NEWS RELEASE

RedHill Biopharma's Positive Opaganib Weight Loss & Diabetes Data Published: Signals Potential $100B Market Disruption

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GLP-1 comparable efficacy: Opaganib's positive results, newly published in the journal Diabetes, Metabolic Syndrome and Obesity, demonstrated weight loss and improved metabolic markers on par with semaglutide in preclinical models

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Novel mechanism of action, formulation and administration: Opaganib is a differentiated oral, non-peptide therapeutic that targets sphingosine kinase-2 (SPHK2), potentially avoiding common Glucagon-like peptide-1 (GLP-1) inhibitor side effects and administration burdens

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Market disruptor potential: The rapidly growing global obesity-diabetes drugs market is projected to be worth around $100 billion by 2034[1] – largely driven by GLP-1 inhibitors like Novo Nordisk's Ozempic® and Wegovy® and Eli Lilly's Trulicity®, Zepbound® and Mounjaro®

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Potential high value and de-risked development pathway: Existing human safety and tolerability data from over 470 subjects, from several clinical programs, may help expedite the FDA pathway to approval; new obesity and diabetes indications add strategic expansion and value to existing development programs in oncology, inflammatory and viral indications

TEL AVIV, Israel and RALEIGH, N.C., April 16, 2025 /PRNewswire/ -- RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced the new **publication**[2] of positive in vivo data, in the journal Diabetes, Metabolic Syndrome and Obesity, in an article entitled "Opaganib Promotes Weight Loss and Suppresses High-Fat Diet (HFD)-Induced Obesity and Glucose Intolerance". The data indicates that opaganib[3] effectively suppresses the loss of metabolic control in mice on a HFD, suggesting that opaganib, alone and in combination with semaglutide, is associated with improved glucose tolerance, decreased deposition of fat, weight loss and the prevention of weight gain rebound after removal of semaglutide.

Dr. Mark Levitt, Chief Scientific Officer at RedHill, said: "Sphingolipid metabolism is implicated in insulin resistance, β-cell disruption, adipocyte function, inflammation and immune regulation, vascular complications and energy metabolism – all significant components of obesity, diabetes and their associated complications. The studies showed that treatment with opaganib markedly suppressed weight gain in mice fed the HFD but not in mice given the control diet (CD). Compared with mice given CD, mice on the HFD demonstrated poor glucose tolerance at 8, 12 and 16 weeks, consistent with the progression of obesity. Importantly, opaganib treatment of the HFD-fed mice abolished this developing glucose intolerance at all times of measurement. Opaganib treatment also reduced the elevation of hemoglobin A1c and the deposition of inguinal fat in HFD-fed mice. Opaganib and semaglutide were equally effective in promoting body weight loss and improving glucose tolerance in obese mice. Opaganib's ability to modulate multiple signaling pathways through simultaneous inhibition of three sphingolipid-metabolizing enzymes in human cells – the first known clinical drug to do so - provides a strong rationale for evaluation of opaganib in obesity-related disorders – and, as a first-in-class, orally administered, non-peptide option, opaganib could potentially represent a game-changing opportunity in the multi-billion-dollar obesity and diabetes market."

The global obesity-diabetes drugs market is projected to be worth around $100 billion by 2034 – largely driven by GLP-1 inhibitors like Novo Nordisk's Ozempic and Wegovy (semaglutide) and Eli Lilly's Trulicity (dulaglutide) and Mounjaro / Zepbound (tirzepatide).

About Opaganib (ABC294640)

Opaganib, a proprietary investigational host-directed and potentially broad-acting drug, is a first-in-class, orally administered sphingosine kinase-2 (SPHK2) selective inhibitor with anticancer, anti-inflammatory and antiviral activity, targeting multiple potential indications, including several cancers, diabetes and obesity-related disorders, gastrointestinal acute radiation syndrome (GI-ARS), chemical exposure indications, COVID-19, Ebola and other viruses as part of pandemic preparedness.

Opaganib's host-directed action is thought to work through the inhibition of multiple pathways, the induction of autophagy and apoptosis, and disruption of viral replication, through simultaneous inhibition of three sphingolipid-metabolizing enzymes in human cells (SPHK2, DES1 and GCS).

Several U.S. government countermeasures and pandemic preparedness programs have selected opaganib for evaluation for multiple indications, including Acute Radiation Syndrome (ARS), Ebola virus disease and others. Funding bodies include the Radiation and Nuclear Countermeasures Program (RNCP), led by the National Institute of Allergy and Infectious Diseases (NIAID), part of the U.S. government Department of Health & Human Services' National Institutes of Health and the Administration for Strategic Preparedness and Response's (ASPR) Center for Biomedical Advanced Research and Development Authority (BARDA).

A Bayer-supported 80-patient placebo-controlled randomized Phase 2 study has also been initiated to evaluate the efficacy of opaganib in combination with Bayer's darolutamide in men with metastatic castrate-resistant prostate cancer (mCRPC), testing the potentially enhancing effect of opaganib in patients with a poor prognosis.

Opaganib has demonstrated antiviral activity against SARS-CoV-2, multiple variants, and several other viruses, such as Influenza A and Ebola. Opaganib delivered a statistically significant increase in survival time when given at 150 mg/kg twice a day (BID) in a United States Army Medical Research Institute of Infectious Diseases (USAMRIID) in vivo Ebola virus study, making it the first host-directed molecule to show activity in Ebola virus disease. Opaganib also recently demonstrated a distinct synergistic effect when combined individually with remdesivir (Veklury®, Gilead Sciences Inc.), significantly improving potency while maintaining cell viability, in a U.S. Army-funded and conducted in vitro Ebola virus study.

Being host-targeted, and based on data accumulated to date, opaganib is expected to maintain effect against emerging viral variants. In prespecified analyses of Phase 2/3 clinical data in hospitalized patients with moderate to severe COVID-19, oral opaganib demonstrated improved viral RNA clearance, faster time to recovery and significant mortality reduction in key patient subpopulations versus placebo on top of standard of care. Opaganib has demonstrated its safety and tolerability profile in more than 470 people in multiple clinical studies and expanded access use. Data from the opaganib global Phase 2/3 study was published in **Microorganisms**.

Opaganib has received several orphan-drug designations from the FDA in oncology and other diseases and has

undergone studies in solid tumors (Phase 1), advanced cholangiocarcinoma (Phase 2a) and prostate cancer. Opaganib also has a Phase 1 chemoradiotherapy study protocol ready for FDA-IND submission.

Opaganib has also shown positive preclinical results in renal fibrosis, and has the potential to target multiple oncology, radioprotection, viral, inflammatory, gastrointestinal and diabetes/obesity-related indications.

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[4], 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 and include, among others, statements regarding the potential effects of opaganib on obesity- and diabetes-related conditions. 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 observations from preclinical studies are not indicative or predictive of results in clinical trials; 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.

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Category: R&D

[1] **https://www.futuremarketinsights.com/reports/obesity-diabetes-drugs-market**
[2] Maines LW, Keller SN, Smith RA, Smith CD. Opaganib Promotes Weight Loss and Suppresses High-Fat Diet-Induced Obesity and Glucose Intolerance. Diabetes Metab Syndr Obes. 2025;18:969-983
https://doi.org/10.2147/DMSO.S514548
[3] Opaganib is an investigational new drug, not available for commercial distribution.
[4] 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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