March 10, 2016

RedHill Biopharma Announces Peer-Reviewed Publication Demonstrating Therapeutic Potential of YELIVA™ in Cholangiocarcinoma Cancer

- **The article was authored by scientists from the Mayo Clinic Cancer Center, the Hollings Cancer Center at the Medical University of South Carolina and Apogee Biotechnology Corporation**
- **RedHill announced in October 2015 positive top-line results from a Phase I study with YELIVA™ (ABC294640) in patients with advanced solid tumors, the majority of which were gastrointestinal cancer patients, including cholangiocarcinoma, pancreatic and colorectal cancers**
- **YELIVA™ is a Phase II-stage, proprietary, first-in-class, orally-administered, sphingosine kinase-2 (SK2) selective inhibitor with anticancer and anti-inflammatory activities, targeting multiple oncology, inflammatory and gastrointestinal indications**
- **The development of YELIVA™ was funded to date primarily by grants and contracts from U.S. federal and state government agencies awarded to Apogee, including the National Cancer Institute, the Department of Health and Human Services Biomedical Advanced Research and Development Authority (BARDA), the Department of Defense and the FDA Office of Orphan Products Development**

TEL-AVIV, Israel, March 10, 2016 (GLOBE NEWSWIRE) -- RedHill Biopharma Ltd. (NASDAQ:RDHL) (TASE:RDHL) ("RedHill" or the "Company"), a biopharmaceutical company primarily focused on the development and commercialization of late clinical-stage, proprietary, orally-administered, small molecule drugs for inflammatory and gastrointestinal diseases, including cancer, today announced the publication of an article evaluating the therapeutic potential of YELIVA™ (ABC294640), the Company's orally-administered first-in-class Sphingosine kinase-2 (SK2) selective inhibitor, in the treatment of cholangiocarcinoma (bile duct cancer). The article, authored by scientists from the Mayo Clinic Cancer Center, the Hollings Cancer Center at the Medical University of South Carolina and Apogee Biotechnology Corporation ("Apogee"), will be published in Oncotarget and is available online on the journal's website.

The article[1], entitled *"Antitumor effect of the novel sphingosine kinase-2 inhibitor ABC294640 is enhanced by inhibition of autophagy and by sorafenib in human cholangiocarcinoma cells,"* found that SK2 is overexpressed in multiple human cholangiocarcinoma cell lines, including a patient-derived line. The article describes non-clinical studies conducted with YELIVA™ (ABC294640) in these cell lines. The results from these studies demonstrated that YELIVA™ inhibited cancer proliferation and induced apoptosis in these cholangiocarcinoma cancer cells. Furthermore, YELIVA™ inhibited STAT3 phosphorylation, one of the key signaling pathways regulating cell proliferation and survival, and also induced autophagy. In addition, YELIVA™ in combination with sorafenib, an FDA-approved multikinase inhibitor for the treatment of hepatocellular carcinoma and renal cell carcinoma (NEXAVAR® marketed by Bayer AG), synergistically inhibited the proliferation of cholangiocarcinoma cells.

The authors concluded that these findings provide preliminary insight into the possible use of YELIVA™ as an anticancer drug for cholangiocarcinoma treatment, as well as novel evidence that SK2 may be a rational therapeutic target in the treatment of this cancer. Additionally, a combination of YELIVA™ with sorafenib and/or autophagy inhibitors may provide novel strategies for the treatment of cholangiocarcinoma.

Reza Fathi, RedHill's Senior VP R&D, said: "We are pleased to announce the publication of this important article in a well-respected, peer-reviewed journal. The findings described in this publication provide further insight into the mechanism of the anticancer activities of YELIVA™, a novel Sphingosine kinase-2 (SK2) inhibitor, and suggest that YELIVA™ could potentially be effective in treating cholangiocarcinoma cancer. Notably, it was found that YELIVA™ inhibited STAT3 phosphorylation, one of the key signaling pathways regulating cholangiocarcinoma cell proliferation and survival. We continue to diligently advance the clinical research of YELIVA™ for multiple indications. We have initiated a Phase I/II study with YELIVA™ in patients with refractory/relapsed diffuse large B-cell lymphoma and plan to initiate two additional Phase II

studies, for multiple myeloma and radioprotection, during 2016. We are planning additional clinical programs with this novel and promising drug candidate for oncology, inflammatory and gastrointestinal indications."

Charles D. Smith, Ph.D., Apogee's President and CEO and a co-author of the article, added: "We are pleased that these results provide a rationale for use of YELIVA™ in a very difficult to treat malignancy. These results further add to the breadth and importance of YELIVA™'s mechanism of action studies in multiple human tumors."

Cholangiocarcinoma is a rare cancer that develops in the bile ducts, characterized by its late diagnosis and high mortality rates. Cholangiocarcinoma is the second most common primary liver tumor, accounting for approximately 10-15% of all hepatobiliary malignancies[2]. Although a rare cancer, the incidence and mortality rates of cholangiocarcinoma have been increasing worldwide in the last three decades. The five year survival rates following diagnosis have not increased during this time period, and remain at 10%[3]. Surgery is the only curative treatment option, but only for the minority of patients diagnosed with early-stage disease.

RedHill announced in October 2015 positive top-line results from a Phase I study with YELIVA™ in patients with advanced solid tumors, the majority of which were gastrointestinal cancer patients, including pancreatic, colorectal and cholangiocarcinoma cancers. Top-line results demonstrated that YELIVA™ can be safely administered to cancer patients at doses that provide circulating drug levels that are predicted to have therapeutic activity, based on levels required in preclinical models. The study included the first-ever longitudinal analysis of plasma S1P levels as a potential pharmacodynamic (PD) biomarker for activity of a sphingolipid-targeted drug. The administration of YELIVA™ resulted in a rapid and pronounced decrease in S1P levels over the first 12 hours, with return to baseline at 24 hours, which is consistent with clearance of the drug, with several patients having prolonged stabilization of disease.

A Phase I/II clinical study was initiated in the U.S. evaluating YELIVA™ in patients with refractory/relapsed diffuse large B-cell lymphoma (DLBCL), including in patients with HIV-related DLBCL. The study is being conducted at the Louisiana State University Health Sciences Center (LSUHSC) in New Orleans and is supported by a grant awarded to Apogee from the NCI Small Business Technology Transfer (STTR) program, as well as additional support from RedHill. The Phase I/II clinical study in patients with refractory/relapsed diffuse large B-cell lymphoma and the Phase I clinical study in cancer patients with advanced solid tumors are registered on www.ClinicalTrials.gov, a web-based service by the U.S. National Institute of Health which provides public access to information on publicly and privately supported clinical studies.

A Phase I/II study with YELIVA™ for the treatment of refractory or relapsed multiple myeloma is planned to be initiated in the second quarter of 2016. The study will be conducted at Duke University Medical Center. The study is supported by a $2 million grant from the NCI Small Business Innovation Research Program (SBIR) awarded to Apogee in conjunction with Duke University, with additional support from RedHill.

A Phase II clinical study to evaluate YELIVA™ as a radioprotectant to prevent mucositis in cancer patients undergoing therapeutic radiotherapy is planned to be initiated in the U.S. during the second half of 2016, subject to regulatory and other conditions.

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[1] The article was authored by Xiwei Ding, Roongruedee Chaiteerakij, Catherine D. Moser, Hassan Shaleh, Jeffrey Boakye, Gang Chen, Albert Ndzengue, Ying Li, Yanling Zhou, Shengbing Huang, Frank A. Sinicrope, Xiaoping Zou, Melanie B. Thomas, Charles D. Smith, Lewis R. Roberts

[2] A. Bergquist et al. *Epidemiology of cholangiocarcinoma,* Best Pract Res Clin Gastroenterol. 2015 Apr;29(2):221-32

[3] S. Rizvi and G. J. Gores, *Pathogenesis, diagnosis, and management of cholangiocarcinoma*, Gastroenterology, vol. 145, no. 6, pp. 1215-1229, 2013.

About YELIVA™ (ABC294640):

YELIVA™ (ABC294640) is a proprietary, first-in-class, orally-administered, sphingosine kinase-2 (SK2) selective inhibitor with anticancer and anti-inflammatory activities, targeting multiple oncology, inflammatory and gastrointestinal indications. By inhibiting the SK2 enzyme, YELIVA™ blocks the synthesis of sphingosine 1-phosphate (S1P), a lipid signaling molecule that promotes cancer growth and pathological inflammation. SK2 is an innovative molecular target for anticancer therapy because of its critical role in catalyzing the formation of S1P, which is known to regulate cell proliferation and activation of inflammatory pathways. YELIVA™ was originally developed by U.S.-based Apogee Biotechnology Corp. and completed multiple successful pre-clinical studies in oncology, inflammation, GI and radioprotection models, as well as the ABC-101

Phase I clinical study in cancer patients with advanced solid tumors. A Phase I/II clinical study evaluating YELIVA™ in patients with refractory/relapsed diffuse large B-cell lymphoma (DLBCL) has been initiated in the U.S. The development of YELIVA™ was funded to date primarily by grants and contracts from U.S. federal and state government agencies awarded to Apogee Biotechnology Corp., including the U.S. National Cancer Institute, the U.S. Department of Health and Human Services' Biomedical Advanced Research and Development Authority (BARDA), the U.S. Department of Defense and the FDA Office of Orphan Products Development.

About RedHill Biopharma Ltd.:

RedHill Biopharma Ltd. (NASDAQ:RDHL) (TASE:RDHL) is a biopharmaceutical company headquartered in Israel, primarily focused on the development and commercialization of late clinical-stage, proprietary, orally-administered, small molecule drugs for the treatment of inflammatory and gastrointestinal diseases, including cancer. RedHill's current pipeline of proprietary products includes: (i) **RHB-105 -** an oral combination therapy for the treatment of *Helicobacter pylori* infection with successful results from a first Phase III study; (ii) **RHB-104 -** an oral combination therapy for the treatment of Crohn's disease with an ongoing first Phase III study and an ongoing proof-of-concept Phase IIa study for multiple sclerosis; (iii) **BEKINDA™ (RHB-102) -** a once-daily oral pill formulation of ondansetron with an ongoing Phase III study in the U.S. for acute gastroenteritis and gastritis and a planned Phase II study for IBS-D; (iv) **RHB-106 -** an encapsulated bowel preparation licensed to Salix Pharmaceuticals, Ltd.; (v) **YELIVA™ (ABC294640) -** an orally-administered first-in-class SK2 selective inhibitor targeting multiple oncology, inflammatory and gastrointestinal indications with a Phase I/II study initiated for refractory/relapsed diffuse large B-cell lymphoma (DLBCL); (vi) **MESUPRON® -** a Phase II-stage first-in-class uPA inhibitor, administered by oral capsule, targeting gastrointestinal and other solid tumors; (vii) **RP101 -** currently subject to an option-to-acquire by RedHill, RP101 is a Phase II-stage first-in-class Hsp27 inhibitor, administered by oral tablet, targeting pancreatic and other gastrointestinal cancers; (viii) **RIZAPORT™ (RHB-103) -** an oral thin film formulation of rizatriptan for acute migraines, with a U.S. NDA currently under discussion with the FDA and marketing authorization received in Germany in October 2015; and (ix) **RHB-101 -** a once-daily oral pill formulation of the cardio drug carvedilol.

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, without limitation, 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; (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 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; (v) the Company's ability to establish and maintain corporate collaborations; (vi) 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; (vii) the interpretation of the properties and characteristics of the Company's therapeutic candidates and of the results obtained with its therapeutic candidates in research, preclinical studies or clinical trials; (viii) the implementation of the Company's business model, strategic plans for its business and therapeutic candidates; (ix) 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; (x) parties from whom the Company licenses its intellectual property defaulting in their obligations to the Company; (xi) estimates of the Company's expenses, future revenues capital requirements and the Company's needs for additional financing; (xii) competitive companies and technologies within the Company's industry; and (xiii) the impact of the political and security situation in Israel on the Company's business. 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 February 25, 2016. All forward-looking statements included in this Press Release are made only as of the date of this Press Release. We assume no obligation to update any written or oral forward-looking statement unless required by law.

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