March 31, 2016

RedHill Biopharma Announces Interim Results from Phase IIa Proof-of-Concept Study Supporting Therapeutic Potential of RHB-104 in Multiple Sclerosis

- **The ongoing CEASE-MS Phase IIa proof-of-concept (PoC), single-arm, open-label study was designed with a series of exploratory endpoints to evaluate the safety and potential efficacy of fixed oral dose RHB-104 as add-on therapy to interferon beta-1a in 18 patients treated for relapsing-remitting multiple sclerosis (RRMS)**
- **Interim results after completion of the 24 week treatment period of the study demonstrated positive safety and clinical signals and support further clinical development based on encouraging preliminary data**
- **Annualized relapse rate (ARR) at 24 weeks was 0.288 in the modified intent-to-treat (mITT) population and 0.0 in the per-protocol (PP) population, comparing favorably with previously reported pivotal studies of interferon beta-1a therapies Avonex® (0.67)[1] and Rebif® (0.87-0.91)[2]**
- **88% of the mITT patient population and 100% of the PP patient population were relapse free at 24 weeks, comparing favorably with previously reported pivotal data on the use of Rebif® (75%) in comparison with Avonex® (63%) as standalone first line therapies[3]; No patients in the CEASE-MS study relapsed after week 8 of treatment**
- **Expanded Disability Status Scale (EDSS) scores, a standard measure of MS disability, indicate the disease was stable during the treatment period and there was a signal of improvement; No increase in total EDSS was observed in any of the patients in the study**
- **With only a single active T1 post gadolinium lesion noted among all patients followed, combined unique active lesions (CUAs) - the primary outcome measure in the study - were almost entirely MRI T2 lesions; Although not powered for efficacy, a reduction in total MRI T2 lesion volume was observed at 24 weeks as compared to baseline, suggesting a decreased burden of disease and comparing favorably with previously reported Avonex®[4] and Rebif®[5] data**
- **No clinically significant change was observed for total CUA lesions at week 24, which is supportive of a stable disease state**
- **RHB-104 was found to be safe and well tolerated, with no drug-related serious adverse events or other clinically relevant or unexpected adverse events**
- **2015 U.S. and worldwide sales of multiple sclerosis therapies were estimated to exceed $12 billion and $17 billion, respectively**
- **RHB-104 is also undergoing a Phase III clinical study for Crohn's disease (the MAP US study), with interim data and safety monitoring board (DSMB) analysis expected in the second half of 2016**

TEL-AVIV, Israel, March 31, 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 encouraging top-line interim results from its ongoing CEASE-MS Phase IIa proof-of-concept (PoC) clinical study evaluating fixed oral dose RHB-104 in patients treated for relapsing-remitting multiple sclerosis (RRMS).

Ira Kalfus MD, Medical Director of RedHill and the CEASE-MS study said: "We are very pleased with the interim results from the ongoing CEASE-MS Phase IIa proof-of-concept study with RHB-104 for relapsing-remitting multiple sclerosis (RRMS). The initial findings from the study, including safety, clinical and MRI, support the therapeutic potential of RHB-104 as add-on therapy in RRMS." **Dr. Kalfus added**: "Although designed as an exploratory proof-of-concept study in a very small patient population and not powered for efficacy, the study interim results demonstrate positive safety data and clinical

signals, supporting additional studies to better investigate the therapeutic potential of RHB-104 in RRMS. 88% of the mITT patient population and 100% of the per-protocol population were relapse free at 24 weeks of treatment. Importantly, a positive efficacy signal was seen in reduction of total T2 lesion volume at 24 weeks compared to baseline. Moreover, EDSS scores were stable with suggestion of improvement. Notably, no patients experienced an increase in total EDSS, further underscoring the therapeutic potential of RHB-104 for the treatment of RRMS. RHB-104 was observed to be safe and well-tolerated with no clinically relevant or unexpected adverse events, further reinforcing our confidence in this therapeutic candidate as we continue to advance the ongoing Phase III MAP US study with RHB-104 for Crohn's disease. We are looking forward to further analyses of the data upon completion of the 48 week CEASE-MS study. Patients are now completing their 24 week follow up treatment period, off RHB-104, and final results of the completed 48 week study are expected during the second half of 2016. Analysis of the completed study will drive next steps in the development path of RHB-104 for MS including identification of the patient population, comparator and clinical endpoints to be investigated in the next study. We would like to thank the patients, investigators and clinical support staff who are participating in this important ongoing study."

Multiple sclerosis (MS) is a chronic inflammatory, demyelinating disease of the central nervous system (CNS) with an unknown etiology, believed to be multifactorial. Thought to be autoimmune, the MS inflammatory process is also consistent with persistent infection. RHB-104 is a proprietary, orally administered, potentially groundbreaking antibiotic combination therapy with potent intracellular, anti-mycobacterial and anti-inflammatory properties. The ongoing CEASE-MS Phase IIa clinical study is a single-arm, open-label PoC study evaluating fixed oral dose RHB-104 as add-on therapy to interferon beta-1a for the treatment of RRMS. This study follows positive pre-clinical research findings and provides clinical evidence of RHB-104's potential as a treatment for MS. The study was designed as an uncontrolled, non-powered, single-arm, open-label PoC study with the objective of evaluating the safety and potential efficacy of RHB-104 using a series of exploratory measures. Eighteen RRMS patients were enrolled in two clinical centers in Israel. The patients received 24 weeks of treatment with RHB-104 and the interim data are presented in this press release. The patients are currently being evaluated for an additional follow-up period of 24 weeks after completing treatment with RHB-104. Independent third parties provided RedHill with the interim data sets and analysis, which remain subject to finalization and completion of the study.

Dr. Radi Shahien MD of Ziv Medical Center in Safed, Israel, Principal Investigator of the CEASE-MS study added: "RRMS is a devastating disease with no known cure, limited treatment options and unknown cause, hence the importance of the development of RHB-104, an intracellularly acting, anti-mycobacterial, anti-inflammatory and orally administered drug candidate. CEASE-MS is a small, open-label, exploratory study intended to investigate the groundbreaking hypothesis that a bacterial induced dysregulated immune system plays a critical role in the pathogenesis of MS. RedHill's CEASE-MS study with RHB-104 is the first clinical study to evaluate the therapeutic potential of a triple antibiotic combination therapy, and specifically these intracellularly acting antibiotics, as add-on therapy in RRMS. The initial analysis of the study's interim results provides encouraging clinical signals as well as important and reassuring safety data. In particular, the reduction of total T2 lesion burden over baseline, a key MS disease burden measurement, as well as relapse-free and stable EDSS data, are positive and meaningful signals, particularly given the small patient population in the study and the early time point of the data generated to date. I find the interim results very promising and am encouraged by the potential efficacy of RHB-104 in treating MS. I look forward to the completion of the study, further analyses and presentation of the final data at the appropriate international medical and academic forums."

"We are very encouraged by these findings which further reinforce the potential role of RHB-104 in the field of auto inflammatory diseases. We are conducting the Phase III MAP US study for Crohn's disease with RHB-104, with interim DSMB analysis expected in the second half of 2016, and the CEASE-MS study adds important information to the body of knowledge about the drug," **stated Dror Ben-Asher, RedHill's Chief Executive Officer.** "With a strong balance sheet and three ongoing Phase III programs in gastroenterology with planned data points in 2016 - RHB-104 for Crohn's disease, RHB-105 for *H. pylori* infection and BEKINDA™ for acute gastroenteritis - RedHill is well positioned for continued growth in 2016 and beyond."

Study Design and Baseline Characteristics

CEASE-MS is an ongoing study with additional data reads due at week 48 once all patients who completed the 24 weeks RHB-104 treatment period, will have completed a 24 week follow-up treatment period with interferon beta-1a, without RHB-104 add-on. All endpoints will be reassessed at that time using patients as their own control for analysis of interferon beta-1a with and without add-on RHB-104 therapy.

18 patients suffering from RRMS were enrolled in the ongoing CEASE-MS study in two sites in Israel, of which 17 patients who completed dose escalation were included in the modified intent-to-treat (mITT) data set. One patient was withdrawn from the study due to prohibited concomitant medication usage. The patients had been treated with interferon beta-1a for an average of approximately five years prior to enrollment in the study, experienced at least one MS relapse within 12 months prior to enrollment or two MS relapses within 24 months prior to enrollment, and had an EDSS score of 6.0 or less at screening, with a mean of 3.06. The per protocol (PP) analysis included ten patients, all of whom completed both the dose escalation and 24 week treatment period without any major protocol deviations.

Annualized Relapse Rate (ARR)

Patients in the study experienced an annualized relapse rate (ARR) of 0.288 in the mITT population and 0.0 in the per-protocol (PP) population, respectively. These results compare favorably with previously reported values for both interferon beta-1a therapies Avonex ® and Rebif®. The pivotal study of Avonex® demonstrated an ARR of 0.67[6], and a different Avonex® study reported ARRs of 0.53 and 0.31 in patients with and without previous history of disease modifying therapy, respectively[7]. The pivotal study of Rebif® demonstrated an ARR of 0.87 - 0.91 (a relapse rate of 1.73 - 1.82 over 2 years, 44 mcg or 22 mcg dose dependent), respectively[8]. In separate studies, reported ARR for Rebif® have ranged from 0.72 in the PRISMS-4 Long Term Efficacy Study[9] and 0.39 as first line therapy in the CARE-MS I study[10].

Relapse During the Study

88% of the mITT patient population and 100% of the PP patient population were relapse free at 24 weeks of treatment with RHB-104. This data compares favorably with previously reported pivotal data on the use Rebif® (75%) in comparison with Avonex® (63%) as standalone first line therapies[11]. Notably, no patients in the CEASE-MS study relapsed after treatment week 8 and there was also marked improvement over historical self-control of the CEASE-MS patients.

Expanded Disability Status Scale (EDSS)

The EDSS scale is a standard for monitoring MS patients. EDSS scores in the study were stable at 24 weeks and were suggestive of improvement. Importantly, no increase in total EDSS was observed in any of the patients in the study.

T2 Lesion Volume and MS Disease Burden

Burden of disease is defined as the total volume of all MRI T2 lesions. T2 lesion load, expected to increase by approximately 11% per year in RRMS if untreated[12], is accepted as an indicator of response and progression in RRMS. Although not powered for efficacy, and conducted over a short period of time in a small number of patients, the CEASE-MS study interim results indicate a reduction in T2 lesion volume at 24 weeks of treatment with RHB-104 as compared to baseline, suggesting reduction in MS disease burden and comparing favorably with previously reported Avonex® and Rebif® data: In a previous study with Rebif®, administered for 24 months as first line treatment of RRMS, median T2 lesion burden was noted to decrease by 6.5% at 24 months[13], while patients treated with RHB-104 as add-on therapy in the CEASE-MS study had a 3.37% decrease in median T2 lesion burden at 24 weeks. Mean T2 lesion burden decreased by 7.56% at 24 weeks in the CEASE-MS study with RHB-104 as add-on therapy, compared with a 10.4% increase in Avonex® treated patients at 12 months[14].

Combined Unique Active Lesions (CUA)

MRI is useful in monitoring MS progression and MRI findings are generally accepted as a surrogate endpoint in MS trials. Combined unique active lesions (CUAs) are defined as active lesions on T1 post-gadolinium, T2 sequences, or both, avoiding double counting. A T2 lesion in this context is defined as a new or enlarging lesion or a lesion reappearing at a site of previous lesion resolution. CUAs served as the primary outcome measure of the CEASE-MS study and among all patients followed, only a single active T1 post gadolinium lesion was noted. Combined unique active lesions (CUAs) in the study were almost entirely driven by changes in T2 lesions, and changes in total CUA lesions at week 24 were not clinically significant. An increase in the average percent change from baseline was observed for total CUA lesions at week 24 yet, as noted above, a positive efficacy signal was seen in reduction of total T2 lesion volume at 24 weeks as compared to baseline. This apparent discrepancy between the average percent change from baseline and the reduction of total T2 lesion volume is best explained by a combination of statistical fluctuation and definitional bias in this small study. Importantly, these MRI findings, along with the presence of only a single active T1 post gadolinium lesion, are consistent with stable radiological and clinical disease.

Safety and Tolerability

Overall, RHB-104 was well tolerated. There were no clinically relevant or unexpected adverse events reported in the study, and none of five serious adverse events (SAEs) seen in the study were related to the study drug. As expected, almost all patients experienced chromaturia (abnormal coloration of the urine). Two subjects withdrew from the study due to adverse events of metallic taste and nausea/vomiting.

Cytokine Levels

Cytokine analysis contribution was generally difficult to assess due to absence of control, the very small patient population and heterogeneity in observed values.

Mycobacterium avium subspecies paratuberculosis (MAP) Status

Development of the RedHill MAP diagnostic is ongoing. It is expected that evaluation of MAP status, using samples collected and stored as part of the ongoing CEASE-MS study, will be performed in conjunction with the development of the diagnostic test.

About Multiple Sclerosis:
Multiple sclerosis (MS) is a chronic inflammatory, demyelinating disease of the central nervous system with an unknown etiology, believed to be multifactorial. A dysfunctional immune system in MS patients causes recurrent inflammatory attacks on the central nervous system (CNS), leading to neurological disability. Diffuse inflammatory and demyelinating lesions, also known as plaques, are the main pathological finding in MS neural tissue. The lesions are primarily found in the spinal cord, optic nerves, brainstem, and periventricular white matter. The symptoms of MS are dictated by the location of the lesions within the CNS. Geographic variation in MS distribution, which cannot be solely explained by population genetics, supports the notion that environmental factors also hold etiological importance. There is currently no known cure for MS, and available treatments are mainly intended to manage or prevent relapses or reduce symptoms. In 2015, there were estimated to be over 900,000 diagnosed patients with MS worldwide. Approximately 85% of MS patients initially exhibit relapse-remitting disease. The 2015 U.S. and worldwide sales of MS therapies were estimated to exceed $12 billion and $17 billion, respectively[15].

About RHB-104:
Currently in a first Phase III study for the treatment of Crohn's disease (the MAP US study) and a second Phase III study which is being prepared (the MAP EU study), RHB-104 is a proprietary and potentially groundbreaking antibiotic combination therapy in oral capsule formulation, with potent intracellular, anti-mycobacterial and anti-inflammatory properties. RHB-104 is based on increasing evidence supporting the hypothesis that Crohn's disease is caused by *Mycobacterium avium subspecies paratuberculosis* (MAP) infection in susceptible patients. Clinical trials conducted with earlier formulations of RHB-104 include an Australian Phase III study conducted by Pfizer. RedHill has conducted several supportive studies with the current formulation of RHB-104 and a long-term population pharmacokinetic (pop-PK) study is ongoing as part of the Phase III MAP US study. RHB-104 is covered by several issued and pending patents. RedHill is also conducting the CEASE-MS Phase IIa, proof-of-concept clinical study, evaluating RHB-104 as an add-on therapy to interferon beta-1a in patients treated for relapsing-remitting multiple sclerosis (RRMS), with top-line interim results announced.

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.

[1] Jacobs LD et al.: Ann Neurol 1996;39:285-294.

[2] 1.73 - 1.82 over 2 years; PRISMS Study Group: Lancet 1998; 352: 1498-504.

[3] EVIDENCE Trial, Panitch H et al.: Neurology 2002;59:1496-1506.

[4] Cohen J A et al.: Oral Fingolimod or Intramuscular Interferon for Relapsing Remitting Multiple Sclerosis. NEJM. 2010, 362: 402-15.

[5] Cohen J A et al.: Alemtuzumab versus Interferon Beta 1a as First-Line Treatment for Patients with Relapsing-Remitting Multiple Sclerosis: a Randomised Controlled Phase 3 Trial. The Lancet. 2012, 380: 1819-28.

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[14] Cohen J A et al.: Oral Fingolimod or Intramuscular Interferon for Relapsing Remitting Multiple Sclerosis. NEJM. 2010, 362: 402-15.

[15] GlobalData PharmaPoint report, 2015.

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