RedHill Biopharma's Phase 2/3 COVID-19 Study of Opaganib Passes Fourth DSMB Review with Unanimous Recommendation to Continue

April 9, 2021

- **Independent Data Safety Monitoring Board unanimously recommends continuation of the global Phase 2/3 study of orally-administered opaganib in severe COVID-19 pneumonia based on review of unblinded safety data from the first 255 treated patients**
- **The 464-patient global Phase 2/3 COVID-19 study is over 75% enrolled, with completion of enrollment expected in the coming weeks**
- **Opaganib potentially minimizes likelihood of resistance due to viral mutations by targeting a human cell component involved in viral replication**

TEL AVIV, Israel and RALEIGH, N.C., April 9, 2021 /PRNewswire/ -- RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced that the global Phase 2/3 study with orally-administered opaganib (Yeliva®, ABC294640)[1] in patients hospitalized with severe COVID-19 pneumonia has received a unanimous recommendation to continue, following a fourth independent Data Safety Monitoring Board (DSMB) safety review. The DSMB's recommendation is based on an analysis of unblinded safety data from the first 255 patients treated for 14 days, extending the total opaganib safety database to approximately 380 patients.

Mark L. Levitt, M.D., Ph.D., Medical Director at RedHill, said: "With approximately 380 patients in the opaganib safety database following this positive fourth DSMB review, we are building a clear picture of the safety profile of opaganib." **Dr. Levitt continued:** "Moreover, adding together the positive Phase 2 data, the successful DSMB futility reviews and the outcomes from compassionate use of opaganib, we look forward with optimism to the reporting of top-line data from the Phase 2/3 study, which will provide the clearest indication to date of opaganib's promise in treating COVID-19."

The global Phase 2/3 randomized, double-blind, parallel-arm, placebo-controlled study of opaganib in patients with severe COVID-19 pneumonia requiring hospitalization and treatment with supplemental oxygen (NCT04467840), is over 75% enrolled in approximately 40 recruiting sites.

RedHill recently announced positive top-line safety and efficacy data from the non-powered U.S. Phase 2 study with opaganib in 40 patients with COVID-19 pneumonia, in which opaganib demonstrated greater improvement in reducing oxygen requirement by end of treatment on Day 14, on top of standard-of-care. The Phase 2 data also showed no material safety differences between the opaganib and placebo on top of standard-of-care treatment arms - further adding to the growing safety database for opaganib.

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

About Opaganib (Yeliva®, ABC294640)

Opaganib, a new chemical entity, is a proprietary, first-in-class, orally-administered, sphingosine kinase-2 (SK2) selective inhibitor with demonstrated dual anti-inflammatory and antiviral activity that targets a host cell component of viral replication, potentially minimizing the likelihood of viral resistance. Opaganib has also shown anticancer activity and has the potential to target multiple oncology, viral, inflammatory, and gastrointestinal indications.

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

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 mitigate pulmonary fibrotic damage, and has shown 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[2].

Opaganib was originally developed by U.S.-based Apogee Biotechnology Corp. and completed multiple successful preclinical studies in oncology, inflammation, GI, and radioprotection models, as well as a Phase 1 clinical study in cancer patients with advanced solid tumors and an additional Phase 1 study in multiple myeloma.

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.

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[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 (Yeliva®, 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 risk of a delay in top-line data from the Phase 2/3 COVID-19 study, that such a study may not be successful, 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] 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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