Press Release

RedHill Biopharma's Opaganib Demonstrates Strong Inhibition of COVID-19 *Delta* Variant

Opaganib demonstrated strong inhibition of COVID-19 Delta variant in a human bronchial epithelial cells model, adding to prior data demonstrating potent inhibition of all COVID-19 variants tested to date

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Opaganib's unique, host-targeted, dual antiviral and anti-inflammatory approach to combatting COVID-19 is expected to maintain effect against other emerging variants

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The global 475-patient Phase 2/3 study with opaganib oral pill in hospitalized COVID-19 patients has completed treatment and follow up phase, with top-line results upcoming

TEL AVIV, Israel and RALEIGH, NC, August 26, 2021, RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced preliminary results of a new preclinical study showing strong inhibition by opaganib (ABC294640)[1] of *Delta* variant replication while maintaining cell viability at relevant concentrations.

Working with the University of Louisville Center for Predictive Medicine, opaganib was studied in a 3D tissue model of human bronchial epithelial cells (EpiAirway™) to evaluate the *in vitro* efficacy of opaganib in inhibiting the *Delta* (Indian) variant. This work adds to the previously reported work that showed opaganib also inhibits *Alpha* (Washington), *Beta* (South African) and *Gamma* (Brazilian) SARS-CoV-2 variants.

"There is growing evidence in support of the possible key role played by sphingosine kinase-2 in the replication of RNA viruses such as SARS-CoV-2, irrespective of mutations at the spike protein. This makes inhibition of this intra-cellular enzyme a promising therapeutic target for treating COVID-19 disease," **said Reza Fathi, PhD., RedHill's Senior VP, R&D**. "We have now accumulated extensive evidence from our preclinical work of opaganib's potent ability to inhibit SARS-CoV-2 variants of

concern, such as Delta, and expect that to extend to new emerging variants. The strong antiviral and anti-inflammatory activities of oral opaganib potentially address both the viral cause and inflammatory effects of COVID-19."

Opaganib, a leading novel small molecule investigational oral pill in development for the treatment of COVID-19, is a unique host targeted, dual antiviral and anti-inflammatory drug that acts on the cause and effect of COVID-19. It is believed to exert its antiviral effect by selectively inhibiting sphingosine kinase-2 (SK2), a key enzyme produced in human cells that may be recruited by the virus to support its replication. Opaganib's global 475-patient Phase 2/3 study in hospitalized patients with COVID-19 has completed its treatment and follow up phase, and study top-line results are upcoming.

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, the opaganib Phase 2/3 study has also passed four Data Safety Monitoring Board reviews, including a futility review, and extends the total opaganib safety database to more than 460 patients. Opaganib previously delivered positive U.S. Phase 2 data in patients with severe COVID-19, presented in June at the World Microbe Forum (WMF) 2021. Additionally, encouraging use of opaganib under compassionate use exemption has been experienced in Israel and Switzerland.

About Opaganib (ABC294640)

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. Opaganib is host-targeted and is expected to be effective against emerging viral variants, having already demonstrated strong inhibition against variants of concern, including *Delta*. 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 completed patient treatment and follow-up, with top-line results upcoming. Opaganib previously delivered positive U.S. Phase 2 data in patients with severe COVID-19, presented in June at the World Microbe Forum (WMF) 2021.

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, 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[3].

The ongoing clinical 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, **Talicia®** for the treatment of *Helicobacter pylori (H. pylori)* infection in adults, and **Aemcolo®** for the treatment of travelers' diarrhea in adults. 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 oral SK2 selective inhibitor targeting multiple indications with a Phase 2/3 program for COVID-19 and Phase 2 studies for prostate cancer and cholangiocarcinoma ongoing; (iii) **RHB-107** (**upamostat**), an oral 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** , 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-head comparison study.

[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.