NEWS RELEASE

RedHill's RHB-102 (BEKINDA®) and Opaganib Granted New Patents in Oncology Setting

5/1/2023

European Patent Office grants RHB-102 patent covering antiemetic extended-release solid dosage forms for the prevention of nausea and vomiting (CINV/RINV), providing protection of RHB-102 to March 2034

Discussions with potential commercialization partners for RHB-102 in the UK and other territories are ongoing

US PTO grants new opaganib combination compositions patent for treatment of cancer

TEL AVIV, Israel and RALEIGH, N.C., May 1, 2023 /PRNewswire/ -- RedHill Biopharma Ltd. (NASDAQ: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced the granting of two new EU and U.S. patents for RHB-102 (BEKINDA)[1] and opaganib[2], respectively, in the oncology setting.

The European Patent Office granted RHB-102 (BEKINDA), a 24-hr bimodal release, once-daily oral tablet formulation of ondansetron, a patent covering antiemetic extended-release solid dosage forms for the prevention of nausea and vomiting (CINV/RINV). The patent provides the potential for UK and EU protection of RHB-102 to March 2034.

"Between 70-80% of patients undergoing chemotherapy or radiotherapy will experience nausea and/or vomiting. The global CINV/RINV market is growing at approximately 6% CAGR and is estimated to be worth over $10 billion by 2031[3]," **said Guy Goldberg, RedHill's Chief Business Officer**. "Following a positive recent UK MHRA scientific advice meeting RHB-102 (BEKINDA) data was deemed supportive of potential submission for marketing approval in the UK

for chemotherapy and radiotherapy induced nausea and vomiting (CINV/RINV). The Company is also considering the potential for RHB-102 in additional territories and discussions with potential commercialization partners in the UK and other territories are ongoing."

Additionally, the U.S. Patent and Trademark Office (USPTO) has granted a new patent for opaganib in respect to combination compositions for treatment of cancer, extending protection to October 2036.

About RHB-102 (BEKINDA):

RHB-102 is a proprietary, bimodal release, once-daily oral pill formulation of the antiemetic drug ondansetron, targeting several gastrointestinal indications. RHB-102 24 mg is intended to provide patients with relief from nausea and vomiting symptoms for a full 24-hour period with a single oral tablet. If approved for marketing by the MHRA, RHB-102 24 mg could become the first oral 24hr extended-release 5-HT3 antiemetic drug in the UK indicated for the treatment of CINV/RINV.

Positive results from two successful late-stage RHB-102 studies at different doses, the U.S. Phase III GUARD gastroenteritis study (RHB-102 24 mg) and the U.S. Phase II IBS-D study (RHB-102 12 mg) were published in **JAMA Network Open**[3] and **The American Journal of Gastroenterology**[4], respectively.

About Opaganib (ABC294640)

Opaganib, a new chemical entity, is an orally administered, first-in-class proprietary selective inhibitor of sphingosine kinase-2 (SK2) with suggested anti-inflammatory, anticancer, radioprotective and antiviral activity.

Opaganib is thought to work through the inhibition of multiple pathways, the induction of autophagy and apoptosis, and disruption of viral replication, through simultaneous inhibition of three sphingolipid-metabolizing enzymes in human cells (SK2, DES1 and GCS).

Opaganib was recently selected by the U.S. Government's Radiation and Nuclear Countermeasures Program (RNCP), led by the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, for the nuclear medical countermeasures product development pipeline as a potential treatment for Acute Radiation Syndrome (ARS). As part of this collaboration, contractors directed and supported by the RNCP will undertake studies, designed in collaboration with RedHill, to test opaganib in established ARS models. In an ARS setting, opaganib is thought to exert its protective effects via an anti-inflammatory mechanism of action involving ceramide elevation and reduction of sphingosine 1-phosphate (S1P) in human cells - suppressing inflammatory damage to normal tissue and thus suppressing toxicity from unintended ionizing radiation exposure. It has also been reported in the literature that inhibition of sphingosine kinase 2 promotes the viability and robustness of hematopoietic stem cells, even in the face of radiation damage, supporting increased survival.

Opaganib has received Orphan Drug designation from the U.S. FDA for the treatment of cholangiocarcinoma and has undergone studies in advanced cholangiocarcinoma (Phase 2a) and prostate cancer. Opaganib also has a Phase 1 chemoradiotherapy study protocol ready for IND submission.

Opaganib has demonstrated broad-acting, host-directed, antiviral activity against SARS-CoV-2, multiple variants, and several other viruses, such as Influenza A. Being host-targeted, and based on data accumulated to date, opaganib is expected to maintain effect against emerging viral variants. In prespecified analyses of Phase 2/3 clinical data in hospitalized patients with moderate to severe COVID-19, oral opaganib demonstrated improved viral RNA clearance, faster time to recovery and significant mortality reduction in key patient subpopulations versus placebo on top of standard of care. Data from the opaganib global Phase 2/3 study has been submitted for peer review and recently published in **medRxiv**.

Opaganib has also shown positive preclinical results in renal fibrosis, and has the potential to target multiple oncology, radioprotection, viral, inflammatory, and gastrointestinal 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, **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, is in late-stage development for treatment of non-hospitalized symptomatic COVID-19, and is 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** (**BEKINDA)**, with expected UK submission for chemotherapy and radiotherapy induced nausea and vomiting, 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**/ **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-102 will not be submitted to the UK's MHRA for approval in CINV/RINV, and if submitted may not be approved and if approved may not be successfully commercialized, 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 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 April 28, 2023, and the Company's Report on Form 6-K filed with the SEC on November 10, 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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[1] RHB-102 (BEKINDA) is an investigational new drug, not available for commercial distribution.

[2] Opaganib is an investigational new drug, not available for commercial distribution.

[3] **https://www.factmr.com/report/chemotherapy-induced-nausea-and-vomiting-cinv-treatment-market**

[4] Plasse TF, Barton G, Davidson E, et al. Bimodal release ondansetron improves stool consistency and symptomatology in diarrhea-predominant irritable bowel syndrome: A randomized, double-blind trial. Am J Gastroenterol 2020;115:1466-73.

[5] Talicia® (omeprazole magnesium, amoxicillin and rifabutin) is indicated for the treatment of H. pylori infection in adults. For full prescribing information see: **www.Talicia.com**.

[6] Aemcolo® (rifamycin) is indicated for the treatment of travelers' diarrhea caused by noninvasive strains of Escherichia coli in adults. For full prescribing information see: **www.aemcolo.com**.

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