Press Release

RedHill Biopharma Receives Approval for Phase 2/3 COVID-19 Study in Russia

Clinical Trial Application approved in Russia for the Phase 2/3 study with opaganib in severe COVID-19 patients following recent approval in the UK and similar submission in Italy

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The Phase 2/3 study aims to enroll 270 subjects in up to 40 clinical sites; enrollment planned to be initiated later this month with potential submission of Emergency Use Authorization application planned for Q4/2020

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In parallel, the U.S. Phase 2a study with opaganib in patients with severe COVID-19 is advancing rapidly with more than 25% of patients enrolled

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Approval also received for a clinical study with opaganib in Israel in up to 50 patients with severe COVID-19

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Treatment of patients with severe COVID-19 under compassionate use showed substantial benefit to such patients compared to a matched case-control group

TEL-AVIV, Israel and RALEIGH, NC, July 16, 2020, RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced approval from the Ministry of Health of the Russian Federation for its Clinical Trial Authorization (CTA) application for a Phase 2/3 study evaluating opaganib (Yeliva®, ABC294640)[1] in patients hospitalized with severe SARS-CoV-2 infection (the cause of COVID-19) and pneumonia. The study was also recently approved in the UK and a similar application is under review in Italy with plans to further expand the study to additional countries.

"We are rapidly advancing the clinical development program with opaganib for COVID-19 and, if successful, plan to submit an application for Emergency Use Authorization in the fourth quarter this year. The Phase 2/3 study with opaganib in patients with severe COVID-19 has already received

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

regulatory approvals in two countries and we are expanding the study to additional countries," **said Gilead Raday, RedHill's Chief Operating Officer.** "With planned initiation of the Phase 2/3 study later this month and with over 25% enrollment in the U.S. Phase 2a study, RedHill is well-positioned at the forefront of the race to bring novel potential beneficial therapies to hospitalized COVID-19 patients."

The multi-center, randomized, double-blind, parallel-arm, placebo-controlled Phase 2/3 study is set to enroll up to 270 patients 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, along with 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 only 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 Company further announced that it has received approval from the Israeli Ministry of Health to initiate a study evaluating opaganib in up to 50 patients with severe COVID-19 infection and pneumonia.

Enrollment is also ongoing for a randomized, double-blind, placebo-controlled Phase 2a clinical study with opaganib in the U.S. (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.

RedHill recently announced that results from the treatment with opaganib of the first patients with severe COVID-19 have 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.

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,

[2] The article was authored by Ramzi Kurd, MD, Shaare-Zedek Medical Center; Eli Ben-Chetrit, MD, Shaare-Zedek Medical Center and Hebrew University Faculty of Medicine; Hani Karameh MD, Shaare-Zedek Medical Center and Maskit Bar-Meir, MD, Shaare-Zedek Medical Center and Hebrew University Faculty of Medicine. See full text here: https://www.medrxiv.org/content/10.1101/2020.06.20.20099010v1?rss=1.

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 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 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).

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-sense single-stranded RNA viruses, similar to coronavirus, and its inhibition may potentially inhibit viral replication. Pre-clinical *in vivo* studies[3] 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[4], **Talicia®** for the treatment of *Helicobacter pylori (H. pylori)* infection in adults[5] and **Aemcolo®** for the treatment of travelers' diarrhea in adults[6]. 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

[3] 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.

[4] Full prescribing information for Movantik® (naloxegol) is available at: www.Movantik.com.

[5] Full prescribing information for Talicia® (omeprazole magnesium, amoxicillin and rifabutin) is available at: www.Talicia.com.

[6] Full prescribing information for Aemcolo® (rifamycin) is available at: www.Aemcolo.com.

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 clinical condition of the patients treated with opaganib will not continue to improve and may worsen, the risk that the U.S. and Israel Phase 2a clinical studies evaluating opaganib will not be successful; the risk that the Company will not initiate the Phase 2/3 study in the UK, Russia or Italy 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 with opaganib in Israel, the U.S., Russia, the UK, Italy 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 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 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, 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; 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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