NEWS RELEASE

Two Leading Labs Confirm RHB-204 MAP-Killing Effect for RedHill's Crohn's Disease Candidate

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In vitro studies, undertaken by two leading microbiology centers, confirm RHB-204's killing capability on Mycobacterium avium subspecies paratuberculosis (MAP) and its MAP-killing comparability to RedHill's RHB-104 in both long-term intracellular culture and spot and phage assays

The two sets of studies, showing confirmed MAP-killing effect and comparability to RHB-104, led by Professor Tim Bull from City St George's University of London, and Prof Irene Grant, Professor of Microbiology and Food Safety, Queen's University Belfast and Dr Hannah Dane, further support development of RHB-204's potential in MAP-related Crohn's disease

In its positive Phase 3 study, RHB-104 met the primary endpoint with statistical significance, showing RHB-104 plus standard of care (SoC) to be 64% more effective than SoC alone in treating Crohn's disease, compared to the placebo (standard of care only) group (p = 0.0048)[1]

RHB-204[2], a proprietary next-generation oral optimized formulation of RHB-104[3], designed for reduced toxicity and side effects and enhanced patient adherence, employs a differentiated, MAP-targeted approach to the treatment of Crohn's disease

RALEIGH, N.C. and TEL AVIV, Israel, Nov. 2, 2026 /PRNewswire/ -- **RedHill Biopharma Ltd.** (NASDAQ: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced the confirmation of RHB-

204's killing capability on Mycobacterium avium subspecies paratuberculosis (MAP), and RHB-204's comparability to RHB-104 MAP-killing, following two sets of in vitro studies, undertaken by leading microbiology centers, in both long-term intracellular culture and spot and phage assays.

The two sets of studies led by Professor Tim Bull from City St George's University of London, and Prof Irene Grant, Professor of Microbiology and Food Safety, Queen's University Belfast and Dr Hannah Dane, support the potential for RHB-204's role in MAP-related Crohn's disease (CD) through demonstrated RHB-204 comparability to RedHill's RHB-104, which met the primary endpoint with statistical significance of its positive Phase 3 clinical trial, 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).

In vitro studies, undertaken by Professor Tim Bull, confirm RHB-204's MAP-killing capability MAP in long term intracellular culture[4] and further demonstrate RHB-204's comparability to RedHill's RHB-104's MAP-killing effect. The positive results were seen across a range of MAP strains, taken from both human Crohn's disease patients and animal carriers of Johne's disease, sometimes referred to as "animal Crohn's", which were suggestive of both potential human and veterinary utility. The studies also showed that RHB-204 did not induce tolerance in the strains during the short exposure periods used in the studies (6 days max), suggesting that further consecutive dosing could add to the effect.

Tim Bull, Professor of Cell and Molecular Biology at City St George's University of London said: "RHB-204 demonstrated a significant MAP-killing effect, similar to RHB-104, against multiple strains of MAP, both human and animal, whilst intracellularly persistent. MAP is remarkably difficult to kill and test against due to its unique biological structure, intracellular lifestyle, and slow growth rate. This data gives a valuable insight into the potential of RHB-204 to treat MAP-related Crohn's disease involving either human or animal derived MAP strains."

Prof. Bull's work adds to the in vitro work undertaken by Rapid-myco Technologies, a world leader in the field and developer of a transformative diagnostic platform for the rapid detection of important and often life-threatening mycobacterial infections of humans and livestock. This work, led by Prof Irene Grant, Professor of Microbiology and Food Safety at Queen's University Belfast and Dr Hannah Dane, showed in vitro that RHB-204 demonstrated comparable MAP killing to RHB-104 in both spot and phage assays. 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[5].

"We know from previous **published** positive Phase 3 clinical testing that RHB-104 delivered a statistically significant 64% improvement over placebo in efficacy in treating Crohn's disease using a MAP-targeted approach. In vitro confirmation of RHB-204's MAP-killing effect and comparability to RHB-104 is another step forward in the

development of RHB-204 for MAP-related CD," **said Reza Fathi, PhD, Senior VP, R&D at RedHill**. "We believe Phase 2-ready RHB-204 could be among the first treatments to be evaluated in an adequately controlled study in a specifically defined MAP-positive Crohn's disease 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[6], 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 hardest to detect bacteria known.

We believe that RedHill's existing collaborations for the provision of cutting-edge MAP detection diagnostics, with two leading European research organizations, may provide the right conditions for a well-designed study in a specifically defined MAP-positive Crohn's disease patient population. Such a study could provide key evidence that could transform CD management and, if RHB-204 is approved, support a therapy addressing both the suspected cause of the disease and its symptoms.

New safe and effective orally administered therapeutic approaches are needed to help improve outcomes in the treatment of Crohn's disease. Up to 40% of CD patients fail to respond to anti-TNF treatment, and over time a similar proportion 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. The CD market is expected to expand significantly, with sales in the United States, Japan, and five major European markets expected to grow at a compound annual growth rate (CAGR) of 3.87% to $19.1 billion by 2033[5].

RHB-204 is patent protected through 2041 and has been granted FDA Fast Track, Orphan Drug and QIDP and EU Orphan designations. Where applicable, the Company intends to explore the potential for additional designations, including FDA breakthrough therapy and pediatric orphan drug designations, which may provide a potential avenue for receiving a priority review voucher (PRV).

RedHill is actively pursuing partnerships and collaborations for this program, including through innovation development grant applications.

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.

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 clinical data from the positive safety and efficacy results achieved in the Phase 3 clinical study of RHB-104 in CD[8], with its potential further demonstrated using mucosal healing imaging, which is widely used in the evaluation of efficacy 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.

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: significantly impairing quality of life and, in some cases, 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 U.S. specialty biopharmaceutical company primarily focused on the development and commercialization of proprietary drugs for gastrointestinal diseases, infectious diseases and oncology. RedHill promotes the FDA-approved gastrointestinal therapies **Rebyota®**, for the prevention of recurrent C. diff infection (rCDI), and the bowel preparation treatment, **Clenpiq®**. 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 anticancer, anti-inflammatory, antiviral and metabolic activity, targeting multiple indications with a track record of U.S. government and academic collaborations intended for medical countermeasure development including for Ebola virus disease, radiation 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 Phase 2-ready proof-of-concept study for GLP-1/GIP receptor agonist-associated GI intolerance, positive results from a first 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; (iii) **RHB-204**, a next-generation optimized formulation of RHB-104, with a Phase 2-ready study for Crohn's disease (based on RHB-104's positive U.S. 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 influenza 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 MAP-killing effect of RHB-204, the design, timing and conduct of any future study of RHB-204 in a MAP-positive CD patient population, the Company's diagnostic collaborations, its partnering, collaboration and grant application efforts, the scope and duration of patent coverage and regulatory designations, and RHB-204's potential as a possible therapeutic option for Crohn's disease. 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 in vitro results are not predictive of results in animals or humans; the risk that the Company may not commence or complete a clinical study of RHB-204 in a MAP-positive CD patient population, or that any such study may be delayed, the risk that MAP detection diagnostics do not perform as expected or are not available on acceptable terms, the anticipated use of NCI grant funding for the planned Phase 1b and Phase 2 trials for opaganib; planned enrollment, timing and design of the Phase 1b and Phase 2 trials and the potential benefits, if any, of opaganib in combination with CAR T-cell therapy; the risk that the NCI funding may be reduced, delayed or terminated, or may be affected by broader uncertainty regarding government funding; the risks arising with trials conducted by a third party not controlled by RedHill; the risk that the trials may be delayed or may not demonstrate safety or efficacy; the risk that the acquisition of commercialization rights for Rebyota® and Clenpiq does not result in the planned commercial growth; the risk that opaganib is not accepted into Ebola virus disease control programs, or if accepted, that it does not demonstrate efficacy; 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 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 commercial products; (v) the Company's ability to establish and maintain corporate collaborations; (vi) 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; (vii) 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; (viii) the implementation of the Company's business model, strategic plans for its business and therapeutic candidates; (ix) 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; (x) parties from whom the Company licenses its intellectual property defaulting in their obligations to the Company; (xi) the Company's ability to collect on its judgement against Kukbo; (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 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] 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.

[2] RHB-204 is an investigational new drug, not available for commercial distribution in the United States.

[3] RHB-104 is an investigational new drug, not available for commercial distribution in the United States.

[4] Data on file.

[5] Data on file.

[6] 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

[7] 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

[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-

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[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.

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