NEWS RELEASE

RedHill's Opaganib Enhances Efficacy of Neuroblastoma Chemo Combination and Augment Anti-Tumor Immunity in Triple-Negative Breast Cancer in Preclinical Studies - New Data Presented at AACR 2026

2026-04-22

New preclinical data, independently presented in two posters at the 2026 American Association for Cancer Research (AACR) Annual Meeting, show positive effects of opaganib[1] as potential add-on therapy in models of neuroblastoma (NB) and triple-negative breast cancer (TNBC)

The positive NB data from studies undertaken by Penn State University's Jeremy Hengst and Apogee Biotechnology, and funded by the Beat Childhood Cancer Foundation and Four Diamonds, indicate that opaganib may enhance the therapeutic efficacy of the oxaliplatin + doxorubicin (OXDOX) chemotherapy combination in high-risk NB by directly destabilizing n-Myc, a key oncogenic driver of neuroblastoma and other solid tumors, through increased ceremide production enhancing programmed cell death (apoptosis) in cancer cells[2]

A second poster from University of Kansas' Colette Worcester describes in vitro model data showing that pre-treatment with opaganib, followed by low-dose diABZI treatment, potentiated the downstream STING-mediated effects and may augment anti-tumor immunity in TNBC, which has the poorest prognosis of the breast cancer subtypes[3]

Opaganib, a novel, potentially broad acting, oral, small molecule drug with demonstrated safety & efficacy profiles[4], is in development for multiple oncology, viral, inflammatory and diabetes and obesity-related indications

RALEIGH, N.C., and TEL-AVIV, Israel, April 22, 2026 /PRNewswire/ -- **RedHill Biopharma Ltd.** (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced the independent presentation of new preclinical data at the 2026 American Association for Cancer Research (AACR) Annual Meeting, showing positive effects of opaganib as potential add-on therapy in models of neuroblastoma (NB) and triple-negative breast cancer (TNBC).

The positive NB data, from studies undertaken by Penn State University's Jeremy Hengst, PhD, and Apogee Biotechnology funded by the Beat Childhood Cancer Foundation and Four Diamonds, indicate that opaganib may enhance the therapeutic efficacy of the oxaliplatin + doxorubicin (OXDOX) chemotherapy combination in high-risk NB. The data showed that opaganib directly destabilized n-Myc, a key oncogenic driver of neuroblastoma and other solid tumors, regulating cell proliferation, differentiation, and apoptosis during embryonic development, a critical factor driving poor outcomes.

A second poster from the University of Kansas' Colette Worcester describes in vitro model data showing that pre-

treatment with opaganib, followed by low-dose diABZI treatment, potentiated the downstream STING-mediated effects and may augment anti-tumor immunity in TNBC, which has the poorest prognosis of the breast cancer subtypes.

Dr. Mark Levitt, Chief Scientific Officer at RedHill said: "These data represent exciting findings that could hold promise for improving outcomes in treating pediatric NB and TNBC, providing additional encouragement for further exploration. Opaganib has previously shown potential as add-on therapy in several preclinical oncology models in combination with chemotherapy. Moreover, the ongoing Phase 2 clinical study of opaganib in combination with darolutamide in advanced prostate cancer could potentially provide paradigm-shifting clinical data in support of the additive use of opaganib in a cancer setting."

Neuroblastoma is the most common infancy cancer with ~5,500 global pediatric cases per year in children aged 0–14. It accounts for 10% of childhood cancers and 15% of pediatric cancer-related deaths in the U.S.[5],[6] Opaganib received FDA Orphan Drug and Rare Pediatric Disease designations for the treatment of neuroblastoma, a rare pediatric cancer, with potential for a Rare Pediatric Disease Priority Review Voucher ("PRV"). Development discussions for this indication are ongoing with Penn State University and the Beat Childhood Cancer consortium.

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.

Peer-reviewed data, published in the journal Diabetes, Metabolic Syndrome and Obesity[7], provides evidence that opaganib uniquely works through the inhibition of multiple pathways implicated in insulin resistance, β-cell disruption, adipocyte function, inflammation / immune regulation, vascular complications, energy metabolism, 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[8]. 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 people 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**.

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[9], with a recent 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 for development for medical countermeasures including radiation and chemical exposure indications such as GI-Acute Radiation Syndrome (GI-ARS), a Phase 2/3 program for hospitalized COVID-19, and a Phase 2 study in prostate cancer in combination with darolutamide; (ii) **RHB-102**, 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.

More information about the Company is available at **www.redhillbio.com** / **X.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 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 effect of opaganib in neuroblastoma and triple negative breast cancer. 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 does not receive a Rare Pediatric Disease Priority Review Voucher; the risk that opaganib is not effective against the indications for which we develop our products; the risk regarding the Company's ability to regain and maintain compliance with Nasdaq's listing requirements, including the minimum bid price requirement and minimum stockholders' equity requirement; the risk that the addition of new revenue generating products or out-licensing transactions will not occur; 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) 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 10, 2025. 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] **Abstract 7879: Opaganib in combination with oxaliplatin and doxorubicin as a novel salvage therapy for relapsed/refractory high-risk neuroblastoma**. **Jeremy Hengst**, **Mohammad Haque**, **Muhammad Younis**, **Thussenthan Walter Angelo**, **Anna Bourne**, **Katherine McClain**, **Meenakshi Shukla**, **Jonathan Lerch**, **Tarlan Arjmandi**, **Eric Cochran**, **Lynn Maines**, **Charles D. Smith**, **Vladimir S. Spiegelman**, **Jacqueline M. Kraveka**, **Giselle L. Saulnier Sholler**. Cancer Res (2026) 86 (7_Supplement): 7879. **https://doi.org/10.1158/1538-7445.AM2026-7879**

[3] Abstract 4323: The SPHK2 inhibitor opaganib potentiates tumor-intrinsic STING activation in triple-negative breast cancer in vitro. Colette R. Worcester, Amrita Mitra, Harsh B. Pathak, Shane R. Stecklein. Cancer Res (2026) 86 (7_Supplement): 4323. **https://doi.org/10.1158/1538-7445.AM2026-4323** Published: 03 April 2026

[4] 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**

[5]**https://www.ncbi.nlm.nih.gov/books/NBK448111/#:~:text=Neuroblastoma%20is%20the%20most%20common,of%20pediatric%20cancer%2Drelated%20deaths**

[6] Yan P, Qi F, Bian L, et al. Comparison of Incidence and Outcomes of Neuroblastoma in Children, Adolescents, and Adults in the United States: A Surveillance, Epidemiology, and End Results (SEER) Program Population Study. Med Sci Monit. 2020;26:e927218. Published 2020 Nov 29. doi:10.12659/MSM.927218.

[7] Maines LW, Keller SN, Smith RA, Smith CD. Opaganib Promotes Weight Loss and Suppresses High-Fat Diet-Induced Obesity and Glucose Intolerance. Diabetes Metab Syndr Obes. 2025;18:969-983. **https://doi.org/10.2147/DMSO.S514548**

[8] **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**

[9] 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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