Press Release

RedHill Biopharma Announces Initiation of Phase IIa Study with ABC294640 (YELIVA®) for Cholangiocarcinoma at Mayo Clinic and MD Anderson

- **YELIVA®, a proprietary, first-in-class SK2 inhibitor, was granted FDA Orphan Drug designation for the treatment of cholangiocarcinoma**

- **Cholangiocarcinoma (bile duct cancer) is a highly lethal malignancy for which there is an urgent need for more effective treatments**

- **A Phase I clinical study with YELIVA® in patients with advanced solid tumors successfully met its primary and secondary endpoints; The study included three cholangiocarcinoma patients who failed prior therapies, of which one had a sustained partial response and the other two had prolonged stable disease**

TEL-AVIV, Israel / RALEIGH, NC, December 22, 2017 RedHill Biopharma Ltd. (NASDAQ: RDHL) (Tel-Aviv Stock Exchange: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company primarily focused on late clinical-stage development and commercialization of proprietary drugs for gastrointestinal diseases and cancer, today announced the initiation of a Phase IIa study with YELIVA® (ABC294640)[1] for the treatment of cholangiocarcinoma.

The single-arm Phase IIa study will evaluate YELIVA® as a single agent in patients suffering from advanced, unresectable intrahepatic, perihilar and extrahepatic cholangiocarcinoma. The study is planned to enroll up to 39 patients at Mayo Clinic major campuses in Arizona and Minnesota and at The University of Texas MD Anderson Cancer Center.

Dr. Mitesh J. Borad, Associate Professor of Medicine and Director of Phase I Drug Development at the Mayo Clinic Cancer Center in Arizona, will act as Principal Investigator of the study. Dr. Borad also serves as a consultant to the Division of Hematology/Oncology,

[1] YELIVA® (ABC294640) is an investigational new drug, not available for commercial distribution.

Department of Internal Medicine and to the Department of Molecular Medicine at Mayo Clinic. Dr. Borad's research is focused on development of novel treatments for patients with biliary and liver cancers and he has served on the National Cancer Institute (NCI) Hepatobiliary Task Force since 2011.

YELIVA® was granted FDA 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®, a new chemical entity, 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.

Cholangiocarcinoma (bile duct cancer) is a highly lethal malignancy for which there is an urgent need for more effective treatments. Approximately 8,000 people are diagnosed with intrahepatic and extrahepatic bile duct cancers annually in the U.S.[2], with recent studies showing an increased incidence of cholangiocarcinoma, mainly attributed to recent advancements in the diagnosis of this disease[3]. 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 diagnosis[4]. Additional treatment options include radiation therapy and chemotherapy. Still, the efficacy of these treatments in cholangiocarcinoma patients is also limited and the prognosis for relapse patients who have failed initial chemotherapy is very poor, with an overall median survival of approximately one year[5]. 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 diagnosis[6].

Following an extensive pre-clinical program, a Phase I clinical study with YELIVA® in patients with advanced solid tumors successfully met its primary and secondary endpoints,

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

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

[4] 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.

[5] 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.

[6] American Cancer Society, Survivor Statistics for Bile Duct Cancers, https://www.cancer.org/content/cancer/en/cancer/bile-duct-cancer/detection-diagnosis-staging/survival-by-stage.html, Jan 20, 2016.

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).

The ongoing 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 YELIVA® (ABC294640):
YELIVA® (ABC294640), a new chemical entity, is a Phase II-stage, proprietary, first-in-class, orally-administered, sphingosine kinase-2 (SK2) selective inhibitor with anticancer and anti-inflammatory activities, targeting 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. 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.

About RedHill Biopharma Ltd.:
RedHill Biopharma Ltd. (NASDAQ: RDHL) (Tel-Aviv Stock Exchange: RDHL) is a specialty biopharmaceutical company, primarily focused on the development and commercialization of late clinical-stage, proprietary drugs for the treatment of gastrointestinal diseases and cancer. RedHill promotes three gastrointestinal products in the U.S.: **Donnatal® -** a prescription oral adjunctive drug used in the treatment of IBS and acute enterocolitis; **Esomeprazole Strontium Delayed-Release Capsules 49.3 mg -** a prescription proton pump inhibitor indicated for adults for the treatment of gastroesophageal reflux disease (GERD) and other gastrointestinal conditions; and **EnteraGam® -** a medical food intended for the dietary management, under medical supervision, of chronic diarrhea and loose stools. RedHill's key clinical-stage development programs include: (i) **TALICIA™ (RHB-105) -** an oral combination therapy for the treatment of *Helicobacter pylori* infection with successful results from a first Phase III study and an ongoing confirmatory Phase III study; (ii) **RHB-104 -** an oral combination therapy with an ongoing first Phase III study for Crohn's disease and a planned pivotal Phase III study for nontuberculous mycobacteria (NTM) infections; (iii) **YELIVA® (ABC294640) -** an orally-administered, first-in-class SK2 selective inhibitor with an ongoing Phase IIa study for cholangiocarcinoma; (iv) **BEKINDA® (RHB-102) -** a once-daily oral pill formulation of ondansetron with successful top-line results from a Phase III study in acute gastroenteritis and gastritis and successful top-line results from a Phase II study in IBS-D; (v) **RHB-106 -** an

encapsulated bowel preparation licensed to Salix Pharmaceuticals, Ltd. and (vi) **MESUPRON** - a Phase II-stage first-in-class, orally-administered protease inhibitor, targeting pancreatic cancer and inflammatory gastrointestinal diseases. 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® and EnteraGam®; (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, 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; (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; and (xiv) competition from other 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. 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.

Company contact:
Adi Frish
Senior VP Business Development & Licensing
RedHill Biopharma
+972-54-6543-112
adi@redhillbio.com

IR contact (U.S.):
Marcy Nanus
Senior Vice President
The Trout Group
+1-646-378-2927
Mnanus@troutgroup.com