NEWS RELEASE

RedHill Announces Positive Phase 2 Study Results with Oral RHB-107 in Non-Hospitalized COVID-19

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Phase 2 part of Phase 2/3 study of once-daily oral RHB-107 in symptomatic COVID-19 successfully met the study's primary endpoint showing good safety and tolerability and highly promising efficacy results

100% reduction in hospitalization due to COVID-19 with zero patients (0/41) on the RHB-107 arms versus 15% (3/20) hospitalized on the placebo-controlled arm

87.8% reduction in reported new severe COVID-19 symptoms after treatment initiation, with only one patient in the RHB-107 treated group 2.4%, (1/41) versus 20% (4/20) of patients in the placebo-controlled arm)

The most common variant among patients in the study was Delta; RHB-107, a novel, investigational oral antiviral serine protease inhibitor, targeting host rather than viral factors, is expected to maintain effect against emerging viral variants

TEL AVIV, Israel and RALEIGH, N.C., March 1, 2022 /PRNewswire/ -- **RedHill Biopharma Ltd.** (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced positive top-line results from the Phase 2 part of the Phase 2/3 study of once-daily oral RHB-107 (upamostat)[1] in non-hospitalized symptomatic COVID-19 patients, predominantly conducted in the U.S. (60/61 patients) as well as South Africa.

Although not powered for efficacy assessment, the study showed highly promising efficacy results delivering a 100% reduction in hospitalization due to COVID-19, with zero patients on RHB-107 hospitalized with COVID-19 (0/41) compared to 15% on the placebo-controlled arm requiring hospitalization (3/20) (nominal p-value=0.0317). Furthermore, the study showed an 87.8% reduction in reported new severe COVID-19 symptoms, with only one patient on RHB-107 (2.4%, 1/41) compared to 20% (4/20) of patients on the placebo-controlled arm experiencing new COVID-19 related severe symptoms (nominal p-value=0.036).

The study met its primary outcome measure, demonstrating a favorable safety and tolerability profile of RHB-107. Study arms were well balanced with respect to baseline disease severity, risk factors and vaccination status. Patients were also tested for the specific viral strain (last patient randomized November 12, 2021), with the most common variant being Delta, found in 62.5% of the patients that had next generation sequencing (NGS).

"These very promising efficacy results, achieved despite a small overall sample size, are impressive. Coupling the efficacy results with successfully meeting the primary endpoint of good safety and tolerability and convenient once-daily dosing, positions oral RHB-107 as a potential highly beneficial treatment for COVID-19 outpatients early in the course of disease in order to reduce symptom severity and prevent disease progression and hospitalization. Given the limitations of current options for early treatment of COVID-19, we are excited to progress the development of RHB-107, subject to additional discussions with regulatory authorities," **said Terry F. Plasse MD, Medical Director at RedHill**. "Equally important is our expectation that RHB-107, with its human cell factor targeting, would maintain its action irrespective of spike protein mutations, thus likely making it a highly desirable variant-agnostic potential treatment option."

The Phase 2/3 multicenter, randomized, double-blind, placebo-controlled, parallel-group study (**NCT04723527**) with RHB-107 is aimed at evaluating treatment in patients with symptomatic COVID-19 early in the course of the disease, with a once-daily oral treatment that can be prescribed and used in the non-hospitalized patient population. The Phase 2 part of the study was designed to evaluate safety for dose selection and to provide preliminary assessment of parameters to be used for efficacy evaluation in Part B. A total of 61 patients were enrolled in Part A and randomized on a 1:1:1 basis to receive one of two dose levels of RHB-107 or a placebo control.

Next steps for the study will follow data submission and discussion with regulators.

About RHB-107 (upamostat)

RHB-107 is a proprietary, first-in-class, orally-administered antiviral, that targets human serine proteases involved in preparing the spike protein for viral entry into target cells. RHB-107 targets host cell factors involved in preparing the spike protein for viral entry into target cells and is therefore expected to be effective against emerging viral variants with mutations in the spike protein. RHB-107 is being evaluated in a Phase 2/3 study for treatment of

patients with symptomatic COVID-19 who do not require inpatient care. RHB-107 has demonstrated strong inhibition of SARS-CoV-2 viral replication in an in vitro human bronchial epithelial cell model. RHB-107 has a strong clinical safety and biodistribution profile, demonstrated in previous clinical studies, including several Phase 1 studies and two Phase 2 studies, demonstrating its clinical safety profile in approximately 200 patients. In addition, RHB-107 inhibits several proteases targeting cancer and inflammatory gastrointestinal disease. RedHill acquired the exclusive worldwide rights to RHB-107, excluding China, Hong Kong, Taiwan and Macao, from Germany's Heidelberg Pharma (FSE: HPHA) (formerly WILEX AG) for all 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 drugs, **Movantik®** for opioid-induced constipation in adults[2], **Talicia®** for the treatment of Helicobacter pylori (H. pylori) infection in adults[3], and **Aemcolo®** for the treatment of travelers' diarrhea in adults[4]. RedHill's key clinical late-stage development programs include: (i) **RHB-204**, with an ongoing Phase 3 study for pulmonary nontuberculous mycobacteria (NTM) disease; (ii) **opaganib (ABC294640)**, a first-in-class, oral SK2 selective inhibitor targeting multiple indications with a Phase 2/3 program for COVID-19 and Phase 2 studies for prostate cancer and cholangiocarcinoma ongoing; (iii) **RHB-107** (**upamostat**), an oral serine protease inhibitor in a U.S. Phase 2/3 study as treatment for symptomatic COVID-19, and targeting multiple other cancer and inflammatory gastrointestinal diseases; (iv) **RHB-104**, with positive results from a first Phase 3 study for Crohn's disease; (v) **RHB-102**, with positive results from a Phase 3 study for acute gastroenteritis and gastritis and positive results from a Phase 2 study for IBS-D; and (vi) **RHB-106**, an encapsulated bowel preparation. More information about the Company is available at **www.redhillbio.com** / **https://twitter.com/RedHillBio**.

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 follow up for Part A and the commencement of Part B of the Phase 2/3 study evaluating RHB-107 in patients with symptomatic COVID-19 will be delayed, not completed or not successful; the risk that RHB-107 and/or opaganib will not be effective against emerging viral variants with mutations in the spike protein; the risk that the Company's Phase 2/3 development program evaluating RHB-107 and/or opaganib will not be successful and that the data from this clinical study will be delayed, if at all; the risk of a delay in receiving data to support emergency use applications or in making such

emergency use applications, if at all; the risk that the Company will not initiate the Phase 2/3 study for RHB-107 in certain geographies, including South Africa, will not expand this study to additional sites in the U.S and that it will not be successful and that enrollment will be delayed; the risk that COVID-19 patients treated with RHB-107 or opaganib will not show any clinical improvement; the development risks of early-stage discovery efforts for a relatively new disease, including difficulty in assessing the efficacy of RHB-107 and opaganib for the treatment of COVID-19, if at all; intense competition from other companies developing potential treatments and vaccines for COVID-19; the effect of a potential occurrence of patients suffering serious adverse events using RHB-107, as well as risks and uncertainties associated with (i) the initiation, timing, progress and results of the Company's research, manufacturing, preclinical 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 preclinical studies or clinical trials (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 Movantik®, 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 and sustain 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, preclinical 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 commercial products 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 events using investigative drugs under the Company's Expanded Access Program; and (xiv) competition from other companies and technologies within the Company's industry. 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 March 18, 2021. 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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[1] RHB-107 (upamostat) is an investigational new drug, not available for commercial distribution in the United States.

[2] Full prescribing information for Movantik® (naloxegol) is available at: **www.Movantik.com**.

[3] Full prescribing information for Talicia® (omeprazole magnesium, amoxicillin and rifabutin) is available at: **www.Talicia.com**.

[4] Full prescribing information for Aemcolo® (rifamycin) is available at: **www.Aemcolo.com**.

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