]. The Phase 3 study also demonstrated the safety and efficacy of concomitant use of RHB-104 with anti-TNFs, immunomodulators and steroids, suggesting that RHB-204 could be a transformative safe and effective, stand-alone or combination, oral therapy[3].

The CD market is expected to expand significantly through 2033, with sales in the United States, Japan, and five major European markets, growing from $13.6 billion to $19.1 billion at a compound annual growth rate (CAGR) of 3.87%[5].

About RHB-204

RHB-204 is a proprietary, fixed-dose oral capsule containing a combination of clarithromycin, rifabutin and clofazimine, at specific doses designed to safely and effectively treat Mycobacterium avium subspecies paratuberculosis-positive (MAP-positive)-related Crohn's disease.

Patent protected until at least 2041, and with an expected pediatric orphan designation (subject to the U.S. Food and Drug Administration (FDA) approval to transfer from RHB-104), RHB-204 is a next-generation formulation of RHB-104 with an optimized formulation for the treatment of CD. It contains the same three antimicrobial agents with potent intracellular, anti-mycobacterial and anti-inflammatory properties, and with an optimized dosing profile, RHB-204 provides the potential for enhanced tolerability, safety and compliance with a 40% pill burden reduction. RHB-204 is supported by a strong foundation of clinical data from the positive safety and efficacy results achieved in the Phase 3 study of RHB-104 in CD, with its potential further demonstrated using mucosal healing imaging, considered to be the gold standard for efficacy evaluation in CD.

Originally developed for the treatment of pulmonary non-tuberculous mycobacteria (NTM) disease 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. Where applicable, the Company intends to explore the potential for additional regulatory process designations, such as breakthrough therapy designation and fast track designations that may provide additional exclusivity or potential for priority review vouchers.

About Crohn's Disease

Crohn's disease (CD) is a form of Inflammatory Bowel Disease (IBD) causing inflammation of digestive tract tissue that can lead to abdominal pain, severe diarrhea, fatigue, weight loss and malnutrition. CD can be highly debilitating and remains a serious burden for both patients and healthcare systems: destroying quality of life and even leading to life-threatening complications. There is no known cure for Crohn's disease. It is estimated that 1 million Americans[9] and approximately 6-8 million people globally have Crohn's disease[10].

Commonly used FDA-approved therapies in the treatment of CD include: Abbvie's Humira® (adalimumab), Janssen's Remicade® (infliximab) and Stelara® (Ustekinumab), BMS's Zeposia® (ozanimod) and Pfizer's Xeljanz® (tofacitinib).

About RedHill Biopharma

RedHill Biopharma Ltd. (NASDAQ: RDHL) is a specialty biopharmaceutical company primarily focused on U.S. development and commercialization of drugs for gastrointestinal diseases, infectious diseases and oncology. RedHill promotes the FDA-approved gastrointestinal drug **Talicia,** for the treatment of Helicobacter pylori (H. pylori) infection in adults[11], with a U.S. co-commercialization agreement with Cumberland Pharmaceuticals (NASDAQ: CPIX). RedHill's key clinical late-stage development programs include: (i) **opaganib (ABC294640)**, a first-in-class, orally administered sphingosine kinase-2 (SPHK2) selective inhibitor with anti-inflammatory, antiviral, metabolic and anticancer activity, targeting multiple indications with U.S. government and academic collaborations for development for medical countermeasures including radiation and chemical exposure indications such as GI-Acute Radiation Syndrome (GI-ARS), a Phase 2/3 program for hospitalized COVID-19, and an ongoing Phase 2 study in prostate cancer in combination with darolutamide; (ii) **RHB-102 (Bekinda)**, with a planned Phase 2 proof-of-concept study for GLP-1/GIP receptor agonist-associated GI intolerance, positive results from a U.S. Phase 3 study for acute gastroenteritis and gastritis, positive results from a U.S. Phase 2 study for IBS-D and potential UK submission for chemotherapy and radiotherapy induced nausea and vomiting. RHB-102 is partnered with Hyloris Pharmaceuticals (EBR: HYL) for worldwide development and commercialization outside North America; (iii) **RHB-204**, a next-generation optimized formulation of RHB-104, with a planned Phase 2 study for Crohn's disease (based

on RHB-104's positive Phase 3 Crohn's disease study results); and (iv) **RHB-107** (**upamostat**), an oral broad-acting, host-directed, serine protease inhibitor with potential for pandemic preparedness, including COVID-19 and also targeting multiple cancer and inflammatory gastrointestinal diseases.

Visit **www.redhillbio.com** / **X.com/RedHillBio** for more information about the Company

Forward Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 and may discuss investment opportunities, stock analysis, financial performance, investor relations, and market trends. Such statements may be preceded by the words "intends," "may," "will," "plans," "expects," "anticipates," "projects," "predicts," "estimates," "aims," "believes," "hopes," "potential" or similar words, and include, among others, statements regarding the potential transferal of pediatric orphan drug designation to RHB-204, the potential for breakthrough therapy designations, fast track designations, additional regulatory exclusivity and priority review vouchers, the potential for partnerships and funding sources for the development of RHB-204, and the potential success of any transactions, commercial programs or development activities. 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 development of RHB-204 for Crohn's disease may not be completed, or if completed may not be approved or may not achieve commercial success; the risk that opaganib is not effective against the indications for which we develop our products; the risk that RHB-102 (Bekinda) does not effectively reduce GLP-1/GIP-related nausea, vomiting and diarrhea; the risk regarding the Company's ability to regain and maintain compliance with Nasdaq's listing requirements, including the minimum bid price requirement; the risk that the addition of new revenue generating products or out-licensing transactions will not occur; the risk that the Company will not receive future milestone payments under its existing agreements or that they will be less than anticipated; the risk of current uncertainty regarding U.S. government research and development funding and that the U.S. government is under no obligation to continue to support development of our products and can cease such support at any time; the risk that acceptance onto the RNCP Product Development Pipeline or other governmental and non-governmental development programs will not guarantee ongoing development or that any such development will not be completed or successful; the risk that the FDA does not agree with the Company's proposed development plans for its programs; the risk that the Company's development programs and studies may not be successful and, even if successful, such studies and results may not be sufficient for regulatory applications, including emergency use or marketing applications, and that additional studies may be required; 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 any necessary commercial companion diagnostics; (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; (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) the Company's ability to collect on its judgement against Kukbo; (xiii) estimates of the Company's expenses, future revenues, capital requirements and needs for additional financing; (xiv) the effect of patients suffering adverse experiences using investigative drugs under the Company's Expanded Access Program; (xv) competition from other companies and technologies within the Company's industry; and (xvi) 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 April 27, 2026. 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] RHB-204 is an investigational new drug, not available for commercial distribution in the United States.
[2] RHB-104 is an investigational new drug, not available for commercial distribution in the United States.
[3] Graham DY, et al. Randomized, Double-Blind, Placebo-Controlled Study of Anti-Mycobacterial Therapy (RHB-104) in Active Crohn's Disease. Antibiotics (Basel). 2024 Jul 25;13(8):694. doi: 10.3390/antibiotics13080694. PMID: 39199994; PMCID: PMC11350828.
[4] Data on file
[5] Non-tuberculous mycobacteria (NTM) lung disease caused by Mycobacterium avium complex (MAC)
[6] DataMonitor - Disease Analysis: Crohn's Disease, September 2024
[7] Singh S, George J, Boland BS, Vande Casteele N, Sandborn WJ. Primary Non-Response to Tumor Necrosis Factor Antagonists is Associated with Inferior Response to Second-line Biologics in Patients with Inflammatory Bowel Diseases: A Systematic Review and Meta-analysis. J Crohns Colitis. 2018 May 25;12(6):635-643. doi: 10.1093/ecco-jcc/jjy004. PMID: 29370397; PMCID: PMC7189966.
[8] Bull T.J., McMinn E.J., Sidi-Boumedine K., Skull A., Durkin D., Neild P., Rhodes G., Pickup R., Hermon-Taylor J. Detection and verification of Mycobacterium avium subsp. paratuberculosis in fresh ileocolonic mucosal biopsy specimens from individuals with and without Crohn's disease. J. Clin. Microbiol. 2003;41:2915–2923. doi: 10.1128/JCM.41.7.2915-2923.2003
[9] Lewis JD, Parlett LE, Jonsson Funk ML, et al. Incidence, prevalence, and racial and ethnic distribution of inflammatory bowel disease in the United States. Gastroenterology. 2023;165:1197–1205. doi:10.1053/j.gastro.2023.07.003
[10] Heydari K, Rahnavard M, Ghahramani S, Hoseini A, Alizadeh-Navaei R, Rafati S, Raei M, Vahidipour M, Salehi F, Motafeghi F, Neshat S, Moosazadeh M, Yousefi M, Pourali A, Rasouli K, Shokrirad S, Lotfi P, Beladi SA, Hadizadeh Neisanghalb M, Sheydaee F, Moghadam S. Global prevalence and incidence of inflammatory bowel disease: a systematic review and meta-analysis of population-based studies. Gastroenterol Hepatol Bed Bench. 2025;18(2):132-146. doi: 10.22037/ghfbb.v18i2.3105. PMID: 40936779; PMCID: PMC12421925.
[11] Talicia® (omeprazole magnesium, amoxicillin and rifabutin) is indicated for the treatment of H. pylori infection in adults. For full prescribing information see: **www.Talicia.com**.

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