NEWS RELEASE

RedHill Biopharma Advancing Opaganib Options for Novel Dual Host Directed and Direct Acting Antiviral Approach for Ebola Outbreak Biodefense Platforms

2026-06-02

Amid the rapidly evolving Ebola virus disease (EVD) outbreak involving the rare Bundibugyo ebolavirus sub-type, for which there are no approved medications or vaccines, RedHill Biopharma is actively discussing potential collaborations for clinical advancement of opaganib[1], including the World Health Organization's (WHO) SOLIDARITY CORE clinical trial platform

Opaganib EVD rationale (analogous to EVD treatment pathway):

- **Phase 3 clinical antiviral activity** (severe COVID-19) showing[2]:
  - 70.2% mortality reduction with opaganib given as add-on to best available standard of care (remdesivir + corticosteroids): 6.98% (n=3/43) opaganib + SoC vs. 23.4% (n=11/47) placebo + SoC (p=0.034))
  - Improved median time to viral RNA clearance by ≥4 days in opaganib-treated patients (median 10 days vs. not reached by Day 14 in placebo, HR 1.34, p=0.043)
  - Demonstrated safety and tolerability profile in 470 clinical trial participants
- **Preclinical EVD activity** (United States Army Medical Research Institute of Infectious Diseases (USAMRIID)-funded studies showed[3]:
  - Opaganib inhibition of EVD in human macrophages
  - Increased survival for opaganib group (one of two animal models)[4]

- Synergistic effect when opaganib combined with Gilead Sciences' remdesivir (Veklury®)

- **Opaganib's potential dual mechanism of action against EVD and filovirus-class activity**[5]:
  - Opaganib's therapeutic target—SPHK2 inhibition—disrupts host-cell components essential for filovirus entry and replication that are conserved across Filoviridae
  - PI3K/Akt pathway inhibition (required for filovirus entry and membrane trafficking)
  - NLRP3 and IL-6/TNFα inflammasome suppression and S1P-mediated vascular permeability reduction (addressing immune dysregulation and vascular leak in viral hemorrhagic fever)
  - Published literature explicitly validates sphingosine kinases as targets for filovirus inhibition[6]

- Opaganib, an investigational SPHK2 inhibitor drug, offers a novel potential approach to strengthen global infectious disease preparedness and biodefense:
  - Host-directed therapeutic (HDT) – providing for a possible two-pronged approach to viral defense with potential for co-administration with direct-acting EVD-focused antivirals (i.e. Gilead's remdesivir and obeldesivir, Regeneron's maftivimab, and Mapp's MBP134) with minimal expected drug-drug interactions
  - Oral administration, ease of storage and distribution supporting clinical evaluation and possible stockpiling requirements

With the WHO suggesting the current outbreak was outpacing response efforts[7], the Company has provided available supply readiness, safety and efficacy data to aid rapid discussions to enable clinical exploration of the potential synergies of opaganib host-directed therapy in addressing a growing global public health threat

TEL AVIV, Israel and RALEIGH, N.C. , June 2, 2026 /PRNewswire/ -- RedHill Biopharma Ltd. (NASDAQ: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced that it is actively discussing potential collaborations for advancement of its investigational oral drug, opaganib, to combat EVD, which can be fatal in approximately half of all cases[8], including the World Health Organization's (WHO) SOLIDARITY CORE clinical trial platform and pharma collaborations. Opaganib is an easily stored, distributed and orally administered, host-directed, small molecule SPHK2 inhibitor with demonstrated antiviral properties in advanced clinical stage.

"Recent remarks from the WHO, and health authorities worldwide, point to the urgent need for options to combat the current Ebola outbreak, involving the rare Bundibugyo ebolavirus sub-type - which appears to be outpacing response efforts. Opaganib has shown a potential dual mechanism of action against EVD and filovirus-class activity, EVD-specific preclinical activity, showing inhibition of EVD, increased survival, and synergistic effects with directing acting antiviral therapy, significantly improving potency while maintaining cell viability, and clinical antiviral evidence of a 70.2% mortality reduction as add-on therapy to the remdesivir + corticosteroids subgroup in our Phase 3 severe COVID-19 trial. This along with its demonstrated clinical safety profile and ability to be easily stored, distributed and administered without the need for complex cold store distribution chains strongly supports the

need for clinical evaluation of opaganib in light of the deadly current outbreak," **said Gilead Raday, Chief Operating Officer and Head of R&D at RedHill**. "Opaganib sits in a distinct category as a host-directed agent which can be added to direct-acting antivirals, representing an opportunity to enhance global infectious disease preparedness and biodefense infrastructure against EVD, while also being preferentially suited to the logistical challenges found on the ground during these tragic outbreaks."

Peer-reviewed published data shows opaganib's host-direction action stems from its ability to simultaneously inhibit three sphingolipid-metabolizing enzymes in human cells (SPHK2, DES1 and GCS), altering the cellular lipid balance and enabling inhibition of replication of viruses like SARS-CoV-2 and Ebola. In EVD specifically, opaganib offers a potential dual mechanism of action; blocking the PI3K/Akt pathway critical for filovirus entry and suppressing NLRP3 inflammasome and reducing IL-6/TNFα and S1P-mediated vascular permeability (addressing immune dysregulation and vascular leak).

Proactively, and upon request, the Company has provided information to relevant government, industry and other organizations, regarding supply readiness and all available clinical and preclinical safety and efficacy data to aid rapid clinical and regulatory discussions.

Opaganib is in development for multiple oncology, viral, inflammatory and diabetes and obesity-related indications. Opaganib is an investigational new drug. It has not been approved by any regulatory authority and is not available for commercial distribution. Inclusion in the WHO CORE platform cannot be guaranteed.

About Ebola virus disease:

According to the Centers for Disease Control and Prevention (CDC), Ebola disease is a rare and often deadly illness, caused by infection by one of a group of four viruses, known as ebolaviruses. Transmission of the disease is mostly through contact with an infected animal (bat or nonhuman primate) or a sick or dead person infected with an ebolavirus. The course of the illness typically progresses from "dry" symptoms initially (such as fever, aches and pains, and fatigue) and then progresses to "wet" symptoms (such as diarrhea, vomiting and unexplained hemorrhaging, bleeding or bruising) as the person becomes sicker. Currently only Inmazeb™ (atoltivimab, maftivimab, and odesivimab-ebgn, Regeneron Pharmaceuticals, Inc.), a combination of three monoclonal antibodies and Ebanga™ (ansuvimab-zykl, Ridgeback Biotherapeutics, LP), a single monoclonal antibody, are FDA-approved to treat EVD. Both are intravenously administered, direct acting, monoclonal antibody antivirals that bind to glycoproteins on the Ebola virus's surface to prevent the virus from entering a person's cells. There is an urgent need for host-directed small molecule therapies that may be effective against multiple strains of ebolavirus, less likely to be impacted by viral mutation, and that are easy to store, distribute and administer, especially in areas where healthcare services and infrastructures may be sub-optimal.

About Opaganib (ABC294640)

Opaganib is a proprietary first-in-class investigational, orally administered sphingosine kinase-2 (SPHK2) selective inhibitor drug. Potentially broad-acting, it is in development for multiple oncology, viral, inflammatory, metabolic (diabetes and obesity) and additional indications.

Opaganib's suggested mechanism of action, **published** in the journal Drug Design, Development and Therapy, is host-directed and potentially broad-acting and is expected to maintain its effect against emerging viral variants. 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 has received Orphan Drug designation from the FDA for the treatment of neuroblastoma and cholangiocarcinoma. A Bayer-supported 80-patient placebo-controlled randomized Phase 2 study is ongoing to evaluate the efficacy of opaganib in combination with Bayer's darolutamide in men with metastatic castrate-resistant prostate cancer (mCRPC), testing the potentially enhancing effect of opaganib in patients with a poor prognosis[9]. Opaganib also has a Phase 1 chemoradiotherapy study protocol ready for FDA-IND submission.

Opaganib has demonstrated its safety and tolerability profile in more than 470 participants in multiple clinical studies and expanded access use, including a large global Phase 2/3 study in hospitalized patients with moderate to severe COVID-19, published in **Microorganisms**[2].

About RedHill Biopharma

RedHill Biopharma Ltd. (NASDAQ: RDHL) is a specialty biopharmaceutical company primarily focused on U.S. development and commercialization of drugs for gastrointestinal diseases, infectious diseases and oncology. RedHill promotes the FDA-approved gastrointestinal drug **Talicia,** for the treatment of Helicobacter pylori (H. pylori) infection in adults[10], with a U.S. co-commercialization agreement with Cumberland Pharmaceuticals (Nasdaq: CPIX). RedHill's key clinical late-stage development programs include: (i) **opaganib (ABC294640)**, a first-in-class, orally administered sphingosine kinase-2 (SPHK2) selective inhibitor with anti-inflammatory, antiviral, metabolic and anticancer activity, targeting multiple indications with U.S. government and academic collaborations intended for medical countermeasure development including for EVD, radiation exposure indications such as GI-Acute Radiation Syndrome (GI-ARS), a Phase 2/3 program for hospitalized COVID-19, and an ongoing Phase 2 study in prostate cancer in combination with darolutamide; (ii) **RHB-102 (Bekinda)**, with a planned Phase 2 proof-of-concept study for GLP-1/GIP receptor agonist-associated GI intolerance, positive results from a U.S. Phase 3 study for acute gastroenteritis and gastritis, positive results from a U.S. Phase 2 study for IBS-D and potential UK submission for chemotherapy and radiotherapy induced nausea and vomiting. RHB-102 is partnered with Hyloris

Pharmaceuticals (EBR: HYL) for worldwide development and commercialization outside North America; (iii) **RHB-204**, a next-generation optimized formulation of RHB-104, with a planned Phase 2 study for Crohn's disease (based on RHB-104's positive Phase 3 Crohn's disease study results); and (iv) **RHB-107** (**upamostat**), an oral broad-acting, host-directed, serine protease inhibitor with potential for pandemic preparedness, including COVID-19 and also targeting multiple cancer and inflammatory gastrointestinal diseases.

Visit **www.redhillbio.com** / **X.com/RedHillBio** for more information about the Company

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 may be preceded by the words "intends," "may," "will," "plans," "expects," "anticipates," "projects," "predicts," "estimates," "aims," "believes," "hopes," "potential" or similar words, and include, among others, statements regarding the potential for opaganib to be accepted into Ebola virus disease control programs or, if accepted, the ability to demonstrate its efficacy. 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 opaganib is not accepted into Ebola virus disease control programs, or if accepted, that it does not demonstrate efficacy; the risk that development of RHB-204 for Crohn's disease may not be completed, or if completed may not be approved or may not achieve commercial success; the risk that opaganib is not effective against the indications for which we develop our products; the risk that RHB-102 (Bekinda) does not effectively reduce GLP-1/GIP-related nausea, vomiting and diarrhea; the risk regarding the Company's ability to regain and maintain compliance with Nasdaq's listing requirements, including the minimum bid price requirement; the risk that the addition of new revenue generating products or out-licensing transactions will not occur; the risk that the Company will not receive future milestone payments under its existing agreements or that they will be less than anticipated; the risk of current uncertainty regarding U.S. government research and development funding and that the U.S. government is under no obligation to continue to support development of our products and can cease such support at any time; the risk that acceptance onto the RNCP Product Development Pipeline or other governmental and non-governmental development programs 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 its programs; the risk that the Company's development programs and studies 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 studies may be required; 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 any necessary commercial companion diagnostics; (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; (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) the Company's ability to collect on its judgement against Kukbo; (xiii) estimates of the Company's expenses, future revenues, capital requirements and needs for additional financing; (xiv) the effect of patients suffering adverse experiences using investigative drugs under the Company's Expanded Access Program; (xv) competition from other companies and technologies within the Company's industry; and (xvi) 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 27, 2026. 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]Opaganib is an investigational new drug, not available for commercial distribution.

[2]Neuenschwander FC, Barnett-Griness O, Piconi S, Maor Y, Sprinz E, Assy N, Khmelnitskiy O, Lomakin NV, Goloshchekin BM, Nahorecka E, et al. Effect of Opaganib on Supplemental Oxygen and Mortality in Patients with Severe SARS-CoV-2 Based upon FIO2 Requirements. Microorganisms. 2024; 12(9):1767. **https://doi.org/10.3390/microorganisms12091767**

[3]Antiviral Activity of Opaganib, a First-in-class Sphingolipid Modulator. Rekha G. Panchal1*, Raina Kumar1, Eric Nguyen1#, LTC Jeffrey Kugelman1, Janet Skerry1, Xiaoli Chi1, Ashley Mcaleese1#, Aura R. Garrison, Mark Levitt, Gilead Raday, Patricia Anderson, Sara Johnston, Reza Fathi, LTC Robert Haupt United States Army Medical Research Institute of Infectious Diseases

[4]Repeat study showed 20% vehicle survival vs. 10% opaganib; mixed results across the two animal models (including the vehicle only group inter study variability) underscore model variability.

[5]Sphingosine Kinases Promote Ebola Virus Infection and Can Be Targeted to Inhibit Filoviruses, Coronaviruses, and Arenaviruses Using Late Endocytic Trafficking to Enter Cells. Corina M. Stewart, Yuxia Bo, Kathy Fu, Mable Chan, Robert Kozak, Kim Yang-Ping Apperley, Geneviève Laroche, Redaet Daniel, André M. Beauchemin, Gary Kobinger, Darwyn Kobasa, and Marceline Côté. ACS Infectious Diseases 2023 9 (5), 1064-1077. DOI: 10.1021/acsinfecdis.2c00416

[6]Sphingosine Kinases Promote Ebola Virus Infection and Can Be Targeted to Inhibit Filoviruses, Coronaviruses, and Arenaviruses Using Late Endocytic Trafficking to Enter Cells. Corina M. Stewart, Yuxia Bo, Kathy Fu, Mable Chan, Robert Kozak, Kim Yang-Ping Apperley, Geneviève Laroche, Redaet Daniel, André M. Beauchemin, Gary Kobinger, Darwyn Kobasa, and Marceline Côté. ACS Infectious Diseases 2023 9 (5), 1064-1077. DOI: 10.1021/acsinfecdis.2c00416

[7]**https://www.reuters.com/business/healthcare-pharmaceuticals/who-chief-tedros-says-there-have-been-220-suspected-deaths-ebola-outbreak-2026-05-25/**

[8]**https://www.who.int/health-topics/ebola#tab=tab_1**

[9]**https://www.redhillbio.com/news/news-details/2025/RedHill-Announces-Initiation-of-Phase-2-Study-of-Opaganib-and-Darolutamide-in-Advanced-Prostate-Cancer/default.aspx**

[10]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**.

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