NEWS RELEASE

RedHill's RHB-102 Progresses in Multiple GI Indications Including GLP-1 Therapy-Related GI Side Effects

2026-01-05

RHB-102[1] is a proprietary, advanced clinical-stage, once-daily, bimodal extended-release, oral tablet formulation of 5-HT3 antagonist, ondansetron, targeting oncology support, acute gastroenteritis and gastritis, IBS-D and GLP-1/GIP-associated gastrointestinal (GI) side effects

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Largey de-risked, RHB-102 development is supported by published positive U.S. Phase 3 & 2 results in gastroenteritis/gastritis and diarrhea-predominant irritable bowel syndrome (IBS-D) respectively, a positive comparative PK clinical study as part of the oncology support (CINV/RINV) program[2], plus decades of ondansetron clinical use (>22 million annual U.S. ER prescriptions[3])

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RHB-102 is clinically aligned, if approved, to improve titration success and reduce the #1 cause of discontinuing diabetes & weight loss therapies like Mounjaro®/Zepbound® & Ozempic®/Wegovy®

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Development planned under the accelerated FDA 505(b)(2) route of RHB-102 (Bekinda®) as a once-daily oral therapy for GLP-1/GIP receptor agonist therapy-associated GI side effects. Phase 2 Proof-of-Concept study designed, and intellectual property expanded

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>2% of Americans take GLP-1 receptor agonist drugs[4] but estimates suggest up to 50% discontinue within 3 months[5], potentially costing an estimated $35 billion in lost market value by 2030[6]

TEL-AVIV, Israel and RALEIGH, N.C., Jan. 5, 2026 /PRNewswire/ -- RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced development progress for RHB-102 (Bekinda®) in multiple GI indications, including its development, via the accelerated FDA 505(b)(2) route, as a once-daily oral ondansetron therapy for GLP-1/GIP receptor agonist therapy-associated GI side effects, such as nausea, vomiting and diarrhea, that are estimated to significantly limit growth in the multi-billion-dollar GLP-1 market.

RHB-102, a patent protected bimodal, immediate and extended-release, once-daily oral formulation of 5HT3 antagonist, ondansetron, is clinically aligned to improve titration success and reduce the #1 cause for early discontinuation of GLP-1/GIP-based diabetes & weight loss therapies like Mounjaro® / Zepbound® and Ozempic® / Wegovy®.

RedHill further announced that it is currently pursuing potential U.S. FDA approval of RHB-102 for oncology support, with additional potential for use in post-operative nausea and vomiting (PONV). If approved by FDA, RHB-102 could be the first oral 24-hour extended-release ondansetron antiemetic drug for the treatment of CINV/RINV. Expansion of RHB-102's intellectual property coverage for relevant indications, including GLP-1-associated nausea and vomiting, has also advanced.

An extensive body of clinical and non-clinical data will be available to support potential FDA approval of RHB-102 for oncology support, as well as gastroenteritis, IBS-D and GLP-1/GIP receptor agonist therapy-associated GI side effects. These data include positive results from the RHB-102 U.S. Phase 3 GUARD gastroenteritis study and the positive Phase 2 IBS-D study, with both studies meeting their primary endpoints, were published in **JAMA Network Open**[7] and **The American Journal of Gastroenterology**[8], respectively. In addition, data from a positive comparative PK clinical study plus any additional outcomes from the planned Phase 2 Proof-of-Concept study in GLP-1/GIP receptor agonist therapy-associated GI side effects, will add to the weight of evidence in support of potential approval in multiple GI indications.

Dr. Terry Plasse, RedHill's Medical Director said: "RHB-102's once-daily oral profile may improve titration success, which we believe may result in reaching and maintaining optimal GLP-1 receptor agonist doses. We have designed a

Phase 2 Proof-of-Concept study of RHB-102 for GLP-1/GIP receptor agonist therapy-associated GI side effects, planned to commence as early as possible this year. The overall aim is to help patients navigate the "danger zone" early months of therapy, where GI-side effects, like nausea, vomiting and diarrhea, are most prevalent. Ultimately, the target is to see fewer patients coming off GLP-1/GIP receptor agonist therapies before they have the chance to deliver their full potential." **Dr. Plasse added**: "RedHill believes that RHB-102 is largely de-risked and supported by prior positive U.S. Phase 3 results in gastroenteritis/gastritis, positive U.S. Phase 2 results for IBS-D, and decades of ondansetron clinical use with more than 22 million U.S. emergency room prescriptions annually. We believe that our patent protected RHB-102 provides a compelling partnership choice with published late-stage data, standard manufacturing, low cost of goods sold and multiple potential indications including GLP-1 receptor agonist–associated GI side effects, acute gastroenteritis & gastritis[9], IBS-D and oncology support (chemotherapy/radiotherapy-induced nausea and vomiting CINV/RINV)."

More than 2% of Americans take GLP-1 receptor agonists, but some estimates suggest up to 50% of patients discontinue GLP-1 within 3 months. GI side-effect-driven discontinuation is considered a key contributor to reductions in forecasted GLP-1 market valuations which, according to Goldman Sachs, could be reduced by an estimated $35 billion by 2030.

About RHB-102 (Bekinda®):

RHB-102 is a proprietary, once-daily, bimodal extended-release, oral tablet formulation of ondansetron, a 5-HT3 antagonist, targeting GLP-1/GIP-associated GI intolerance, oncology support (CINV/RINV), acute gastroenteritis and gastritis, and IBS-D.

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[10], with a recent co-commercialization agreement in the U.S. with Cumberland Pharmaceuticals. 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, 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 a Phase 2 study in prostate cancer in combination with darolutamide; (ii) **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); (iii) **RHB-102**, 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 Pharma (EBR: HYL) for worldwide development and commercialization outside North America; 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.

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, and include, among others, statements regarding the potential impact of Talicia. 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-102 to address gastrointestinal (GI) intolerance in obesity and diabetes therapy may not commence, be completed or, if completed, may not be sufficient for approval and, if approved, may not be a commercial success; the risk that opaganib may not replicate its potential to mitigate resistance in CLL therapy; the risk that the strategic transaction with Cumberland will not bring the currently anticipated benefits to RedHill's global Talicia business or to RedHill's financial position, costs or its broader strategic objectives; the risk regarding the Company's ability to maintain compliance with Nasdaq's listing requirements, including the minimum stockholders' equity requirement; 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 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.

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Category: R&D

[1] RHB-12 is an investigational new drug, not available for commercial distribution in the United States.

[2] Data on file

[3] Cairns C, Kang K. National Hospital Ambulatory Medical Care Survey: 2021 emergency department summary tables. Available from: **https://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NHAMCS/doc21-ed-508.pdf**.

[4] FAIR Health. Obesity and GLP-1 Drugs: A Claims-Based Analysis. FAIR Health White Paper; May 27, 2025.

[5] Issue Brief (Real-World Trends in GLP-1 Treatment Persistence and Prescribing for Weight Management, May 2024)

[6] **https://www.goldmansachs.com/insights/articles/the-anti-obesity-drug-market-may-prove-smaller-than-expected**

[7] Silverman RA, House SL, Meltzer AC, et al. Bimodal Release Ondansetron for Acute Gastroenteritis Among Adolescents and Adults: A Randomized Clinical Trial. JAMA Netw Open. 2019;2(11):e1914988. doi:10.1001/jamanetworkopen.2019.14988

[8] Plasse TF, Barton G, Davidson E, et al. Bimodal release ondansetron improves stool consistency and symptomatology in diarrhea-predominant irritable bowel syndrome: A randomized, double-blind trial. Am J Gastroenterol 2020;115:1466-73.

[9] Acute gastroenteritis and gastritis are characterized by inflammation of the mucus membranes of the gastrointestinal tract, most commonly caused by viral infection, with symptoms including nausea, vomiting, diarrhea and abdominal pain.

[10] 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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