



April 4, 2017

RedHill Biopharma Receives FDA Orphan Drug Designation for YELIVA® for the Treatment of Cholangiocarcinoma

- | **Orphan Drug designation allows RedHill to benefit from various development incentives to develop YELIVA® (ABC294640) for cholangiocarcinoma, as well as a seven-year marketing exclusivity period for the indication, if approved for marketing**
- | **A Phase IIa clinical study with YELIVA® in patients with advanced, unresectable, intrahepatic and extrahepatic cholangiocarcinoma is planned to be initiated in the third quarter of 2017**
- | **Cholangiocarcinoma (bile duct cancer) is a highly lethal malignancy for which there is a strong need for more effective systemic treatments; the 5-year relative survival rate for patients with cholangiocarcinoma ranges between 2% to 30%, depending on the tumor type and stage at diagnosis**
- | **A Phase I study with YELIVA® in patients with advanced solid tumors successfully met its primary and secondary endpoints; of the three cholangiocarcinoma patients in the Phase I study, one patient had a sustained partial response and the other two had prolonged stable disease**
- | **RedHill is pursuing several Phase I/II clinical studies with YELIVA®, targeting multiple oncology and inflammatory indications, some of which are supported by National Cancer Institute (NCI) grants awarded to Apogee Biotechnology and U.S. universities**
- | **YELIVA® is a proprietary, first-in-class, orally-administered sphingosine kinase-2 (SK2) selective inhibitor, with anti-cancer and anti-inflammatory activities**

TEL-AVIV, Israel, April 04, 2017 (GLOBE NEWSWIRE) -- RedHill Biopharma Ltd. (NASDAQ:RDHL) (Tel-Aviv Stock Exchange:RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company primarily focused on the development and commercialization of late clinical-stage, proprietary, orally-administered, small molecule drugs for gastrointestinal and inflammatory diseases and cancer, today announced that the U.S. Food and Drug Administration (FDA) has granted YELIVA® (ABC294640) Orphan Drug designation for the treatment of cholangiocarcinoma.

The Orphan Drug designation allows RedHill to benefit from various development incentives to develop YELIVA® for this indication, including tax credits for qualified clinical testing, waiver of a prescription drug user fee (PDUFA fee) upon submission of a potential marketing application and, if approved, a seven-year marketing exclusivity period for the treatment of cholangiocarcinoma.

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. 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.

Mark L. Levitt, MD, PhD, RedHill's Medical Director, Oncology, said: "Cholangiocarcinoma is a cancer with a poor prognosis. Patients suffering from this disease have very few treatment options, and they are of limited efficacy. Based on promising preclinical data, as well as results from three previously treated cholangiocarcinoma patients who took part in the Phase I study with YELIVA®, we are hopeful that YELIVA® could potentially provide a much-needed new treatment option for patients. We are very pleased with the Orphan Drug designation and are advancing our preparations for a Phase IIa study to evaluate the safety and efficacy of YELIVA® in patient suffering from unresectable, intrahepatic and extrahepatic cholangiocarcinoma, which we plan to initiate in the third quarter of this year."

Cholangiocarcinoma (bile duct cancer) is a highly lethal malignancy for which there is a strong need for more effective systemic treatments. Approximately 8,000 people are diagnosed with intrahepatic and extrahepatic bile duct cancers annually in the U.S.¹, with recent studies showing an increased incidence of cholangiocarcinoma, mainly attributed to recent advancements in diagnosis of this disease². Surgery with complete resection remains the only curative therapy for cholangiocarcinoma, however only a minority of patients are classified as having a resectable tumor at the time of diagnosis³. Additional treatment options include radiation therapy and chemotherapy; however, the efficacy of these treatments in cholangiocarcinoma patients is also limited. Despite overall advances in the ability to diagnose and treat

patients with cholangiocarcinoma, the prognosis for these relapse patients who have failed initial chemotherapy remains very poor, with an overall median survival of approximately one year⁴. The 5-year relative survival rates of intrahepatic and extrahepatic cholangiocarcinoma patients range between 2% to 30%, depending on the tumor type and stage at diagnosis⁵.

Final results from the Phase I study with YELIVA® in patients with advanced solid tumors confirmed that the study, conducted at the Medical University of South Carolina (MUSC) Hollings Cancer Center, successfully met its primary and secondary endpoints, demonstrating that the drug is well-tolerated and can be safely administered to cancer patients at doses that provide circulating drug levels that are predicted to have therapeutic activity.

Of the three patients with cholangiocarcinoma treated in the Phase I study, all of whom had prior therapy, one subject achieved a sustained partial response (Overall Survival (OS) = 20.3 months) and the other two subjects had prolonged stable disease (OS = 17.6 and 16.3 months).

RedHill plans to initiate a Phase IIa clinical study with YELIVA® in patients with advanced, unresectable, intrahepatic and extrahepatic cholangiocarcinoma in the third quarter of 2017. The single-arm study will evaluate YELIVA® as a single agent in cholangiocarcinoma patients with a primary endpoint of determining the response rate of cholangiocarcinoma to this treatment.

A Phase II study with YELIVA® for the treatment of advanced hepatocellular carcinoma (HCC) is ongoing at MUSC Hollings Cancer Center. The study is supported by a \$1.8 million grant from the NCI, awarded to MUSC, which is intended to fund a broad range of studies on the feasibility of targeting sphingolipid metabolism for the treatment of a variety of solid tumor cancers, with additional support from RedHill.

A Phase Ib/II study with YELIVA® for the treatment of refractory or relapsed multiple myeloma is ongoing 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 Biotechnology Corp. (Apogee), in conjunction with Duke University, with additional support from RedHill.

A Phase I/II clinical study evaluating YELIVA® in patients with refractory/relapsed diffuse large B-cell lymphoma as well as Kaposi sarcoma patients is ongoing at the Louisiana State University Health Sciences Center. The study is supported by a grant from the NCI awarded to Apogee, with additional support from RedHill.

A Phase Ib study to evaluate YELIVA® as a radioprotectant for prevention of mucositis in head and neck cancer patients undergoing therapeutic radiotherapy is planned to be initiated in the third quarter of 2017.

A Phase II study to evaluate the efficacy of YELIVA® in patients with moderate to severe ulcerative colitis is planned to be initiated in the second half of 2017.

About YELIVA® (ABC294640):

YELIVA® (ABC294640) is a Phase II-stage, proprietary, first-in-class, orally-administered, sphingosine kinase-2 (SK2) selective inhibitor with anti-cancer and anti-inflammatory activities. RedHill is pursuing with YELIVA® multiple clinical programs in oncology, inflammatory and gastrointestinal indications. By inhibiting SK2, 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. The Phase I 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, with several patients having prolonged stabilization of disease. YELIVA® received Orphan Drug designation from the U.S. FDA for the treatment of cholangiocarcinoma. 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) (Tel-Aviv Stock Exchange:RDHL) is a specialty 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 gastrointestinal and inflammatory diseases and cancer.

RedHill has a U.S. co-promotion agreement with Concordia for **Donnatal**[®], a prescription oral adjunctive drug used in the treatment of IBS and acute enterocolitis. RedHill's clinical-stage pipeline 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, a completed proof-of-concept Phase IIa study for multiple sclerosis and QIDP status for nontuberculous mycobacteria (NTM) infections; (iii) **BEKINDA**[®] (**RHB-102**) - a once-daily oral pill formulation of ondansetron with an ongoing Phase III study for acute gastroenteritis and gastritis and an ongoing Phase II study for IBS-D; (iv) **RHB-106** - an encapsulated bowel preparation licensed to Salix Pharmaceuticals, Ltd.; (v) **YELIVA**[®] (**ABC294640**) - a Phase II-stage, orally-administered, first-in-class SK2 selective inhibitor targeting multiple oncology, inflammatory and gastrointestinal indications; (vi) **MESUPRON** - a Phase II-stage first-in-class, orally-administered protease inhibitor, targeting pancreatic cancer and other solid tumors and (vii) **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. More information about the Company is available at: www.redhillbio.com.

*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 successfully market **Donnatal**[®], (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 of the results obtained with its therapeutic candidates in research, preclinical 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; and (xii) estimates of the Company's expenses, future revenues capital requirements and the Company's needs for additional financing; (xiii) competitive companies and technologies within the Company's industry. 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 23, 2017. 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.*

¹ American Cancer Society, Bile Duct Cancer: www.cancer.org/acs/groups/cid/documents/webcontent/003084-pdf.pdf, Jan 20, 2016.

² Gores GJ. Cholangiocarcinoma: current concepts and insights. *Hepatology* (Baltimore, Md). 2003 May;37(5):961-9.

³ Banales JM et al. Expert consensus document: Cholangiocarcinoma: current knowledge and future perspectives consensus statement from the European Network for the Study of Cholangiocarcinoma (ENS-CCA), *Nat Rev Gastroenterol Hepatol*. 2016;13:261-280.

⁴ Valle J, Wasan H, Palmer DH, et al. Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. *New Eng J Med* 2010;362:1273-81.

⁵ Howlader N, Noone AM, Krapcho M, Miller D, Bishop K, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2013, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2013/, based on November 2015 SEER data submission, posted to the SEER web site, April 2016.

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