Press Release

Publication of Data from Severe COVID-19 Patients Shows Substantial Benefit to Patients Treated with RedHill's Opaganib Compared to Matched Case-Control Group

Analysis of treatment outcomes in five severe COVID-19 patients showed substantial benefit to patients treated with opaganib under compassionate use in both clinical outcomes and inflammatory markers as compared to a matched case-control group from the same hospital

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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

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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

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

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A randomized, double-blind, placebo-controlled study with opaganib in up to 40 patients with severe COVID-19 initiated at leading medical centers across the U.S.

TEL-AVIV, Israel and RALEIGH, NC, June 24 2020, RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced that results from the treatment of the first severe COVID-19 patients with its investigational drug, opaganib (Yeliva®, ABC294640)[1], have been published in medRxiv.

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

The article[2], entitled 'Compassionate Use of Opaganib For Patients with Severe COVID-19' was published under an expedited process and is available publicly.

Mark L. Levitt, M.D., Ph.D., Medical Director at RedHill, stated: "We are very encouraged by the analysis from severe COVID-19 patients treated with opaganib to date, demonstrating substantial benefit to patients in both clinical outcomes and inflammatory markers as compared to a matched case-control group. This data further supports our intensive efforts to rapidly advance the development of opaganib via the recently initiated Phase 2a clinical study under IND with the FDA and the Phase 2/3 study in European and other countries which we expect to initiate shortly, as well as through ongoing and planned compassionate use programs."

Seven patients with severe[3] COVID-19 were treated with opaganib under compassionate use in a leading hospital in Israel. Prior to treatment initiation, these patients were hospitalized and required treatment with supplemental oxygen via high-flow nasal cannula while being treated with standard-of-care. Opaganib was given on top of standard-of-care therapy. Five patients were included in the final published analysis[4] of the active arm. An investigator-selected matched case-control group of patients with similar baseline characteristics at the same hospital was identified for comparison (n=18).

A comparison of outcomes between patients treated with opaganib and the matched case-controls treated with standard-of-care alone for both clinical and inflammatory measures revealed:

- All patients in the opaganib-treated group were discharged from hospital on room air, without having required mechanical ventilation, whereas 33% of patients in the 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 control group.
- Improvement in lymphocyte counts was faster in opaganib-treated patients as compared to patients in the control group.

[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.

[3] Definition based on U.S. Food and Drug Administration (FDA) guidance published on May 12, 2020.

[4] Of the six patients who received more than one day of opaganib, one patient improved rapidly and was discharged from the hospital after only two doses. Hence, five patients who were administered more than one day of opaganib were included in the active group. A seventh patient was started on hydroxychloroquine, azithromycin and opaganib within 24 hours, and had all 3 drugs stopped due to diarrhea after only one day of treatment with opaganib. Eighteen matched case-controls (same sex, same severity and similar background medication) from the treating hospital were retrospectively identified.

- C-reactive protein (an inflammatory marker) showed faster improvement in the opaganib treated group as compared to the control group.

- In this cohort of severe COVID-19 patients, opaganib was found safe and well tolerated and improvement in clinical and laboratory parameters was demonstrated for opaganib-treated patients compared to matched case-controls.

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

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.

In parallel, the Company has submitted Clinical Trial Applications (CTA) in Russia, Italy and the UK for a multi-center, randomized, double-blind, parallel-arm, placebo-controlled Phase 2/3 study with opaganib in patients hospitalized with severe COVID-19. This study is planned to commence shortly and enroll up to 270 subjects across up to 40 clinical sites in these European and other countries.

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 coronavirus, and its inhibition may potentially inhibit viral replication. Pre-clinical *in vivo* studies[5] 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.

[5] 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.

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[6], **Talicia®** for the treatment of *Helicobacter pylori (H. pylori)* infection in adults[7] and **Aemcolo®** for the treatment of travelers' diarrhea in adults[8]. 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," "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.

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

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

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

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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