Press Release

RedHill Biopharma Announces Planned Expansion of Opaganib Global Phase 2/3 COVID-19 Study to the U.S.

Following review of data from the U.S. Phase 2 study by the FDA, RedHill plans to expand the global Phase 2/3 study of orally-administered opaganib for severe COVID-19 to the U.S.

--

The study has enrolled over 50% of the targeted 464 patients globally; U.S. study activities expected to expand the study to a total of 8 countries and approximately 40 recruiting sites; Top-line results expected in the second quarter

--

Opaganib demonstrated dual anti-inflammatory and antiviral activity and targets a human cell component involved in viral replication and is therefore expected to be effective against emerging viral variants with mutations in the spike protein

TEL AVIV, Israel and RALEIGH, NC, February 23, 2021, RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced its plans to expand the Company's global Phase 2/3 study of opaganib[1] in patients with severe COVID-19 to the U.S., following U.S. Food and Drug Administration (FDA) review of the data from the U.S. Phase 2 study of opaganib and receipt of its recommendations.

Expansion of the global Phase 2/3 study to the U.S. will entail adjustments to the protocol based on the FDA's recommendations and ongoing discussions. The expansion of the study to the U.S. will help further speed-up enrollment, expanding the study to a total of 8 countries and approximately 40 recruiting sites, with additional sites and countries being added. The 464-patient study is over 50% enrolled and is expected to deliver top-line data in the second quarter of 2021.

The global Phase 2/3 study recently underwent a positive DSMB futility review, which is suggestive that the study has the potential for a positive outcome. RedHill recently announced positive top-line safety and efficacy data from the non-powered U.S. Phase 2 study with opaganib in patients with

COVID-19 pneumonia, in which opaganib demonstrated greater improvement in reducing oxygen requirement by end of treatment on Day 14 across key primary and secondary efficacy outcomes. The Phase 2 data also showed no material safety differences between the opaganib and placebo treatment arms - further adding to the growing safety database for opaganib.

Opaganib is a novel, orally-administered sphingosine kinase-2 (SK2) inhibitor with demonstrated antiviral, anti-inflammatory, and anti-thrombotic activity, that targets a human cell component involved in viral replication and is therefore expected to be effective against emerging viral variants with mutations in the spike protein.

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 U.S. Phase 2 study.

Preclinical data have demonstrated anti-inflammatory, antiviral and anti-thrombotic activities of opaganib, with the potential to ameliorate inflammatory lung disorders, such as pneumonia, and mitigate pulmonary fibrotic damage. 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. Opaganib also demonstrated reduced blood clot length, weight and total thrombus score in a preclinical model of Acquired Respiratory Distress Syndrome. Additionally, preclinical *in vivo* studies[2] 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.

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 and includes statements regarding the timing of the reporting of a full analysis of the data from the U.S. Phase 2 trial evaluating opaganib, the timing of potential emergency use applications for opaganib and the timing of reporting of top-line data for the global Phase 2/3 study with opaganib. 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 Company's COVID-19 Phase 2/3 study evaluating opaganib will not be successful; the risk of a delay in receiving top-line data from the Phase 2/3 study and in receiving data to support emergency use applications or in making such emergency use applications, if at all; the risk that data received from the Phase 2/3 study, even if successful, will not be sufficient to support filing or approval of emergency use applications or other marketing applications in certain or all geographical regions; the risk that the full analysis of data from the U.S. Phase 2 clinical study evaluating opaganib will be delayed or will differ from the preliminary data; the risk that the Company will not initiate the Phase 2/3 study for opaganib in certain geographies, will not expand this study to additional countries and that it will not be successful

and that enrollment will be delayed; the risk that the Phase 2/3 study will not provide a clear picture of opaganib's potential in treating severe COVID-19; the risk that other COVID-19 patients treated with opaganib will not show any clinical improvement; 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 severe 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, 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 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.

Company contact:
Adi Frish
Chief Corporate & Business Development Officer
RedHill Biopharma
+972-54-6543-112
adi@redhillbio.com

Media contacts:
U.S.: Bryan Gibbs, Finn Partners
+1 212 529 2236
bryan.gibbs@finnpartners.com
UK: Amber Fennell, Consilium
+44 (0) 7739 658 783
fennell@consilium-comms.com

[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.