NEWS RELEASE

RedHill Announces First Patient Enrolled in U.S. Government-Supported COVID-19 Study

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First patient enrolled in the global, 300-patient, Phase 2 adaptive platform trial arm of RHB-107 (upamostat)[1] for early COVID-19 outpatient treatment, funded through non-dilutive external sources, including the U.S. Department of Defense

The study is expected to be completed by the end of 2024

RHB-107 successfully met the primary endpoint of safety and tolerability and delivered promising efficacy results, including marked reduction in hospitalization due to COVID-19 in a U.S. Phase 2 study[2]

RHB-107 is a novel, oral, once-daily, host-directed potential broad-acting antiviral expected to act independently of viral spike protein mutations[3]

RALEIGH, N.C. and TEL-AVIV, Israel, April 24, 2024 /PRNewswire/ -- **RedHill Biopharma Ltd.** (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced that the first patient has been enrolled in the Austere environments Consortium for Enhanced Sepsis Outcomes' (ACESO) U.S. government-supported PROTECT multinational platform trial for early COVID-19 outpatient treatment. RHB-107 (upamostat) is the first drug being tested in this platform study. Funded through non-dilutive external sources, including the U.S. Department of Defense, the PROTECT study is expected to be conducted in the U.S., Thailand, Ivory Coast, South Africa and Uganda, and is estimated to be completed by the end of 2024.

"Enrollment of the first patient in the study marks an important milestone for RHB-107 in the 300-patient U.S. government-supported PROTECT platform study, which could add significant validating data to the previous marked reduction in hospitalizations due to COVID-19 seen in the RHB-107 arm of our earlier U.S. Phase 2 study," said **Gilead Raday, RedHill's Chief Operating Officer and Head of R&D**. "RHB-107 is a novel, potentially broad-acting, host-directed antiviral that is expected to act independently of viral spike protein mutations. If approved, RHB-107 could provide a much-needed additional option for use in the early COVID-19 treatment space, alongside Paxlovid. Additionally, with both RHB-107 and opaganib recently demonstrating distinct synergistic effect when combined individually with remdesivir in an in vitro Ebola study, we are making encouraging progress with our pipeline assets for pandemic preparedness."

Data from RHB-107's previous U.S. Phase 2 study showed a 100% reduction in hospitalization due to COVID-19, with zero patients (0/41) on the RHB-107 arms versus 15% (3/20) hospitalized for COVID-19 on the placebo-controlled arm (nominal p-value=0.0317). The study also showed an approximately 88% reduction in reported new severe COVID-19 symptoms after treatment initiation, with 2.4% of the RHB-107 treated group (1/41) versus 20% (4/20) of patients in the placebo-controlled arm (nominal p-value=0.036) reporting new severe COVID-19 symptoms. Further post-hoc analysis showed faster recovery periods from severe COVID-19 symptoms with a median of 3 days to recovery with upamostat compared to 8 days with the placebo.

The ACESO PROTECT study is an adaptive, randomized, double blind, multi-site Phase 2 platform trial, being conducted by researchers from ACESO and partner organizations, and administered by the Henry M. Jackson Foundation for the Advancement of Military Medicine (HJF). The study will compare investigational products (IPs) to control, in standard-risk, non-hospitalized adult SARS-CoV-2 infected participants with at least two moderate-severe symptoms at baseline. RHB-107 is the initial drug being evaluated in the early treatment arm of the study. The primary efficacy assessment in the early treatment indication will be time to sustained alleviation or resolution of COVID-19 symptoms. Participants will be followed for a period of up to 12 weeks.

Selection of IPs for inclusion in the ACESO PROTECT study is based on review of the preclinical and early clinical data, evaluating safety, tolerability, and efficacy. Selection is also based on route of administration and product availability.

RHB-107's development for COVID-19 runs parallel to the development of opaganib, RedHill's other novel oral drug, for Acute Radiation Syndrome, being done in collaboration with, and funded by, the U.S. government's National Institutes of Health Radiation and Nuclear Countermeasures Program. Both RHB-107 and opaganib also recently demonstrated distinct synergistic effect when combined individually with remdesivir, significantly improving potency while maintaining cell viability, in a U.S. Army-funded and conducted in vitro Ebola virus study.

About RHB-107 (upamostat)

RHB-107 is a proprietary, first-in-class, once-daily orally administered investigational antiviral, that targets human serine proteases involved in preparing the spike protein for viral entry into target cells. Because it is host-cell targeted, RHB-107 is expected to also be effective against emerging viral variants with mutations in the spike protein. RHB-107 is well tolerated; in the initial COVID-19 study, among 41 patients only one reported a drug-related adverse reaction (a mild, self-limited, rash).

In addition, RHB-107 inhibits several proteases targeting cancer and inflammatory gastrointestinal disease. RHB-107 has undergone several Phase 1 studies and two Phase 2 studies, demonstrating its clinical safety profile in approximately 200 patients[4].

RedHill acquired the exclusive worldwide rights to RHB-107, excluding China, Hong Kong, Taiwan and Macao, from Germany's Heidelberg Pharma AG (FSE: HPHA) (formerly WILEX AG) for all indications.

About HJF

The Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. (HJF), now celebrating its 40th anniversary, is a global nonprofit organization with the mission to advance military medicine. HJF's scientific, administrative and program operations services empower investigators, clinicians, and medical researchers around the world to make discoveries in all areas of medicine. HJF serves as a trusted and responsive link between the military medical community, federal and private partners, and the millions of warfighters, veterans, and civilians who benefit from military medicine. For more information, visit **www.hjf.org.**

About ACESO

The Austere environments Consortium for Enhanced Sepsis Outcomes (ACESO) aims to improve survival for patients with sepsis in resource-limited settings through development of host-based technology solutions and evidence-based clinical management strategies. Founded in 2010, ACESO brings together a consortium comprised of academic, non-profit, governmental, and industry partners that is administered by HJF. ACESO has established a global clinical research network to develop and deliver cutting-edge tools and strategies to save lives in austere settings.

For more information, visit **www.aceso-sepsis.org**.

About RedHill Biopharma

RedHill Biopharma Ltd. (Nasdaq: RDHL) is a specialty biopharmaceutical company primarily focused on gastrointestinal and infectious diseases. RedHill promotes the gastrointestinal drugs **Talicia®**, for the treatment of Helicobacter pylori (H. pylori) infection in adults[5], and **Aemcolo®**, for the treatment of travelers' diarrhea in adults[6]. 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 pandemic preparedness, 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** / **twitter.com/RedHillBio**.

Forward Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. 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, the risk that the ACESO PROTECT study for RHB-107 may not be completed or, if completed, may not be successful or, even if successful, may not be sufficient support for regulatory applications, including emergency use or marketing applications, that additional COVID-19 studies for RHB-107 are likely to be required, and that we will not be successful in obtaining further non-dilutive development funding for RHB-107. Such risks and uncertainties also include those associated with the risk that the Company will not successfully commercialize its products, that the growth in prescriptions will not continue and the addition of new generating products will not occur, and that we will not be successful in increasing sales of our commercial products, including due to market and other conditions; 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 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 28, 2023. 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.

This project was supported by the Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense (JPEO-CBRND) Joint Project Lead for Enabling Biotechnologies (JPL CBRND EB) in collaboration with the Defense Health Agency (DHA) COVID funding initiative for The Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Contract W911QY-20-9-0004 for this effort.

The views expressed in this press release reflect the results of research conducted by the author and do not necessarily reflect the official policy or position of the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., the Department of the Navy, Department of the Army, Department of Defense, nor the United States Government. References to non-federal entities or their products do not constitute or imply Department of

Defense or Army endorsement of any company, organization, or product. To the Company's knowledge, the study protocol is in compliance with all applicable federal regulations governing the protection of human subjects.

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Category: R&D

[1] RHB-107 (upamostat) is an investigational new drug, not available for commercial distribution in the United States.

[2] **https://www.ijidonline.com/article/S1201-9712(22)00638-5/fulltext**

[3] Preliminary data from a recent in vitro study

[4] **https://www.ijidonline.com/article/S1201-9712**(22)00638-5/fulltext

[5] 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**.

[6] Aemcolo® (rifamycin) is indicated for the treatment of travelers' diarrhea caused by noninvasive strains of Escherichia coli in adults. For full prescribing information see: **www.aemcolo.com**.

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