NEWS RELEASE

RedHill Biopharma's Oral Opaganib Significantly Improves Viral Clearance in Phase 2/3 Study in Severely Ill Hospitalized COVID-19 Patients

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- In a prespecified analysis of all Phase 2/3 study patients with positive PCR at screening, opaganib improved the median time to viral RNA clearance by at least 4 days; Median of 10 days for viral clearance in the opaganib arm vs. clearance median not reached by end of 14-day treatment in placebo arm (Hazard Ratio 1.34; nominal p-value=0.043, N=437/463)

- Opaganib is the first oral novel drug candidate to show improved viral RNA clearance in patients with severe COVID-19 pneumonia; Provides clinical evidence supporting opaganib's potential antiviral activity

- Results achieved in a severely ill hospitalized patient population with a median of 11-days from onset of symptoms - a patient population much further advanced than mild-moderate outpatients with less than 5 days from symptom onset, for which oral anti-viral medications have recently been approved

- Results add to opaganib's 62% reduction in mortality seen in a post-hoc analysis of the Phase 2/3 study and are being provided to regulators as part of ongoing discussions on potential pathways to approval in multiple countries

TEL AVIV, Israel and RALEIGH, N.C., Jan. 13, 2022 /PRNewswire/ -- **RedHill Biopharma Ltd.** (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced new data from a prespecified

analysis of all oral opaganib's[1] Phase 2/3 study patients with positive PCR at screening, demonstrating that opaganib improved the median time to viral RNA clearance by at least 4 days. Treatment with opaganib resulted in viral RNA clearance in a median of 10 days while the median for clearance in the placebo arm was not reached by the end of 14-days treatment for placebo (Hazard Ratio 1.34; nominal p-value=0.043, N=437/463).

"Opaganib is the first oral novel drug candidate to demonstrate SARS-CoV-2 viral RNA clearance in hospitalized patients with severe COVID-19 pneumonia. It also provides the first clinical demonstration of opaganib's potential antiviral activity, supporting the 62% reduction in mortality seen in the post-hoc analysis of a large subset of patients from the Phase 2/3 study and confirming the viral inhibition observed in preclinical testing against Delta and other variants," **said Dr. Mark Levitt, RedHill's Chief Scientific Officer.** "It is important to note that these results were achieved in a severely ill hospitalized patient population and following an 11-day median time from onset of symptoms - an entirely different patient population from the mild-moderate outpatients with less than 5 days from symptom onset, for whom oral antivirals have been recently approved. It is also important to keep in mind that as opaganib's proposed mechanism of action targets a host factor, its activity is not expected to be affected by mutations in the spike protein emerging with new viral variants, including Omicron."

Opaganib was studied in a global Phase 2/3 study in hospitalized patients with severe COVID-19 pneumonia (NCT04467840) with positive PCRs at screening obtained for 437 out of 463 patients (the remaining patients could not be included in this prespecified analysis due to lack of PCR results at screening). Results from a post-hoc analysis of data from 251 study participants requiring a Fraction of inspired Oxygen (FiO2) up to and including 60% at baseline (54% of the study participants) demonstrated that treatment with oral opaganib resulted in a 62% reduction in mortality as well as improved outcomes in time to room air, median time to hospital discharge, and likelihood of intubation and mechanical ventilation in this large group of hospitalized, moderately severe COVID-19 patients.

RedHill is vigorously pursuing the development program for opaganib and is in ongoing discussions with multiple regulatory agencies regarding potential pathways to approval.

About Opaganib (ABC294640)

Opaganib, a new chemical entity, is a proprietary, first-in-class, orally-administered, sphingosine kinase-2 (SK2) selective inhibitor, with proposed 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 positive preclinical results in renal fibrosis, and also has the potential to target multiple oncology, viral, inflammatory, and gastrointestinal indications.

Opaganib previously delivered positive U.S. Phase 2 data in patients with moderate to severe COVID-19, submitted for peer review and recently published in medRxiv.

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. Patient accrual, treatment and analysis in this study are ongoing.

Opaganib demonstrated potent antiviral activity against SARS-CoV-2, the virus that causes COVID-19, inhibiting viral replication of the original SARS-CoV-2 and variants tested to date in an in vitro model of human lung bronchial tissue. Additionally, preclinical in vivo studies have demonstrated opaganib's potential to decrease renal fibrosis, have shown decreased fatality rates from influenza virus infection, and amelioration of bacteria-induced pneumonia lung injury by reducing the levels of IL-6 and TNF-alpha in bronchoalveolar lavage fluids[2].

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[3], **Talicia®** for the treatment of Helicobacter pylori (H. pylori) infection in adults[4], and **Aemcolo®** for the treatment of travelers' diarrhea in adults[5]. 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**/ **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, without limitation, the risk of regulatory feedback regarding the opaganib Phase 2/3 data packages submitted to the regulatory authorities , the risk that further analysis of the top-line results of the Phase 2/3 COVID-19 study for opaganib results in findings inconsistent with the data disclosed in this release; the risk that no further COVID-19 studies for opaganib will be commenced, and if commenced, may not be successful; the risk that any additional studies for opaganib in COVID-19 patients, even if successful, will not be sufficient for regulatory applications, including emergency use or marketing applications, and that additional COVID-19 studies for opaganib will be required by regulatory authorities to support such potential applications and the use or marketing of opaganib for COVID-19 patients, the risk 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 Talicia®, 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, 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.

Category: R&D

[1.] Opaganib is an investigational new drug, not available for commercial distribution.
[2.] 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.
[3.] Full prescribing information for Movantik® (naloxegol) is available at: **www.Movantik.com**.
[4.] Full prescribing information for Talicia® (omeprazole magnesium, amoxicillin and rifabutin) is available at: **www.Talicia.com**.
[5.] Full prescribing information for Aemcolo® (rifamycin) is available at: **www.Aemcolo.com**.

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