RedHill Biopharma's Opaganib COVID-19 Study Passes Second Independent Committee Review

October 7, 2020

Second pre-scheduled independent Safety Monitoring Committee (SMC) review unanimously recommends continuation without change of the U.S. Phase 2 study with opaganib in COVID-19

--

The U.S. Phase 2 study is 75% enrolled with data expected later this quarter

--

In parallel, enrollment advancing rapidly in the global COVID-19 Phase 2/3 study with opaganib

--

Global emergency use authorization applications are planned, subject to positive clinical results

TEL AVIV, Israel and RALEIGH, N.C., Oct. 07, 2020 (GLOBE NEWSWIRE) -- RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced that the U.S. Phase 2 study with opaganib (Yeliva®, ABC294640)[1] in patients hospitalized with severe COVID-19 pneumonia has passed its second pre-scheduled safety review by the independent Safety Monitoring Committee (SMC) with a unanimous recommendation to continue the study without change. The SMC's recommendation is based on an unblinded analysis of safety data from the first 24 patients treated in the study for at least seven days. The study is 75% enrolled.

The U.S. Phase 2 study with opaganib (NCT04414618), ongoing in eight clinical trial sites, is planned to complete enrollment this month, with data expected to follow before the end of this year. The Phase 2 study is not powered for efficacy and is focused on safety evaluation and identifying a signal of efficacy.

In parallel, the global Phase 2/3 study with opaganib in patients with severe COVID-19 pneumonia (NCT04467840) is rapidly enrolling across 15 study sites and is on track to enroll up to 270 patients. This study is focused on, and powered for, efficacy evaluation. The study has been approved in the UK, Italy, Russia, Mexico, Brazil and Israel, with further expansion ongoing.

"Passing this second pre-scheduled independent safety review, involving data from 60% of the patients in the study, is an important milestone in the ongoing development of opaganib as a potential therapy for patients with severe COVID-19," **said Mark L. Levitt, M.D., Ph.D., Medical Director at RedHill**. "We are rapidly building more data and experience with opaganib, with the safety database from opaganib studies now numbering close to 200 patients. This further supports the ongoing global Phase 2/3 study which is focused on delivering efficacy and is on track to enroll up to 270 patients by the end of the year."

RedHill is in discussions with U.S. government agencies around potential funding to support the rapid advancement of opaganib toward potential emergency use approval and manufacturing scale-up.

About Opaganib (ABC294640, Yeliva®)
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, 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 in a global Phase 2/3 study and a U.S. Phase 2 study for the treatment of severe COVID-19.

Preclinical data have demonstrated both anti-inflammatory and antiviral activities of opaganib, with the potential to reduce 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. 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.

Under a compassionate use program, patients with COVID-19 (as classified by the WHO ordinal scale) were treated with opaganib in a leading hospital in Israel. Data from the treatment of these first patients with severe COVID-19 with opaganib have been published[2]. Analysis of treatment outcomes suggested substantial benefit to patients treated with opaganib under compassionate use in both clinical outcomes and inflammatory markers as compared to a retrospective matched case-control group from the same hospital. All patients in the opaganib-treated group were discharged from hospital on room air without requiring intubation and mechanical ventilation, whereas 33% of the matched case-control group required intubation and mechanical ventilation. Median time to weaning from high-flow nasal cannula was reduced to 10 days in the opaganib-treated group, as compared to 15 days in the matched case-control group.

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 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 a planned pivotal Phase 3 study for pulmonary nontuberculous mycobacteria (NTM) infections; (ii) **opaganib (Yeliva®)**, a first-in-class 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-104**, with positive results from a first Phase 3 study for Crohn's disease; (iv) **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; (v) **RHB-107**, a Phase 2-stage first-in-class, serine protease inhibitor, targeting cancer and inflammatory gastrointestinal diseases and is also being evaluated for COVID-19 and (vi) **RHB-106**, an encapsulated bowel preparation. More information about the Company is available at www.redhillbio.com.

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 that the Company's Phase 2/3 study evaluating opaganib will not be successful; the risk that the antiviral activity of opaganib shown in the preclinical human lung cell model will not be demonstrated in clinical trials; the risk of a delay in receiving data to support emergency use applications; the risk that other COVID-19 patients treated with opaganib will not show any clinical improvement; the risk that clinical trials with opaganib in Brazil, Israel, the U.S., Italy, Russia, the UK, Mexico or elsewhere for the treatment of COVID-19, if conducted at all, will not show any improvement in patients; the risk of a delay in applying for emergency use authorizations, if at all; 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 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 under compassionate use programs, 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
Senior VP Business Development & Licensing
RedHill Biopharma
+972-54-6543-112
adi@redhillbio.com

IR contact (U.S.):
Timothy McCarthy, CFA, MBA
Managing Director, Relationship Manager
LifeSci Advisors, LLC
+1-212-915-2564
tim@lifesciadvisors.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.

Source: RedHill Biopharma Ltd.