Press Release

RedHill Biopharma Expands Opaganib COVID-19 Phase 2/3 Study with Clinical Trial Applications in Italy and UK

The multi-center, randomized, double-blind, parallel-arm, placebo-controlled Phase 2/3 clinical study with opaganib in 270 severe COVID-19 patients is planned to be conducted in up to 40 clinical sites across Russia, Italy, the UK and additional countries

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In parallel, a clinical study of opaganib in up to 40 severe COVID-19 patients has been approved by the FDA and is open for recruitment in the U.S.

TEL-AVIV, Israel and RALEIGH, NC, June 18 2020, RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced that it has submitted Clinical Trial Applications (CTA) with the UK Medicines & Healthcare Products Regulatory Agency (MHRA) and the Italian Medicines Agency (AIFA) for a Phase 2/3 clinical study evaluating opaganib (Yeliva®, ABC294640)[1] in patients hospitalized with severe SARS-CoV-2 infection, the cause of COVID-19, and pneumonia.

Mark L. Levitt, M.D., Ph.D., Medical Director at RedHill, said: "We are quickly advancing the preparations for a global, multi-center powered Phase 2/3 study with opaganib for COVID-19. In line with the global shift from a focus on compassionate use programs to adequately controlled clinical studies, our highest priority is on generating robust data in a controlled setting for regulatory purposes. Following our submission of the Clinical Trial Application in Russia last week, we have submitted similar applications in the UK and Italy, and we are looking to expand the study to additional countries and start treating patients soon. This study, along with the ongoing Phase 2a study in the U.S., should allow us to enroll patients faster to evaluate the efficacy of opaganib against COVID-19 and bring this promising therapy one step closer to those who need it."

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

The multi-center, randomized, double-blind, parallel-arm, placebo-controlled Phase 2/3 study is planned to enroll up to 270 subjects with severe COVID-19 pneumonia requiring hospitalization and treatment with supplemental oxygen. Subjects will be randomized at a 1:1 ratio to receive either opaganib or placebo, on top of 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 when approximately 100 subjects have been evaluated for the primary endpoint.

The Company currently plans to conduct the study in up to 40 clinical sites across Russia, Italy, the UK and additional countries.

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

The Company previously announced encouraging preliminary findings from six COVID-19 patients requiring high-flow supplemental oxygen treated with opaganib in Israel under compassionate use. All six patients analyzed demonstrated pronounced clinical improvement following treatment initiation with opaganib, substantial improvement in biomarkers, including decreased required supplemental oxygen, higher lymphocyte counts and decreased C-reactive protein (CRP) levels. All six patients analyzed were weaned from supplemental oxygen and discharged from the hospital on room air without having to receive mechanical ventilation.

To date, a total of 141 subjects have been dosed with opaganib 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 U.S. Food and Drug Administration (FDA) approved expanded access requests for oncology patients and under the expanded access for COVID-19 patients in Israel, establishing safety and tolerability in humans both in the U.S. and ex-U.S.

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.

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 SK2 in the replication-transcription complex of positive-strand single-stranded RNA viruses, similar to SARS-CoV-2, 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.

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 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 is also being evaluated for the treatment of SARS-CoV-2 infection (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-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. 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,"

[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.

"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 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. 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, the clinical condition of the patients treated with opaganib will not continue to improve and may worsen, the risk that the U.S. Phase 2a clinical study evaluating opaganib will not be successful; the risk that the Company will not initiate a the Phase 2/3 study in Russia, Italy and the UK and will not expand this study to a multinational study with sites in additional countries, the risk that other COVID-19 patients treated with opaganib will not show any clinical improvement, the risk that clinical trials of opaganib in Israel, the U.S., Russia, Italy, the UK or elsewhere for the treatment of COVID-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 other 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 commercial products; (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 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; (xiv) competition from other companies and technologies within the Company's industry; and (xv) the hiring and maintaining employment 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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