NEWS RELEASE

RedHill Announces a New Patent Covering Opaganib in Combination with Immune Checkpoint Inhibitors, Valid Through 2040

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New Chinese patent notice of allowance issued covering opaganib in combination with immune checkpoint inhibitors (ICIs) as a method of inducing an anti-cancer immune response**[1]**. Provides protection for opaganib's potential use in combination with a range of approved and in-development (ICIs) across a growing range of indications**[2]** through 2040

ICIs have become a cornerstone in cancer treatment, having been hailed as a major breakthrough by oncologists, with the global ICI market expected to exceed $100 billion by 2028, including Merck's Keytruda (pembrolizumab) and BMS' Yervoy (ipilimumab)**[3]**

Opaganib, a host-directed and potentially broad acting twice-daily oral, small molecule with a demonstrated safety & efficacy profile, is in development for multiple oncology, viral and inflammatory indications, including COVID-19, Ebola, acute respiratory distress syndrome (ARDS) and two U.S. government-sponsored countermeasures programs for Acute Radiation Syndrome (ARS) and Sulfur Mustard exposure

TEL-AVIV, Israel and RALEIGH, N.C., June 3, 2024 /PRNewswire/ -- RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced the issue of a new Chinese patent notice of allowance for opaganib[4] in combination with immune checkpoint inhibitors (ICIs) as a method of

inducing an anti-cancer immune response, providing protection for opaganib's potential use with a range of approved and in-development immune checkpoint inhibitors (ICIs) across a growing range of indications through 2040. The patent will be issued by the Chinese National Intellectual Property Administration (CNIPA) (Chinese Patent Application No.: 202080013805.3 issued May 24, 2024).

"ICIs have become a cornerstone in cancer treatment, having been hailed as a major breakthrough by oncologists, with the global ICI market expected to exceed $100 billion by 2028, including Merck's Keytruda (pembrolizumab) and BMS' Yervoy (ipilimumab)," **said Guy Goldberg, RedHill's Chief Business Officer**. "This exciting new patent is based on compelling data from a range of in vivo experiments showing significant improvements in outcomes in combination with selected ICIs. China has been a world leader in embracing ICI-based therapy[5] and this is an important addition to the strong patent portfolio protecting opaganib."

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 prostate cancer and cholangiocarcinoma (bile duct cancer), gastrointestinal acute radiation syndrome (GI-ARS), Sulfur Mustard exposure, COVID-19, Ebola and other viruses as part of pandemic preparedness.

Opaganib's host-directed action 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 has been selected for evaluation by two U.S. government countermeasures programs for Acute Radiation Syndrome (ARS) and Sulfur Mustard exposure, both funded by the NIH: The Radiation and Nuclear Countermeasures Program (RNCP), led by the National Institute of Allergy and Infectious Diseases (NIAID), part of the HHS National Institutes of Health, for the nuclear medical countermeasures (MCM) product development pipeline selected opaganib for development as a potential treatment for Acute Radiation Syndrome (ARS); and the Chemical Medical Countermeasures (Chem MCM) Program and Chemical Countermeasures Research Program (CCRP), managed respectively by the Administration for Strategic Preparedness and Response (ASPR) / Biomedical Advanced Research and Development Authority (BARDA) and NIH/NIAID selected opaganib for evaluation as a potential medical countermeasure (MCM) against Sulfur Mustard exposure.

Opaganib has demonstrated antiviral activity against SARS-CoV-2, multiple variants, and several other viruses, such as Influenza A and Ebola. Opaganib delivered a statistically significant increase in survival time when given at 150 mg/kg twice a day (BID) in a United States Army Medical Research Institute of Infectious Diseases (USAMRIID) in vivo Ebola virus study, making it the first host-directed molecule to show activity in Ebola virus disease. Opaganib also

recently demonstrated a distinct synergistic effect when combined individually with remdesivir (Veklury®, Gilead Sciences Inc.), significantly improving potency while maintaining cell viability, in a U.S. Army-funded and conducted in vitro Ebola virus study.

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. Opaganib has demonstrated its safety and tolerability profile in more than 470 people in multiple clinical studies and expanded access use. Data from the opaganib global Phase 2/3 study was published in **medRxiv**.

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 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[6], and **Aemcolo®**, for the treatment of travelers' diarrhea in adults[7]. 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 U.S. government collaborations for development for Acute Radiation Syndrome (ARS) and Sulfur Mustard exposure, 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, with non-dilutive external funding covering the entirety of the RHB-107 arm of the 300-patient Phase 2 adaptive platform trial, 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** / **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 and may discuss investment opportunities, stock analysis, financial performance, investor relations, and market trends. Such statements, including, but not limited to, statements regarding the intended use of net proceeds from the offering, 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 the risk that the Company will not comply with the listing requirements of the Nasdaq Capital Market ("Nasdaq") to remain listed for trading on Nasdaq, 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 8, 2024. 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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Logo: **https://mma.prnewswire.com/media/1334141/RedHill_Biopharma_Logo.jpg**

[1] The allowed claims cover a pharmaceutical composition comprising opaganib and immune checkpoint inhibitors anti-PD-L1 antibody, an anti-PD-1 antibody, and/or an anti-CTLA4 antibody, the combination of opaganib and anti-PD1/anti-PDL1 for treatment of melanoma; combination of opaganib and anti-CTL4 for treatment of lung cancer.

[2] Jin Y, Li H, Zhang P, Yu M, Zhang H, Li X. The regulatory approvals of immune checkpoint inhibitors in China and

the United States: A cross-national comparison study. Int J Cancer. 2023 Jun 1;152(11):2351-2361. doi: 10.1002/ijc.34427. Epub 2023 Jan 18. PMID: 36632000. **https://pubmed.ncbi.nlm.nih.gov/36632000/**

[3] GlobalData: Thematic Intelligence: Immuno-oncology (2023). Report Code: GDHCHT393, May 2023

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

[5] Jin Y, Li H, Zhang P, Yu M, Zhang H, Li X. The regulatory approvals of immune checkpoint inhibitors in China and the United States: A cross-national comparison study. Int J Cancer. 2023 Jun 1;152(11):2351-2361. doi: 10.1002/ijc.34427. Epub 2023 Jan 18. PMID: 36632000.

[6] 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**.

[7] 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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