



NEWS RELEASE

RedHill Announces Publication of Positive Phase 2 Study Results with Once-Daily Oral RHB-107 in Non-Hospitalized COVID-19

1/3/2023

Positive data from a U.S. Phase 2 study of once-daily oral RHB-107 (upamostat) in symptomatic COVID-19 published in the peer-reviewed International Journal of Infectious Diseases

RHB-107 successfully met the primary endpoint of safety and tolerability and delivered promising efficacy results, including faster recovery from severe COVID-19 symptoms (median of 3 days to recovery vs. 8 days with placebo) and 100% reduction in hospitalization due to COVID-19

RHB-107, a novel, broad-acting, host-directed, once-daily oral antiviral, is expected to act independently of viral spike protein mutations including Omicron BA.5 sub-variant ^[1]

Inclusion of once-daily oral RHB-107 in a multinational platform trial for COVID-19 outpatients pending. Discussions for external non-dilutive funding for additional Phase 3 COVID-19 development advancing

Several collaborative projects, with government and non-government bodies, on a range of preclinical studies against other viral targets for pandemic preparedness ongoing and under discussion

TEL AVIV, Israel and RALEIGH, NC, Jan. 3, 2023 /PRNewswire/ -- RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or

the "Company"), a specialty biopharmaceutical company, today announced publication of positive data from a Phase 2 study of once-daily oral investigational RHB-107 (upamostat)^[2] in non-hospitalized symptomatic COVID-19 patients, in the peer-reviewed International Journal of Infectious Diseases^[3]. The study showed that RHB-107 successfully met the primary endpoint of safety and tolerability and delivered promising efficacy results, despite the small number of patients in each treatment group, including faster recovery from severe COVID-19 symptoms and 100% reduction in hospitalization due to COVID-19.

Data showed a 100% reduction in hospitalization due to COVID-19, with zero patients (0/41) on the RHB-107 arms versus 15% (3/20) hospitalized on the placebo-controlled arm (nominal p-value=0.0317). The study also showed an approx. 88% reduction in reported new severe COVID-19 symptoms after treatment initiation, with only 2.4% of the RHB-107 treated group (1/41) versus 20% (4/20) of patients in the placebo-controlled arm (nominal p-value=0.036) reporting new severe COVID-19 symptoms. Further analysis showed faster recovery from severe COVID-19 symptoms with a median of 3 days to recovery with upamostat vs. 8 days with placebo.

"It is highly satisfying to see this study, and the exciting results it produced, published in this important journal. These data, achieved despite a small overall sample size, are impressive. Showing both safety and efficacy signals, in a highly convenient once-daily oral therapy, positively positions investigational RHB-107 as a potentially very useful treatment for COVID-19 outpatients to reduce symptom severity and prevent disease progression and hospitalization," **said Terry F. Plasse MD, Medical Director at RedHill**. "Given the growing awareness of the limitations of existing options for early treatment of COVID-19, it is vital that we do not stop our efforts to bring new options forward – especially those in which we have already observed broad-acting, host-directed variant-agnostic abilities."

The Phase 2 multicenter, randomized, double-blind, placebo-controlled, parallel-group study with once-daily oral RHB-107 in non-hospitalized patients with symptomatic COVID-19 (NCT04723537) evaluated safety and tolerability, provided evidence for dose selection, and provided preliminary assessment of parameters to be used for efficacy evaluation in a Phase 3 study. A total of 61 patients were enrolled and randomized on a 1:1:1 basis to receive one of two dose levels of RHB-107 or a placebo control.

Advanced discussions are ongoing regarding inclusion of once-daily oral RHB-107 in a multinational platform trial for COVID-19 outpatients. Discussions for external non-dilutive funding for Phase 3 COVID-19 development, in addition to the platform study, are also advancing.

About RHB-107 (upamostat)

RHB-107 is a proprietary, first-in-class, once-daily orally administered investigational antiviral, that targets human serine proteases involved in preparing the spike protein for viral entry into target cells. Because it is host-cell

targeted, RHB-107 is expected to also be effective against emerging viral variants with mutations in the spike protein.

Top-line results from Part A of the Phase 2/3 study (NCT04723537) evaluating treatment with RHB-107 in non-hospitalized patients with symptomatic COVID-19 early in the course of the disease, showed a 100% reduction in hospitalization due to COVID-19, with zero patients (0/41) on the RHB-107 arms versus 15% (3/20) hospitalized on the placebo-controlled arm. The study also showed an approx. 88% reduction in reported new severe COVID-19 symptoms after treatment initiation, with only one patient in the RHB-107 treated group 2.4%, (1/41) versus 20% (4/20) of patients in the placebo-controlled arm. Further analysis showed faster recovery from severe COVID-19 symptoms with a median of 3 days to recovery with upamostat vs. 8 days with placebo.

In addition, RHB-107 inhibits several proteases targeting cancer and inflammatory gastrointestinal disease. 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 (ABC294640)**, a first-in-class oral broad-acting, host-directed, SK2 selective inhibitor targeting multiple indications, including for pandemic preparedness, with a Phase 2/3 program for hospitalized COVID-19 and a Phase 2 program in oncology and a radiation protection program ongoing; (iii) **RHB-107 (upamostat)**, an oral broad-acting, host-directed serine protease inhibitor with potential for pandemic preparedness and is in Phase 3-stage development as treatment for non-hospitalized 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; and (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. 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 that RHB-107 will not be included in the multinational platform trial for COVID-19 outpatients, the risk that RHB-107 will not be shown to be a broad acting, host-directed candidate therapy for pandemic preparedness, the risk that a pivotal Phase 3 trial for RHB-107 will not be initiated or that such trial be successful and, even if successful, such study and results may not be sufficient for regulatory applications, including emergency use or marketing applications, and that additional COVID-19 studies may be required by regulatory authorities to support such potential applications and the use or marketing of rhb-107 for COVID-19 patients, that 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 17, 2022. 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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Category: R&D

[1] Preliminary data from a recent in vitro study

[2] RHB-107 (upamostat) is an investigational new drug, not available for commercial distribution in the United States.

[3] Manuscript accepted for publication and will be available on-line as soon as proofing is finalized

[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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