Press Release

RedHill Biopharma Announces Positive Recommendation from Independent Committee to Continue U.S. Phase 2 COVID-19 Study, and Approval of COVID-19 Phase 2/3 Study in Italy

A pre-scheduled independent Safety Monitoring Committee (SMC) has recommended that the U.S. Phase 2 COVID-19 study with opaganib continue with no changes; the study is more than 50% enrolled and enrollment is planned to be completed in the coming weeks

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The global Phase 2/3 COVID-19 study with opaganib, being conducted in parallel to the U.S. Phase 2 study, received approval in Italy; this study has also been approved in the UK, Russia and Mexico, and is under review in additional countries

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The first patients have been enrolled in the global Phase 2/3 study with opaganib, which is set to enroll up to 270 patients hospitalized with severe COVID-19 pneumonia across up to 40 clinical sites

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Potential submission of global emergency use applications as early as Q4/2020

TEL AVIV, Israel and RALEIGH, NC, August 27, 2020, RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced that its U.S. Phase 2 study with opaganib (Yeliva®, ABC294640)[1] in patients hospitalized with severe COVID-19 pneumonia, has successfully passed the first scheduled independent Safety Monitoring Committee (SMC) review. The SMC reviewed unblinded safety data from the first 12 patients treated for at least seven days, recommending that the study continue without change. The study is more than 50% enrolled and enrollment is expected to be completed in the coming weeks. The next scheduled SMC review will take place once 24 patients complete at least seven days of treatment.

The Company also announced it has received approval from the Italian Medicines Agency (AIFA) for its Clinical Trial Authorization (CTA) application for the global Phase 2/3 study evaluating opaganib in patients hospitalized with severe COVID-19 pneumonia, for which patient enrollment has already commenced.

"The independent SMC's recommendation to continue the U.S. Phase 2 COVID-19 study without changes is another important step in advancing opaganib as a potential therapy for patients with severe COVID-19. The SMC recommendation further validates the general safety database that we have from treating patients with opaganib, which now numbers more than 140," **said Gilead Raday, RedHill's Chief Operating Officer**. "In parallel, enrollment of the first patients in our global Phase 2/3 study, together with approval for the study in Italy, are additional encouraging steps in our efforts to provide patients with an urgently needed treatment option. Subject to positive data from the studies, we aim to apply for emergency use authorizations as early as the fourth quarter of this year."

To date, the global Phase 2/3 study has been approved in the UK, Italy, Russia and Mexico, with review ongoing in additional countries and further expansion planned. The multi-center, randomized, double-blind, parallel-arm, placebo-controlled Phase 2/3 study (NCT04467840) is set to enroll up to 270 patients with severe COVID-19 pneumonia requiring hospitalization and treatment with supplemental oxygen. Subjects are randomized at a 1:1 ratio to receive either opaganib or placebo, in addition to standard-of-care therapy. The primary endpoint of the study is to evaluate the proportion of patients requiring intubation and mechanical ventilation by Day 14. An unblinded futility interim analysis will be conducted by an independent data safety monitoring board (DSMB) when approximately 100 subjects have been evaluated for the primary endpoint.

The U.S. Phase 2 clinical study with opaganib, which is not powered for statistical significance, is a randomized, double-blind, placebo-controlled study (NCT04414618), set to enroll up to 40 patients with severe COVID-19 pneumonia requiring hospitalization and supplemental oxygen.

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, viral, inflammatory, and gastrointestinal indications. By inhibiting SK2, opaganib impacts multiple cellular pathways which are associated with cancer growth, viral replication, and pathological inflammation.

Opaganib was originally developed by U.S.-based Apogee Biotechnology Corp. and completed multiple successful preclinical 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 2a study in advanced cholangiocarcinoma and in a Phase 2 study in prostate cancer. Opaganib is also being evaluated for the treatment of coronavirus (COVID-19).

Results from the treatment of the first patients with severe COVID-19 with opaganib have recently been published[2]. Analysis of treatment outcomes in five patients with severe COVID-19 showed substantial benefit to patients treated with opaganib under compassionate use in both clinical outcomes and inflammatory markers as compared to a retrospective matched case-control group from the same hospital. All patients in the opaganib-treated group were discharged from hospital without requiring mechanical ventilation, whereas 33% of the matched case-control group required mechanical ventilation. Median time to weaning from high-flow nasal cannula was reduced to 10 days in the opaganib-treated group, as compared to 15 days in the matched case-control group.

Preclinical 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 preclinical studies support the potential role of SK2 in the replication-transcription complex of positive-sense single-stranded RNA viruses, similar to coronavirus, and its inhibition may potentially inhibit viral replication. Preclinical *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.

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-204**, with a planned pivotal Phase 3 study for pulmonary nontuberculous mycobacteria (NTM) infections; (ii) **opaganib (Yeliva®)**, a first-in-class SK2 selective inhibitor targeting multiple indications with a Phase 2/3 program for COVID-19 and ongoing Phase 2 studies for prostate cancer and cholangiocarcinoma; (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-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 and is

also being evaluated for COVID-19. 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 the U.S. Phase 2 clinical study evaluating opaganib will not be successful and the risk that completion of enrollment for this clinical study will be delayed; the risk that the Company will not initiate the Phase 2/3 study in certain geographies, will not expand this study in additional countries and that it will not be successful; the risk that other COVID-19 patients treated with opaganib will not show any clinical improvement; the risk that clinical trials with opaganib in Israel, the U.S., Italy, Russia, the UK, Mexico or elsewhere for the treatment of COVID-19, if conducted at all, will not show any improvement in patients; the risk of a delay in applying for emergency use authorizations; 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 or the development of a commercial companion diagnostic for the detection of Mycobacterium avium subspecies paratuberculosis (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 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 experiences 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] Opaganib is an investigational new drug, not available for commercial distribution.
[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.