Press Release

RedHill Biopharma Announces First Patient Dosed in U.S. Phase 2/3 COVID-19 Outpatient Study with RHB-107

The U.S. Phase 2/3 study with once-daily, orally-administered RHB-107 (upamostat) evaluates treatment of patients with symptomatic COVID-19 who do not require hospitalization - the vast majority of patients

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RHB-107 is a novel serine protease inhibitor targeting human cell factors involved in viral entry, and is therefore expected to be effective against emerging viral variants with mutations in the spike protein

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The RHB-107 Phase 2/3 study allows patients to remain in the comfort of their home while being monitored at a level previously possible only in a hospital setting

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In parallel, top-line data from global Phase 2/3 study in hospitalized patients with opaganib, RedHill's second COVID-19 candidate, is expected Q2/2021

TEL AVIV, Israel and RALEIGH, NC, February 17, 2021, RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced that the first patient was dosed in its U.S. Phase 2/3 study of orally-administered RHB-107 (upamostat)[1], an investigational new drug for patients with symptomatic COVID-19 who do not require hospital care.

Dror Ben-Asher, RedHill's CEO said: "RedHill is rapidly advancing two Phase 3-stage, orally-administered, novel molecules for the treatment of COVID-19: RHB-107 for outpatient use and opaganib for hospitalized patients. With these two promising and complementary shots on goal across the disease severity spectrum, RedHill is positioned at the very forefront of COVID-19 therapeutic research, aiming to address both existing and emerging mutations."

The U.S. Phase 2/3 study (NCT04723527) is aimed at evaluating treatment with RHB-107 in patients with symptomatic COVID-19 early in the course of the disease, with a simple once-daily oral treatment in an outpatient setting.

RHB-107 is a novel, potent inhibitor of serine proteases, that 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 demonstrated strong inhibition of SARS-CoV-2 viral replication in an *in vitro* human bronchial epithelial cell model and previous preclinical work demonstrated potential tissue-protective action. Previous clinical studies of RHB-107 included several Phase 1 and Phase 2 studies in different indications, demonstrating its clinical safety profile in approximately 200 patients.

"Dosing of the first patient in the Phase 2/3 study of RHB-107 in patients with symptoms but not needing hospital care, the largest COVID-19 patient group, is a key step forward in RedHill's efforts to help combat the widespread effects of this pandemic. Together with opaganib, we now have two novel, orally-administered compounds, with unique mechanisms of action, in advanced development for treating patients at different stages of COVID-19 disease," **said Terry F. Plasse MD, Medical Director at RedHill**. "The ability to treat patients early in the course of COVID-19 disease, with an oral therapy designed to be used outside the hospital, and with a compound expected to be effective against emerging viral variants, has the potential to be a game-changer in managing this disease. The ground-breaking design of the study allows us to collect data at a level previously possible only in hospital while enabling patients to stay in the comfort of their homes and decreasing exposure risk of this highly contagious disease."

This study is a 2-part, multicenter, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the safety and efficacy of RHB-107. The first part of the study is designed for dose selection and is planned to enroll 60 patients. The second part of the study is planned to enroll 250 patients and will evaluate time to sustained recovery from illness as the primary endpoint. Each patient will be tested for specific viral strain.

The study is unique in a COVID-19 trial setting in its extensive use of telemetry and electronic patient-reported outcome (ePRO) data collection and is based on the latest FDA guidance for symptom monitoring. Following the patients' initial visit to a medical facility, a research-trained nurse will make periodic home visits to study patients to collect samples for safety and virology monitoring. This innovative use of home-based safety and efficacy monitoring technologies, together with home nursing support, enables patients to participate in the study from home with the benefit of hospital-level monitoring, enhancing patient comfort and markedly decreasing the risk of SARS-CoV-2 exposure to medical staff and other members of the public.

In parallel, the late-stage development program for RedHill's second COVID-19 drug candidate, opaganib[2] in patients hospitalized with severe COVID-19, is progressing rapidly. Recently announced

top-line results from the U.S. Phase 2 study of opaganib demonstrated safety and positive efficacy data across key primary and secondary endpoints. The global Phase 2/3 study continues to enroll, having recently received a positive DSMB futility review, with top-line data and potential subsequent global emergency use authorization applications expected in the second quarter of 2021.

About RHB-107 (upamostat)

RHB-107 is a proprietary, first-in-class, orally-administered potent inhibitor of several serine proteases, with demonstrated antiviral and potential tissue-protective effects. 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 U.S. Phase 2/3 study for treatment of patients with symptomatic COVID-19 who do not require inpatient care. In addition, RHB-107 has potential in targeting cancer, inflammatory lung diseases and gastrointestinal diseases. 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 (Yeliva®, ABC294640)**, a first-in-class 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**), a 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** (**Bekinda®**), 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 enrollment in the Company's 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 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 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 opaganib in certain geographies, will not expand this study to additional countries and that it will not be successful and that enrollment will be delayed; the risk that other 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 disease that is still little understood, 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 opaganib under compassionate use programs, 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 4, 2020. 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.

Company contact:
Adi Frish
Chief Corporate & Business Development Officer
RedHill Biopharma
+972-54-6543-112
adi@redhillbio.com

Media contacts:
U.S.: Bryan Gibbs, Finn Partners
+1 212 529 2236
bryan.gibbs@finnpartners.com
UK: Amber Fennell, Consilium
+44 (0) 7739 658 783
fennell@consilium-comms.com

[1] RHB-107 (upamostat) is an investigational new drug, not available for commercial distribution in the United States.
[2] Opaganib (Yeliva®, ABC294640) 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.