Press Release

RedHill Biopharma Announces Last Patient Randomized in Part A of Ongoing Phase 2/3 COVID-19 Study of Once-Daily Oral RHB-107 in Non-Hospitalized Patients

Recruitment completed for Part A of the Phase 2/3 study of once-daily orally-administered RHB-107 (upamostat) for patients with symptomatic COVID-19 who do not require hospital care

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Top-line results for Part A of the study, designed to evaluate safety and tolerability of RHB-107 and dose selection, expected in Q1/ 22

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RHB-107 is a novel, investigational antiviral serine protease inhibitor targeting human cell factors and is expected to be effective against emerging viral variants

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In parallel, data packages for opaganib, RedHill's other advanced novel oral COVID-19 drug candidate, have been submitted in the U.S., EU, UK and other territories, ahead of planned regulatory advice

TEL AVIV, Israel and RALEIGH, NC, November 15, 2021, RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced that the last patient has been enrolled in Part A of the Phase 2/3 study with novel, once-daily, orally-administered pill RHB-107 (upamostat)[1] for non-hospitalized patients with symptomatic COVID-19. The study is being conducted in the U.S. and South Africa.

The Phase 2/3 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 study is a 2-part, multicenter, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the safety and efficacy of RHB-107. The study is designed to evaluate time to sustained recovery from illness as the primary endpoint and for dose selection. A total of 61 patients have been enrolled in Part A and randomized on a 1:1:1 basis to receive one of two doses of upamostat or placebo. Based on safety and tolerability

results of part A, a dose for part B will be selected, and patients will be randomized 3:2 to active vs. placebo. Patients are also tested for specific viral strain. Top-line results from Part A of the study are expected in the first quarter of 2022, with Part B of the study expected to follow subsequent to discussions with regulators.

"Once again, we see a rise in COVID-19 infections in many countries across the world – and the need for effective, simple and safe oral therapies that can be used outside the hospital setting, and that can work across COVID-19 variants, is significant," **said Terry F. Plasse MD, Medical Director at RedHill**. "Completing randomization for Part A of the RHB-107 Phase 2/3 study is an important step forward for this elegant, once-daily novel oral pill as a potential treatment of COVID-19 in the community."

RHB-107 is a novel antiviral drug candidate 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 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 and Phase 2 studies in different indications, in approximately 200 patients.

In parallel, data packages for opaganib[2], RedHill's other advanced novel oral COVID-19 drug candidate – have been submitted to regulators in various territories including the U.S., EU, UK and others, ahead of planned regulatory advice. Opaganib's global Phase 2/3 study in patients hospitalized with severe COVID-19 demonstrated a 62% reduction in mortality as well as improved outcomes in time to room air and median time to hospital discharge in a sub-group of 251 moderately severe patients, comprising 54% of the study participants.

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 human 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. 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. RedHill acquired the exclusive worldwide rights to RHB-107, excluding China, Hong Kong, Taiwan and Macao, from Germany's Heidelberg Pharmaceuticals (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[3], **Talicia®** for the treatment of *Helicobacter pylori (H. pylori)* infection in adults[4], and **Aemcolo®** for the treatment of travelers' diarrhea in adults[5]. 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] Opaganib is an investigational new drug, not available for commercial distribution in the United States.
[3] Full prescribing information for Movantik® (naloxegol) is available at: www.Movantik.com.
[4] Full prescribing information for Talicia® (omeprazole magnesium, amoxicillin and rifabutin) is available at: www.Talicia.com.
[5] Full prescribing information for Aemcolo® (rifamycin) is available at: www.Aemcolo.com.