RedHill Biopharma's Second COVID-19 Candidate, RHB-107, Cleared by FDA for Phase 2/3 Study in Symptomatic COVID-19 Disease

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FDA clears IND application for Phase 2/3 study with RedHill's second novel COVID-19 candidate, RHB-107 (upamostat), an orally administered novel serine protease inhibitor, with demonstrated antiviral and potential tissue-protective effects

The Phase 2/3 study is designed to evaluate outpatient-based treatment of patients with symptomatic COVID-19 disease - the vast majority of treated patients

RHB-107 has demonstrated strong inhibition of SARS-CoV-2 viral replication in a human bronchial cell model and targets a host cell component involved in viral replication, minimizing potential for resistance due to viral mutations

In parallel, RedHill is rapidly advancing its development program with opaganib in severe COVID-19 pneumonia; The U.S. Phase 2 study is fully enrolled with topline data expected within weeks, and a global Phase 2/3 study which is more than 50% enrolled, with topline data expected in Q1/2021 in support of potential emergency use applications

TEL AVIV, Israel and RALEIGH, N.C., Nov. 17, 2020 /PRNewswire/ -- RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced that the U.S. Food and Drug Administration (FDA) has cleared the Company's Investigational New Drug (IND) application for a Phase 2/3 study evaluating orally administered RHB-107 (upamostat)[1] in patients with symptomatic COVID-19 who do not require hospitalization.

"This is a significant milestone in our efforts to combat the effects of the COVID-19 pandemic. The ability to treat patients earlier in the course of COVID-19 disease, using an oral therapy that enables treatment outside of a hospital setting, is of critical importance given the large proportion of patients that are not hospitalized but are still very much at risk of disease progression," **said Terry F. Plasse MD, Medical Director at RedHill**. "With RHB-107 and opaganib[2], RedHill has two novel, late-stage, oral therapeutic candidates with potential to reduce the impact of COVID-19 disease, both of which target host cell components, potentially minimizing the likelihood of resistance due to emergence of viral mutations."

RHB-107 is a proprietary, first-in-class, orally administered potent inhibitor of several serine proteases, with demonstrated antiviral and potential tissue-protective effects. This combined antiviral and potential tissue-protective action make it a promising candidate for evaluation as a treatment for COVID-19 disease. RHB-107 has demonstrated strong inhibition of SARS-CoV-2 viral replication in an *in vitro* human bronchial cell model and its safety profile has been demonstrated in approximately 200 people, including in Phase 2 studies in oncology indications. RedHill licensed RHB-107 (formerly Mesupron) from Heidelberg Pharma AG (FWB: HPHA, formerly Wilex AG).

The randomized, parallel-group double-blind Phase 2/3 study is expected to start enrolling patients early next year. The study will enroll patients with symptomatic diagnostically confirmed COVID-19 who do not require inpatient care. RHB-107 will be administered once daily for 14 days, with patients receiving follow-up for eight weeks from first dosing. The primary endpoints will be time to recovery from symptomatic illness compared to placebo, as well as safety and tolerability of RHB-107. Several secondary and exploratory endpoints will also be assessed.

The late-stage development program for RedHill's other COVID-19 candidate, opaganib, in patients with severe COVID-19 pneumonia includes: The U.S. Phase 2 study (NCT04414618) is now fully enrolled and expected to report topline data in the coming weeks; and the global Phase 2/3 study (NCT04467840) which is more than 50% enrolled and is on track to enroll up to 270 patients and report topline data in support of potential emergency use applications in the first quarter of 2021. Both studies are randomized, double-blind, parallel-arm, placebo-controlled trials with opaganib in patients

with severe COVID-19 pneumonia requiring hospitalization and treatment with supplemental oxygen.

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. This combined antiviral and potential tissue-protective action make it a strong candidate for evaluation as a treatment for COVID-19 disease. In addition, RHB-107 has potential in targeting cancer, inflammatory lung diseases and gastrointestinal diseases, and 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 (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 with non-cancer pain[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 investigational development programs include: (i) **RHB-204**, with a planned Phase 3 study for pulmonary nontuberculous mycobacteria (NTM) disease; (ii) **opaganib (Yeliva®)**, 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-104**, with positive results from a first Phase 3 study for Crohn's disease; (iv) **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; (v) **RHB-107** (**upamostat**), a Phase 2-stage first-in-class, serine protease inhibitor, targeting cancer and inflammatory gastrointestinal diseases and is also being evaluated for COVID-19 and (vi) **RHB-106**, an encapsulated bowel preparation. More information about the Company is available at www.redhillbio.com.

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, 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 U.S. Phase 2 clinical study evaluating opaganib will not be successful and the risk that the data from this clinical study will be delayed 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 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 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.

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

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

[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.

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