Press Release

RedHill Biopharma Announces Last Patient Out for Phase 2/3 COVID-19 Study of Oral Opaganib

Patient follow-up completed for the 475-patient global Phase 2/3 study of oral opaganib for severe COVID-19

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Top-line results expected in the coming weeks

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Opaganib, a novel, dual antiviral and anti-inflammatory investigational COVID-19 pill, demonstrated potent inhibition of Beta and Gamma variants and is expected to be effective against emerging variants, including Delta and Delta Plus

TEL AVIV, Israel and RALEIGH, NC, July 19, 2021, RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty pharma company that is a leader in the development of novel oral therapies for COVID-19, today announced that all treatment and follow-up has now been completed in the 475-patient global Phase 2/3 study with opaganib (ABC294640)[1] in patients hospitalized with severe COVID-19 pneumonia (NCT04467840). Top-line results are expected in the coming weeks.

Opaganib is a novel, host-targeted, dual antiviral and anti-inflammatory investigational pill in advanced clinical development for the treatment of severe COVID-19. Opaganib recently demonstrated potent *in vitro* inhibition of the *Beta* (South African) and *Gamma* (Brazilian) variants and based on its unique host-targeted mechanism and the preliminary results from this study, we believe opaganib is likely to also maintain its activity against emerging variants, including *Delta* and *Delta Plus*. Positive U.S. Phase 2 efficacy data has also previously been announced.

"Emerging data is showing that variants are capable of evading vaccines' effects. Not only does this threaten efforts to control the pandemic, but it also brings into sharp focus the urgent need for effective oral COVID-19 therapies capable of working despite the emergence of variants. This makes the completion of this study even more significant, given its potential to be a game-changer in the

treatment of COVID-19," **said Mark L. Levitt, MD, Ph.D., Medical Director at RedHill**. "We can now concentrate on getting all the data collected, cleaned and collated in the database ready for analysis and subsequent reporting. This means we are weeks away from knowing if we are a big step closer to having a paradigm-shifting oral therapy for hospitalized COVID-19 patients."

The primary endpoint of the global Phase 2/3 study, approved in 10 countries, is the proportion of patients breathing room air without oxygen support by Day 14. The study has also captured additional important outcome measures, such as the time to hospital discharge, improvement according to the World Health Organization Ordinal Scale for Clinical Improvement and incidence of intubation and mortality.

Evaluations of blinded blended intubation and mortality rates from the Phase 2/3 study have been encouraging compared to reported rates of mortality from large platform studies such as RECOVERY, and other studies in similar patient populations[2]. Furthermore, four independent DSMB recommendations to continue the study have been received following three unblinded safety reviews and an unblinded futility analysis. Additionally, encouraging use of opaganib under compassionate use exemption has been experienced in Israel and Switzerland.

The Company maintains ongoing discussions with the FDA, EMA and other regulators, on potential pathways to approval, with next steps to be guided by study results. Discussions are also ongoing with potential partners who are interested in the rights to opaganib in various countries.

About Opaganib (ABC294640[3])

Opaganib, a new chemical entity, is a proprietary, first-in-class, orally-administered, sphingosine kinase-2 (SK2) selective inhibitor, with dual anti-inflammatory and antiviral activity, that is host-targeted and is therefore expected to be effective against emerging viral variants. Opaganib has also shown anticancer activity and has the potential to target multiple oncology, viral, inflammatory, and gastrointestinal indications.

Opaganib is being evaluated as a treatment for COVID-19 pneumonia in a global Phase 2/3 study that has now completed patient treatment and follow-up. Opaganib has also demonstrated positive safety and efficacy signals in preliminary top-line data from a 40-patient U.S. Phase 2 study.

Opaganib has also 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 demonstrated potent antiviral activity against SARS-CoV-2, the virus that causes COVID-19, completely inhibiting viral replication in an *in vitro* model of human lung bronchial tissue. Additionally, preclinical *in vivo* studies have demonstrated opaganib's potential to ameliorate inflammatory lung disorders, such as pneumonia, and have shown decreased fatality rates from

influenza virus infection and amelioration of *Pseudomonas aeruginosa*-induced lung injury by reducing the levels of IL-6 and TNF-alpha in bronchoalveolar lavage fluids[4].

The ongoing studies with opaganib are registered on www.ClinicalTrials.gov, a web-based service by the U.S. National Institute of Health, which provides public access to information on publicly and privately supported clinical studies.

About RedHill Biopharma

RedHill Biopharma Ltd. (Nasdaq: RDHL) is a specialty biopharmaceutical company primarily focused on gastrointestinal and infectious diseases. RedHill promotes the gastrointestinal drugs, **Movantik®** for opioid-induced constipation in adults[5], **Talicia®** for the treatment of *Helicobacter pylori (H. pylori)* infection in adults[6], and **Aemcolo®** for the treatment of travelers' diarrhea in adults[7]. RedHill's key clinical late-stage development programs include: (i) **RHB-204**, with an ongoing Phase 3 study for pulmonary nontuberculous mycobacteria (NTM) disease; (ii) **opaganib (ABC294640)**, a first-in-class SK2 selective inhibitor targeting multiple indications with positive Phase 2 COVID-19 data and an ongoing Phase 2/3 program for COVID-19 and Phase 2 studies for prostate cancer and cholangiocarcinoma ongoing; (iii) **RHB-107 (upamostat)**, a serine protease inhibitor in a U.S. Phase 2/3 study as treatment for symptomatic COVID-19, and targeting multiple other cancer and inflammatory gastrointestinal diseases; (iv) **RHB-104**, with positive results from a first Phase 3 study for Crohn's disease; (v) **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; and (vi) **RHB-106**, an encapsulated bowel preparation. More information about the Company is available at www.redhillbio.com / https://twitter.com/RedHillBio.

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 the delay in top-line data from the Phase 2/3 COVID-19 study for opaganib, that the Phase 2/3 COVID-19 study for opaganib may not be successful and, even if successful, such study and results may not be sufficient for regulatory applications, including emergency use or marketing applications, and that additional COVID-19 studies for opaganib are likely to be required by regulatory authorities to support such potential applications and the use or marketing of opaganib for COVID-19 patients, that opaganib will not be effective against emerging viral variants, 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 (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 events 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 18, 2021. 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] Based on preliminary blinded blended data from 463 patients. The Company did not conduct a head-to-head comparison study in the same patient population. The theoretical comparison between the global Phase 2/3 study with opaganib and

reported rates of mortality from large platform studies such as RECOVERY, and other studies in similar patient populations, serves as a general benchmark and should not be construed as a direct and/or applicable comparison as if the Company conducted a head-to-hear comparison study.

[3] Yeliva remains the prospective brand name for opaganib

[4] 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.

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

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

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