RedHill Biopharma Receives Allowances for U.S. Patent Applications Covering Opaganib and RHB-107 for COVID-19

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- **The two patents protect opaganib and RHB-107 for the treatment of COVID-19 until at least 2041 once granted**
- **Enrollment in opaganib's global Phase 2/3 study in hospitalized patients with severe COVID-19 is almost 100% complete**
- **RHB-107's ongoing Phase 2/3 study is enrolling U.S. non-hospitalized patients with symptomatic COVID-19 that do not require supplemental oxygen**
- **Opaganib and RHB-107 are novel, oral, host-targeted drug candidates expected to be effective against emerging viral variants**
- **Opaganib and RHB-107 potentially cover the vast majority of affected COVID-19 patients**

TEL AVIV, Israel and RALEIGH, NC, May 26, 2021 /PRNewswire/ -- RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced receipt of two Notices of Allowance from the U.S. Patent and Trademark Office (USPTO) covering opaganib[1] and RHB-107 (upamostat)[2] as methods for the treatment of COVID-19 caused by the SARS-CoV-2 virus.

Both opaganib and RHB-107 are novel COVID-19 therapeutic candidates, in oral pill form, with dual mechanism of action effects. Both are host-targeted and are therefore expected to be effective against emerging viral variants with various mutations in the spike protein.

"There is an urgent need for oral COVID-19 treatments for patients inside and outside of the hospital setting," **said Danielle T. Abramson, Ph.D., VP, Intellectual Property & Research at RedHill**. "With two novel oral COVID-19 therapeutics in late clinical-stage development, RedHill stands at the forefront of research for COVID-19 treatments. We are very pleased with the new intellectual property protection which extends until at least 2041. The Company has also filed for protection under the Patent Cooperation Treaty (PCT) and has the option of applying in the member countries thereof."

Enrollment in opaganib's global Phase 2/3 study in hospitalized patients with severe COVID-19 (NCT04467840) is almost 100% complete. RHB-107's Phase 2/3 study is ongoing in non-hospitalized patients with symptomatic COVID-19 (NCT04723527) who do not require supplemental oxygen. Together, this covers potential treatment for the vast majority of affected patients.

In view of the upcoming completion of enrollment, RedHill is evaluating the regulatory path for opaganib with a focus on those countries currently most affected by COVID-19. The regulatory path, including potential submissions of emergency use applications in those countries, is subject to whether the data generated by the ongoing Phase 2/3 study is sufficiently positive and supportive as well as the specific requirements in each country. The strength of the safety and efficacy data generated from the opaganib studies will be key to regulatory applications. Additional studies to support the potential of such applications and the use or marketing of opaganib are likely to be required. For example, the FDA has indicated we will need to complete additional studies to support applications in the U.S. Evaluations and discussions continue with the FDA, EMA and regulators in other countries.

About Opaganib (Yeliva®, 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, 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 is 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 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 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[3].

Originally developed by Apogee Biotechnology Corp., opaganib's development 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 RHB-107 (upamostat)

RHB-107 is a proprietary, first-in-class, orally-administered potent inhibitor of several serine proteases, with antiviral and potential tissue-protective effects. RHB-107 targets human cell factors involved in preparing the spike protein for viral entry into target cells and is therefore expected to be effective against emerging viral variants with mutations in the spike protein. RHB-107 is being evaluated in a U.S. Phase 2/3 study for treatment of non-hospitalized patients with symptomatic COVID-19 who do not require supplemental oxygen. In addition, RHB-107 has potential in targeting cancer, inflammatory lung diseases and gastrointestinal diseases. RHB-107 has undergone several Phase 1 studies and two Phase 2 studies, demonstrating its clinical safety profile in approximately 200 patients. RedHill acquired the exclusive worldwide rights to RHB-107, excluding China, Hong Kong, Taiwan and Macao, from Germany's Heidelberg Pharmaceuticals (FSE: HPHA) (formerly WILEX AG) for all indications.

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[4], **Talicia®** for the treatment of *Helicobacter pylori (H. pylori)* infection in adults[5], and **Aemcolo®** for the treatment of travelers' diarrhea in adults[6]. 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 completion of enrollment for the Phase 2/3 COVID-19 study for opaganib and the Phase 2/3 COVID-19 study for RHB-107, 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 and the Phase 2/3 COVID-19 study for RHB-107 may not be successful and, even if successful, such studies 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, and for RHB-107 may be required, by regulatory authorities to support such potential applications and the use or marketing of opaganib and/or RHB-107, as the case may be, for COVID-19 patients, that opaganib and RHB-107 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] RHB-107 (upamostat) is an investigational new drug, not available for commercial distribution.

[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.

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

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

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

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