NEWS RELEASE

RedHill Receives Positive FDA Feedback on Pathway to Approval of Groundbreaking RHB-204 for Crohn's Disease

2025-07-21

The positive FDA feedback allows for:

- A novel Phase 2 RHB-204[1] study, planned to be the first ever clinical study in a specifically defined Mycobacterium avium subspecies paratuberculosis infected (MAP-positive) Crohn's disease (CD) patient population
- Groundbreaking approach testing MAP as a root cause of CD, supporting RHB-204 as a potential paradigm-shifting therapy treating both the suspected cause of Crohn's disease and its symptoms
- RedHill has initiated two new collaborations with leading academic centers utilizing cutting-edge rapid and accurate MAP detection diagnostics – the lack of which has previously been a major barrier to advancing the Company's novel anti-MAP Crohn's disease program
- Innovative design enables a smaller sample size allowing for lower study costs and faster time to completion

Funding for this ground-breaking program expected to be non-dilutive; Grant application submitted and discussions ongoing for additional non-dilutive financing

Patent protected through 2041, orally-administered RHB-204, a next-generation optimized formulation of RedHill's RHB-104 designed to further enhance tolerability, safety and patient adherence, is supported by positive RHB-104[2] Phase 3 safety and efficacy results, which delivered a statistically significant 64% improvement in efficacy[3]

Expected transferal of pediatric orphan drug designation to RHB-204 as well as potential for breakthrough therapy designation, fast track designation, additional regulatory exclusivity and priority review voucher

The multibillion-dollar Crohn's disease market is expected to expand significantly, with sales in the key markets growing from $13.6 billion in 2024 to over $19 billion in 2033[4], presenting significant commercial potential for new, paradigm changing, FDA-approved therapies

RALEIGH, N.C. and TEL AVIV, Israel, July 21, 2025 /PRNewswire/ -- RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced that it received positive feedback from the U.S. Food and Drug Administration (FDA), following a scheduled Type C meeting, in which the FDA provided guidance on the pathway to approval for the Company's potentially groundbreaking RHB-204 Crohn's disease (CD) development program.

The positive FDA feedback allows for the planned RHB-204 Phase 2 study to be the first ever clinical trial in Crohn's disease to test a specifically defined population of Mycobacterium avium subspecies paratuberculosis infected (MAP-positive) CD patients. Testing MAP as a root cause of Crohn's, this groundbreaking approach could potentially make RHB-204, if approved, a paradigm-shifting new therapy treating both the suspected cause of the disease and its symptoms.

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 bacteria on the planet. The Company is collaborating with two leading academic centers for the provision of cutting-edge MAP detection diagnostics, supporting the study's novel design and the potential future commercial application of RHB-204.

The Phase 2 study is expected to have primary endpoints of mucosal remission (considered by FDA as a new gold standard in efficacy evaluation in Crohn's disease), correlated with MAP status and clinical remission, per FDA guidance. These endpoints are supported by the positive RHB-104 Phase 3 study safety and efficacy results. The endpoints and expected use of imaging and cutting-edge MAP detection methods to correlate mucosal healing with MAP infection eradication, enable a potentially smaller sample size allowing for substantially lower study costs and faster time to completion.

Patent protected until 2041, RHB-204, is a novel next-generation optimized formulation of Phase 3-stage RHB-104,

designed to support enhanced tolerability, safety and adherence, with a 40% pill burden reduction, and thus, potentially, better outcomes. The development of RHB-204 is supported by a strong foundation of 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. The data from this study, published in the peer-reviewed journal, Antibiotics[5], 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.

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[5]. Additionally, 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.

The CD market is expected to expand significantly over the 2024–2033 forecast period, 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%[4].

Funding for this ground-breaking program is expected to be non-dilutive. RedHill is actively pursuing partnering and collaborations for this program, including via an innovation development grant application already submitted and ongoing discussions with non-dilutive external funding sources. RHB-204 is expected to benefit from the transferal of pediatric orphan drug designation from RHB-104 and, 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. According to the Cleveland Clinic, experts estimate that more than three-quarters of a million Americans and approximately 6-8 million people globally have Crohn's disease

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 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 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 NTM disease caused by 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. RedHill has protection for RHB-204, and its use in treating pulmonary MAC disease, until 2041.

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[6], with submission planned for marketing authorization in other territories. 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 and antiviral activity, targeting multiple indications with U.S. Government and academic collaborations for development for radiation and chemical exposure indications such as Gastrointestinal-Acute Radiation Syndrome (GI-ARS), a Phase 2 study in prostate cancer in combination with Bayer's darolutamide and a Phase 2/3 program for hospitalized COVID-19 patients; (ii) RHB-204, an all-in-one, fixed-dose, orally administered, combination antibiotic therapy with a planned Phase 2 study for Crohn's disease and Phase 3-stage for pulmonary nontuberculous mycobacterial (NTM) disease; (iii) RHB-104, with positive results from a first Phase 3 study for Crohn's disease; (iv) RHB-107 (upamostat), an oral broad-

acting, host-directed, serine protease inhibitor with potential for pandemic preparedness, is in late-stage development as a treatment for non-hospitalized symptomatic COVID-19 and is also targeting multiple other cancer and inflammatory gastrointestinal diseases; and (v) RHB-102, with potential UK submission for chemotherapy and radiotherapy induced nausea and vomiting, positive results from a Phase 3 study for acute gastroenteritis and gastritis and positive results from a Phase 2 study for IBS-D. RHB-102 is partnered with Hyloris Pharma (EBR: HYL) for worldwide development and commercialization outside North America.

More information about the Company is available at **www.redhillbio.com** / **X.com/RedHillBio**.

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. 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: market and other conditions; the Company's ability to regain and maintain compliance with the Nasdaq Capital Market's listing requirements; the risk that the addition of new revenue generating products or out-licensing transactions will not occur; 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 of market and other conditions and 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) 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 10, 2025. 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.

[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.] DataMonitor - Disease Analysis: Crohn's Disease, September 2024.

[5.] 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.

[6.] 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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