



NEWS RELEASE

## RedHill Announces New USPTO Notice of Patent Allowance for Opaganib and EU Patent Grant for RHB-102 (BEKINDA®)

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USPTO issues Notice of Allowance for a new opaganib patent covering sphingosine kinase 2 inhibition treatment for Ebola virus disease, supporting opaganib protection until October 2035

Additionally, European Patent Office grants new RHB-102 patent covering ondansetron extended-release solid dosage forms for treating either nausea, vomiting or diarrhea symptoms, providing protection of RHB-102 across multiple indications until March 2035

TEL-AVIV, Israel and RALEIGH, N.C., Sept. 5, 2023 /PRNewswire/ -- RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced that the U.S. Patent and Trademark Office (USPTO) had issued a Notice of Allowance for a new opaganib<sup>[1]</sup> patent covering sphingosine kinase 2 inhibition treatment for Ebola virus disease, supporting opaganib protection until October 2035. The Company also announced that the European Patent Office has granted RHB-102 (BEKINDA)<sup>[2]</sup> a new patent, covering ondansetron extended-release solid dosage forms for treating either nausea, vomiting or diarrhea symptoms. This new patent is expected to provide protection of RHB-102 across multiple indications until March 2035.

**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, vomiting and diarrhea 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**<sup>[3]</sup> and **The American Journal of Gastroenterology**<sup>[4]</sup>, respectively.

### **About Opaganib (ABC294640)**

Opaganib, a proprietary investigational host-directed and potentially broad-acting drug, is a first-in-class, orally administered sphingosine kinase-2 (SPHK2) selective inhibitor with anticancer, anti-inflammatory and antiviral activity, targeting multiple potential diseases, including gastrointestinal acute radiation syndrome (GI-ARS), COVID-19, other viruses as part of pandemic preparedness, and cholangiocarcinoma (bile duct cancer).

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 (SPHK2, 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 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 FDA-IND submission.

Opaganib has demonstrated 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**<sup>®</sup>, for the treatment of Helicobacter pylori (H. pylori) infection in adults<sup>[5]</sup>, and **Aemcolo**<sup>®</sup>, for the treatment of travelers' diarrhea in adults<sup>[6]</sup>. RedHill's key clinical late-stage development programs include: (i) **opaganib (ABC294640)**, a first-in-class oral broad-acting, host-directed SPHK2 selective inhibitor with potential for pandemic preparedness, targeting multiple indications with a U.S. Government collaboration for development for Acute Radiation Syndrome (ARS), a Phase 2/3 program for hospitalized COVID-19, and a Phase 2 program in oncology; (ii) **RHB-107 (upamostat)**, an oral broad-acting, host-directed, serine protease inhibitor with potential for pandemic preparedness is in late-stage development as a treatment for non-hospitalized symptomatic COVID-19, and is also targeting multiple other cancer and inflammatory gastrointestinal diseases; (iii) **RHB-102**, with potential 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; (iv) **RHB-104**, with positive results from a first Phase 3 study for Crohn's disease; and (v) **RHB-204**, a Phase 3-stage program for pulmonary nontuberculous mycobacteria (NTM) disease.

More information about the Company is available at: [www.redhillbio.com](http://www.redhillbio.com) / [twitter.com/RedHillBio](https://twitter.com/RedHillBio).

## **Forward Looking Statements**

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements, including, but not limited to, statements regarding the intended use of net proceeds therefrom, may be preceded by the words "intends," "may," "will," "plans," "expects," "anticipates," "projects," "predicts," "estimates," "aims," "believes," "hopes," "potential" or similar words and include statements regarding anticipated the addition of new revenue generating products, out-licensing of the Company's development pipeline assets, timing of opaganib's development for Acute Radiation Syndrome, non-dilutive development funding from RHB-107 and its inclusion in a key platform study. 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, market and other conditions, the risk that the addition of new revenue generating products or out-licensing transactions will not occur; the risk that acceptance onto the RNCP Product Development Pipeline will not guarantee ongoing development or that any such development will not be completed or successful; the risk that the FDA does not agree with the Company's proposed development plans for opaganib for any indication, the risk that observations from preclinical studies are not indicative or predictive of results in clinical trials; the risk that the FDA pre-study requirements will not be met and/or that the Phase 3 study of RHB-107 in COVID-19 outpatients will not be approved to commence or if approved, will not be completed or, should that be the case, that we will not be successful in obtaining alternative non-dilutive development funding for RHB-107, the risk that HB-107's late-stage development for non-hospitalized COVID-19 will not benefit from the resources redirected from the terminated RHB-204 Phase 3 study, that 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 and RHB-107 are likely to be required, as well as risks and uncertainties associated with the risk that the Company will not successfully commercialize its products; as well as risks and uncertainties associated with (i) the initiation, timing, progress and results of the Company's research, manufacturing, pre-clinical 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 pre-clinical studies or clinical trials or the development of a commercial companion diagnostic for the detection of MAP; (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 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, pre-clinical 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 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 experiences using

investigative drugs under the Company's Expanded Access Program; (xiv) competition from other companies and technologies within the Company's industry; and (xv) the hiring and employment commencement date of executive managers. 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. 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] Opaganib is an investigational new drug, not available for commercial distribution.

[2] RHB-102 (BEKINDA) is an investigational new drug, not available for commercial distribution.

[3] Silverman RA, House SL, Meltzer AC, et al. Bimodal Release Ondansetron for Acute Gastroenteritis Among Adolescents and Adults: A Randomized Clinical Trial. *JAMA Netw Open*. 2019;2(11):e1914988.  
doi:10.1001/jamanetworkopen.2019.14988

[4] Plasse, Terry F. MD<sup>1</sup>; Barton, Gary MD<sup>2</sup>; Davidson, Evelyne MD<sup>3</sup>; Abramson, Danielle PhD<sup>1</sup>; Kalfus, Ira MD<sup>1</sup>; Fathi, Reza PhD<sup>1</sup>; Raday, Gilead MS<sup>1</sup>; Harris, M. Scott MD<sup>4</sup>. Bimodal Release Ondansetron Improves Stool Consistency and Symptomatology in Diarrhea-Predominant Irritable Bowel Syndrome: A Randomized, Double-Blind, Trial. *The American Journal of Gastroenterology* 115(9):p 1466-1473, September 2020. | DOI: 10.14309/ajg.0000000000000727

[5] Talicia<sup>®</sup> (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<sup>®</sup> (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](http://www.aemcolo.com)

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