Press Release

Six COVID-19 Patients Treated with RedHill's Opaganib Under Compassionate Use Show Objective Clinical Improvement

Preliminary data in moderate-to-severe COVID-19 patients treated with opaganib show measurable clinical improvement in all six patients analyzed, including decreased requirement for supplemental oxygenation, higher lymphocyte counts and decreased CRP

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Five of the six patients have been weaned from oxygen altogether, the sixth patient continues to improve, and three out of the six were discharged from the hospital

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Opaganib has been well tolerated and no patient required mechanical ventilation following treatment with opaganib

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

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IND submitted to the FDA for a randomized clinical study in COVID-19 patients in the U.S.; Clinical studies also planned in Israel and Italy; discussions ongoing for compassionate use and clinical programs in additional countries

TEL-AVIV, Israel and RALEIGH, N.C., April 27, 2020, RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today provided an additional update on the compassionate use program with its investigational drug, opaganib (Yeliva®, ABC294640)[1], in patients with confirmed SARS-CoV-2 infection (the cause of COVID-19) in Israel.

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 and were treated with standard-

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

of-care (mostly hydroxychloroquine). All patients required supplemental oxygenation and were hypoxic despite being treated with supplemental oxygen.

Preliminary findings from all six patients analyzed have shown that all the patients demonstrated objective significant measurable clinical improvement within days following treatment initiation with opaganib, including a decrease in required supplemental oxygenation, higher lymphocyte counts, a sign of improvement from virus-induced lymphopenia, and decreased C-reactive protein (CRP) levels, an important inflammatory biomarker correlated with lung lesions which could reflect disease severity[2]. Opaganib was well tolerated and showed clinical improvement both with and without hydroxychloroquine.

Five of the six patients analyzed were weaned from oxygen, and three were discharged from the hospital within days of treatment initiation. The 6th patient, whose therapy was initiated more recently, is improving. To date, two patients have safely completed 14 days of opaganib therapy, which has been well tolerated.

A 7th patient who was treated with hydroxychloroquine and azithromycin suffered from side effects of diarrhea, which resolved quickly following cessation of all therapies. This patient received only 1 day of opaganib dosing and therefore was not included in this analysis.

"These preliminary findings are highly encouraging, show clinical improvement in the first COVID-19 patients treated with opaganib and provide preliminary support for the tolerability of opaganib and its potential efficacy in COVID-19 patients," **said Mark L. Levitt, MD, Ph.D., Medical Director at RedHill.** "We have submitted to the FDA an application to initiate a clinical study with opaganib in the U.S. and are also working on expanding access to opaganib through compassionate use and clinical programs in additional countries."

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

RedHill recently announced that it has submitted an Investigational New Drug (IND) application to the FDA to evaluate the safety and efficacy of opaganib in a randomized, double-blind, placebo-controlled Phase 2a study in patients hospitalized with positive SARS-CoV-2 and pneumonia in the U.S.

A total of 131 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., and under the existing FDA-approved expanded access requests from physicians for

[2] Ling W. C-reactive protein levels in the early stage of COVID-19. Med Mal Infect. 2020 Mar 31. pii: S0399-077X(20)30086-X.

individual oncology patients, establishing safety and tolerability in humans both in the U.S. and ex-U.S.

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[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.

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-viral and anti-inflammatory 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) in confirmed COVID-19 patients in Israel. 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

[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.

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 oncology, inflammatory and gastrointestinal indications, with an ongoing Phase 1/2a study for cholangiocarcinoma; (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 and the Company's discussions to increase the accessibility of opaganib under compassionate use program authorizations 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 the Company will not expand access to opaganib under compassionate use and clinical development programs in other territories, 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., 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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