Press Release

RedHill Biopharma Receives FDA Approval for COVID-19 Clinical Study with Opaganib in the U.S.

The randomized, double-blind, placebo-controlled study aims to enroll up to 40 patients with moderate-to-severe COVID-19 pneumonia in the U.S.

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All six analyzed moderate-to-severe COVID-19 patients treated with opaganib under compassionate use in Israel were weaned from oxygen and discharged from the hospital

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Opaganib's unique mechanism of action has both anti-inflammatory and anti-viral activities, targeting a critical host factor, minimizing potential development of resistance due to viral mutations

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Continued progress towards compassionate use and clinical programs in additional countries

TEL-AVIV, Israel and RALEIGH, NC, May 8, 2020, 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 approved its Investigational New Drug (IND) application for a Phase 2a clinical study evaluating its investigational drug, opaganib (Yeliva®, ABC294640)[1], in patients with confirmed moderate-to-severe SARS-CoV-2 infection (the cause of COVID-19).

Kevin Winthrop, MD, M.P.H., Professor of Infectious Diseases and Public Health at the OHSU-PSU School of Public Health and Principal Investigator of the study, said: "We are pleased to offer opaganib to hospitalized patients as part of a clinical study and are hopeful to meet the strong unmet need for treatments to decrease the severity and duration of respiratory symptoms due to COVID-19."

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

Mark L. Levitt, MD, Ph.D., Medical Director at RedHill, added: "We are grateful to the FDA for the timely review of our IND and look forward to initiating the study. There is a strong scientific rationale for the potential efficacy of opaganib in the treatment of COVID-19, including pre-clinical data demonstrating that opaganib may inhibit viral replication and reduce levels of IL-6 and TNF-alpha, important mediators of inflammation that are elevated in moderate-to-severe COVID-19 patients. This is coupled with encouraging preliminary data from the compassionate use program in Israel, which demonstrated objective measurable clinical improvement in all six patients analyzed, including a decrease in required supplemental oxygenation, higher lymphocyte counts, and decreased CRP levels."

A total of 139 subjects have been dosed with opaganib to date in ongoing and completed Phase 1 and Phase 2 clinical studies in oncology indications, in pharmacokinetic studies in healthy volunteers in the U.S., under the existing FDA-approved expanded access requests from physicians for individual oncology patients and under expanded access for COVID-19 patients in Israel, establishing safety and tolerability in humans both in the U.S. and ex-U.S.

The randomized, double-blind, placebo-controlled Phase 2a study aims to enroll up to 40 patients with moderate-to-severe SARS-CoV-2 infection and pneumonia requiring hospitalization and supplemental oxygenation. The Company expects to promptly initiate patient enrollment. Patients will be randomized at a 1:1 ratio to receive either opaganib or placebo on-top of standard-of-care. The primary objective of the study is to evaluate the reduction in total oxygen requirement over the course of treatment for up to 14 days. Secondary endpoints include time to 50% reduction in oxygen requirements, the proportion of patients without fever at Day 14, and proportion with negative nasal swabs at Day 14. This clinical trial is not powered for statistical significance.

Preliminary findings from six moderate-to-severe COVID-19 patients treated with opaganib in Israel under compassionate use have shown that all the patients demonstrated both subjective and objective significant measurable clinical improvement within days following treatment initiation with opaganib, including decreased required supplemental oxygenation, higher lymphocyte counts and decreased C-reactive protein (CRP) levels. All six patients analyzed were weaned from oxygen and discharged from the hospital. Opaganib has been well tolerated and showed clinical improvement both with and without hydroxychloroquine. At the time of treatment initiation, all of the patients were hospitalized, suffered from moderate-to-severe acute respiratory symptoms related to SARS-CoV-2 infection, were hypoxic, and required supplemental oxygen while being treated with standard-of-care, mostly hydroxychloroquine.

To find out more about RedHill Biopharma's Expanded Access policy, please visit: www.redhillbio.com/expandedaccess.

Pre-clinical data have demonstrated both anti-inflammatory and anti-viral activities of opaganib, with the potential to reduce lung inflammatory disorders, such as pneumonia, and mitigate pulmonary

fibrotic damage. Several prior pre-clinical studies support the potential role of sphingosine kinase-2 (SK2) in the replication-transcription complex of positive-strand single-stranded RNA viruses, similar to coronavirus, and its inhibition may potentially inhibit viral replication. Pre-clinical *in vivo* studies[2] have demonstrated that opaganib decreased fatality rates from influenza-virus infection and ameliorated *Pseudomonas aeruginosa*-induced lung injury by reducing the levels of IL-6 and TNF-alpha in bronchoalveolar lavage fluids.

About Opaganib (ABC294640, Yeliva®)

Opaganib, a new chemical entity, is a proprietary, first-in-class, orally-administered, sphingosine kinase-2 (SK2) selective inhibitor with anticancer, anti-inflammatory and anti-viral activities, targeting multiple oncology, inflammatory and gastrointestinal indications. By inhibiting SK2, opaganib blocks the synthesis of sphingosine 1-phosphate (S1P), a lipid-signaling molecule that promotes cancer growth and pathological inflammation. By inhibiting SK2, opaganib potentially blocks viral replication complex and pathological inflammation. Opaganib was originally developed by U.S.-based Apogee Biotechnology Corp. and completed multiple successful pre-clinical studies in oncology, inflammation, GI and radioprotection models, as well as a Phase 1 clinical study in cancer patients with advanced solid tumors. Opaganib received Orphan Drug designation from the U.S. FDA for the treatment of cholangiocarcinoma and is being evaluated in a Phase 1/2a in advanced cholangiocarcinoma and in a Phase 2 study in prostate cancer. Opaganib is also being evaluated for the treatment of coronavirus (COVID-19). The development of opaganib has been supported by grants and contracts from U.S. federal and state government agencies awarded to Apogee Biotechnology Corp., including from the NCI, BARDA, the U.S. Department of Defense and the FDA Office of Orphan Products Development.

About RedHill Biopharma

RedHill Biopharma Ltd. (Nasdaq: RDHL) is a specialty biopharmaceutical company primarily focused on gastrointestinal 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-104**, with positive results from a first Phase 3 study for Crohn's disease; (ii) **RHB-204**, with a planned pivotal Phase 3 study for pulmonary nontuberculous mycobacteria (NTM) infections; (iii) **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; (iv) **Opaganib (Yeliva®)**, a first-in-class SK2 selective inhibitor, targeting multiple

[2] Xia C. et al. Transient inhibition of sphingosine kinases confers protection to influenza A virus infected mice. Antiviral Res. 2018 Oct; 158:171-177. Ebenezer DL et al. Pseudomonas aeruginosa stimulates nuclear sphingosine-1-phosphate generation and epigenetic regulation of lung inflammatory injury. Thorax. 2019 Jun;74(6):579-591.

[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.

indications, with an ongoing Phase 1/2a study for cholangiocarcinoma and a development program for COVID-19; (v) **RHB-106**, an encapsulated bowel preparation, and (vi) **RHB-107**, a Phase 2-stage first-in-class, serine protease inhibitor, targeting cancer and inflammatory gastrointestinal diseases. 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, including forward-looking statements regarding the preliminary findings from the treatment of COVID-19 patients with opaganib, the Company's discussions to increase the accessibility of opaganib under compassionate use program authorizations as well as potential emergency clinical development programs. The treatment with opaganib in Israel is administered under a compassionate use program in accordance with the Israeli Ministry of Health guidelines. The findings to date are only preliminary, are based on clinical results of a very limited number of patients, and are not part of a clinical study. There is no guarantee that these patients will continue to show clinical improvement or that other patients will show similar clinical improvement. 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 clinical condition of the patients treated with opaganib will not continue to improve and may worsen, the risk that other COVID-19 patients treated with opaganib will not show any clinical improvement, the risk that clinical trials of opaganib in the U.S., Israel, Italy or elsewhere for the treatment of COV-19, if conducted at all, will not show any improvement in patients, 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 the compassionate use programs 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 or 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® and Movantik®; (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 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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