Press Release

RedHill Biopharma Announces Phase Ib/II Study with YELIVA™ Initiated for Multiple Myeloma at a Leading U.S. Academic Medical Center

- **The Phase Ib/II clinical study is intended to evaluate the safety and efficacy of YELIVA™ (ABC294640) in patients with refractory or relapsed multiple myeloma and is supported by a $2 million grant from the National Cancer Institute (NCI), awarded to Apogee Biotechnology Corp., with additional support from RedHill**

- **YELIVA™ is a proprietary, first-in-class, orally-administered sphingosine kinase-2 (SK2) selective inhibitor, with anti-cancer and anti-inflammatory activities**

- **RedHill is pursuing several clinical studies with YELIVA™, targeting multiple inflammatory and oncology indications, including a Phase II study for the treatment of advanced hepatocellular carcinoma to be initiated in the coming weeks at the Medical University of South Carolina (MUSC) and additional clinical centers, supported by an NCI grant awarded to MUSC with additional support from RedHill**

- **Final positive results from the Phase I study with YELIVA™ in patients with advanced solid tumors confirmed that the study 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**

- **Worldwide sales of multiple myeloma therapies are estimated to exceed $12 billion in 2016**

TEL-AVIV, Israel, September 8, 2016 RedHill Biopharma Ltd. (NASDAQ: RDHL) (TASE: RDHL) ("RedHill" or the "Company"), a biopharmaceutical company primarily focused on development and commercialization of late clinical-stage, proprietary, orally-administered, small molecule drugs for gastrointestinal and inflammatory diseases and cancer, today announced that a Phase Ib/II clinical study evaluating YELIVA™ (ABC294640) in patients with refractory or relapsed multiple myeloma has been initiated.

The open-label, dose escalation Phase Ib/II study is being conducted at Duke University Medical Center and will enroll up to 77 patients with refractory or relapsed multiple myeloma who have previously been treated with proteasome inhibitors and immunomodulatory drugs.

Dr. Yubin Kang, MD, Associate Professor in the Division of Hematologic Malignancies and Cellular Therapy in the Department of Medicine at Duke University School of Medicine, is the lead investigator for the study.

The study is supported by a $2 million grant from the National Cancer Institute (NCI) Small Business Innovation Research Program (SBIR) awarded to Apogee Biotechnology Corp. (Apogee), in conjunction with Duke University, with additional support from RedHill.

YELIVA™ is a proprietary, first-in-class, orally-administered, sphingosine kinase-2 (SK2) selective inhibitor with anti-cancer and anti-inflammatory activities. 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.

RedHill is pursuing with YELIVA™ multiple clinical programs in oncology, inflammatory and gastrointestinal indications.

"We are very pleased that this study with YELIVA™ has been initiated at Duke University. Award of the NCI funding to support the study and the interest in the product by a major research university confirms the potential promise of YELIVA™ in this serious, chronic disease," **said Terry Plasse, MD, RedHill's Medical Director.** "The clinical study follows a successful preclinical study demonstrating that sphingosine kinase-2 is overexpressed in multiple myeloma cell lines and in human specimens, and that its inhibition may fight the disease. This is the second Phase I/II study initiated with YELIVA™. We expect to initiate additional clinical studies in the coming months, including studies in advanced hepatocellular carcinoma and prevention of mucositis in head and neck cancer patients undergoing therapeutic radiotherapy. Given YELIVA™'s unique mechanism of action, we continue to evaluate its therapeutic potential for multiple oncology, inflammatory and gastrointestinal indications, as a single agent and in combination with other oncology drugs."

The primary objectives of the first portion of the study (Phase Ib) are to assess safety and determine the maximum tolerated dose (MTD) in refractory or relapsed multiple myeloma patients. Secondary objectives include assessment of antitumor activity and determination of the pharmacokinetic (PK) and pharmacodynamic (PD) properties of YELIVA™ in this group of patients. The Phase Ib will be conducted at Duke University Division of Hematologic Malignancies and Cellular Therapy.

The primary objectives of the second portion of the study (Phase II) are to assess the overall treatment response rate and overall survival. Secondary objectives include evaluating the treatment response to YELIVA™ in patients with refractory or relapsed multiple myeloma

after three cycles of treatment and evaluation of pharmacodynamic markers. The Phase II portion will be conducted at multiple sites and will be managed by the Duke Cancer Network.

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), 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.

Among the 16 subjects that were assessable for response by RECIST 1.1 criteria (Response Evaluation Criteria in Solid Tumors), one subject had a partial response with a progression-free survival of 16.9 months, and six subjects had stable disease with a progression-free survival of between 3.5 and 17.6 months. Of the three patients with cholangiocarcinoma, one had a partial response and the other two had stable disease, one for over a year. YELIVA™ was well tolerated over a prolonged period at doses inducing the expected pharmacodynamic effects.

A Phase II study with YELIVA™ for the treatment of advanced hepatocellular carcinoma is planned to be initiated in the coming weeks. The study will be conducted at MUSC Hollings Cancer Center and additional clinical centers in the U.S. It is supported by a $1.8 million grant from the NCI awarded to MUSC, 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, including the Phase II study with YELIVA™, and will be further supported by additional funding from RedHill.

A clinical study to evaluate YELIVA™ as a radioprotectant for prevention of mucositis in head and neck cancer patients undergoing therapeutic radiotherapy is also planned.

A Phase I/II clinical study evaluating YELIVA™ in patients with refractory/relapsed diffuse large B-cell lymphoma (DLBCL) was initiated at the Louisiana State University Health Sciences Center (LSUHSC) in New Orleans in June 2015 and is expected to resume later this year following administrative hold and pending a protocol amendment aimed at improving overall recruitment. The study is supported by a grant awarded to Apogee from the NCI, as well as additional support from RedHill.

The studies with YELIVA™ (ABC294640) 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.

About Multiple Myeloma:

Multiple myeloma is a malignant plasma cell disorder which is usually not curable[1]. Symptomatic multiple myeloma is characterized by a clonal proliferation of plasma cells

[1] Ludwig, H., *et al.* Survival and years of life lost in different age cohorts of patients with multiple myeloma. *J Clin Oncol* 28, 1599-1605 (2010).

preceding clinical findings that include bone lesions, fractures, anemia, renal failure and hypercalcemia[2]. Approximately 30,000 new cases of multiple myeloma are expected to be diagnosed in the U.S. in 2016, accounting for 1.8% of all cancers. The 5-year survival rate of myeloma is estimated at 48.5% and approximately 95,000 people are living with myeloma in the United States[3]. The risk of multiple myeloma increases as people age. Most patients diagnosed with this cancer are at least 65 years old[4], making treatment with the most effective therapies problematic. The worldwide sales of multiple myeloma therapies are estimated to exceed $12 billion in 2016[5].

About YELIVA™ (ABC294640):

YELIVA™ (ABC294640) is a Phase II-stage, proprietary, first-in-class, orally-administered, sphingosine kinase-2 (SK2) selective inhibitor with anticancer and anti-inflammatory activities. RedHill is pursuing with YELIVA™ multiple clinical programs in 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. 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/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 gastrointestinal and inflammatory diseases and 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 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,

[2] Kyle, R.A. & Rajkumar, S.V. Multiple myeloma. *Blood* 111, 2962-2972 (2008).

[3] 'Surveillance, Epidemiology, and End Results Program', Myeloma

[4] American Cancer Society, Multiple Myeloma (January 2016)

[5] GlobalData Pharma eTrack, multiple myeloma estimated market size (September 2016)

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 uPA inhibitor, 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, orally-administered Hsp27 inhibitor, 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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