NEWS RELEASE

RedHill Announces Collaboration with a Leading U.S. Academic Medical Center to Develop Opaganib as a Countermeasure Against Phosgene Inhalation Injury

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The collaboration outlines plans for multiple in vivo studies, designed to test opaganib as a potential medical countermeasure to treat phosgene inhalation injury. The collaboration aims to determine whether opaganib can advance into further definitive U.S. government-sponsored development under the FDA's Animal Rule pathway to approval

Used as a chemical weapon during World War I, phosgene, a toxic, colorless chemical, is today widely used in industrial processes for the manufacture of plastics and pesticides. The U.S. Environmental Protection Agency (EPA) identified 123 sites in the United States that could potentially expose millions of people to phosgene due to plant malfunction or bioterrorism[1]

Phosgene inhalation can be extremely dangerous, causing significant, even fatal, respiratory injury. No known approved antidote or reversal agent currently exists, and, if approved, opaganib may provide potential for stockpiling for emergency use in the event of a major public safety incident

With multiple U.S. government collaborations for chemical and medical countermeasures and pandemic preparedness, RedHill's opaganib is a novel, host-directed, potentially broad acting, orally administered small molecule, clinical-stage drug with demonstrated safety & efficacy profiles, being developed for various oncology,

viral infections, inflammatory diseases and chemical and nuclear/radioprotection indications

TEL AVIV, Israel and RALEIGH, N.C., Oct. 22, 2024 /PRNewswire/ -- RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced the signing of a collaborative research agreement with Duke University School of Medicine outlining plans for multiple in vivo studies. The program is designed to test opaganib[2] as a potential medical countermeasure to treat phosgene inhalation injury, aimed at providing results sufficient to advance opaganib into further definitive U.S. government-sponsored development under the U.S. Food and Drug Administration's (FDA) Animal Rule pathway to approval. The FDA Animal Rule allows for the use of pivotal animal model efficacy studies to support FDA approval of new drugs when human clinical trials are not ethical or feasible. Under this research agreement, RedHill will provide required drug quantities for animal studies, analytical support to quantify drug concentrations in plasma samples, and share dosing regimen with the Achanta Lab at Duke University.

"Opaganib is currently being tested, by various governmental research bodies, in multiple areas that urgently require new chemical and medical countermeasure therapeutic options," **said Dr. Satya Achanta, D.V.M., Ph.D., Assistant Professor in the Department of Anesthesiology at Duke University School of Medicine.** "Our research will help determine whether there is a potential protective role of opaganib in limiting damage caused by phosgene inhalation."

"Notably used as a chemical weapon during World War I, phosgene, a toxic, colorless chemical, is today widely used in industrial processes for the manufacture of plastics and pesticides. The U.S. Environmental Protection Agency (EPA) identified 123 sites in the United States that could expose millions of people to phosgene potentially due to plant malfunction or bioterrorism," **said Gilead Raday, RedHill's Chief Operating Officer and Head of Research and Development**. "This exciting collaboration with Duke University School of Medicine could pave the way to a potential therapy for the acute respiratory distress syndrome (ARDS) phosgene inhalation can cause, which can be extremely dangerous, causing significant, even fatal, injury. No known approved antidote or reversal agent currently exists, and, if approved, opaganib may provide potential for stockpiling for emergency use in the event of a major public safety incident."

What is Phosgene inhalation injury

Phosgene inhalation injury occurs when someone breathes in phosgene gas ($COCl_2$), a toxic chemical primarily used in industrial processes. Phosgene has a distinct odor, similar to freshly mown grass or hay. However, only 10% of

the population may detect this odor at lower concentrations. The combination of its unassuming odor and poor human detection makes phosgene particularly dangerous. At higher concentrations, it is extremely dangerous, even fatal, and is a cause of acute respiratory distress syndrome (ARDS). It is believed that no antidotes or reversal agents exist at this time. Phosgene was notably used as a chemical weapon during World War I.

Today, phosgene use in industry is ubiquitous - being used in the production of polymers, plastics and pesticides. Global estimates indicate that more than 12 million metric tons are produced annually[3]. Despite its widespread use, some regions poorly regulate its production, and concern exists for its potential as a weapon of bioterrorism. Given its severe toxicity and high mortality, research is primarily limited to an Animal Rule pathway to approval, which allows for the use of pivotal animal model efficacy studies to support FDA approval of new drugs when human clinical trials are not ethical or feasible.

The EPA identified 123 sites in the United States that could expose millions of people to phosgene if the plant malfunctions or becomes a target of bioterrorism.

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), Sulfur Mustard exposure, 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).

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 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, and gastrointestinal indications.

About RedHill Biopharma

RedHill Biopharma Ltd. (Nasdaq: RDHL) is a specialty biopharmaceutical company primarily focused on gastrointestinal and infectious diseases. RedHill promotes the gastrointestinal drug **Talicia®,** for the treatment of Helicobacter pylori (H. pylori) infection in adults[4]. RedHill's key clinical late-stage development programs include: (i) **opaganib (ABC294640)**, a first-in-class oral broad-acting, host-directed SPHK2 selective inhibitor with potential for chemical and medical countermeasure and pandemic preparedness use, targeting multiple indications with a U.S. government collaboration for development for Acute Radiation Syndrome (ARS), a Phase 2/3 program for hospitalized COVID-19, and a Phase 2 program in oncology; (ii) **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, with non-dilutive external funding covering the entirety of the RHB-107 arm of the 300-patient Phase 2 adaptive platform trial, and is also targeting multiple other cancer and inflammatory gastrointestinal diseases; (iii) **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; (iv) **RHB-104**, with positive results from a first Phase 3 study for Crohn's disease; and (v) **RHB-204**, a Phase 3-stage program for pulmonary nontuberculous mycobacteria (NTM) disease.

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 in the treatment of phosgene inhalation injury. 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 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 that acceptance onto the RNCP Product Development Pipeline 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 opaganib for any indication; the risk that observations from preclinical studies are not indicative or predictive of results in clinical trials; the risk that the FDA pre-study requirements will not be met and/or that the Phase 3 study of RHB-107 in COVID-19 outpatients will not be approved to commence or if approved, will not be completed or, should that be the case, that we will not be successful in obtaining alternative non-dilutive development funding for RHB-107; the risk that RHB-107's late-stage development for non-hospitalized COVID-19 will not benefit from the resources redirected from the terminated RHB-204 Phase 3 study, and that the Phase 2/3 COVID-19 study for RHB-107 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 COVID-19 studies for opaganib and RHB-107 are likely to 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 a commercial companion diagnostic for the detection of MAP; (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® and Aemcolo®; (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 8, 2024. 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

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[1] **https://www.ncbi.nlm.nih.gov/books/NBK589660/**

[2] Opaganib is an investigational new drug, not available for commercial distribution.

[3] **https://www.ncbi.nlm.nih.gov/books/NBK589660/**

[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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