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All HCV Patients Treated with a Single SC Administration of 4 mg/kg of RG-101 Responded with Mean Viral Load Reduction of 4.8 log10 at Day 29 and 9/14 Patients are Below the Limit of Quantification at Day 57

-Extended Follow-Up Shows 4/14 Patients Treated with a Single SC Dose of 2 mg/kg of RG-101 are Target Not Detected at Day 85 -
- Study Enrolled HCV Patients with Multiple Genotypes, Liver Fibrosis Status and Prior Treatment History -
- Conference Call Today at 8:00 a.m. EST to Discuss Results -

LA JOLLA, Calif., Feb. 9, 2015 /PRNewswire/ -- Regulus Therapeutics Inc. (*NASDAQ:RGLS*), a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs, today announced top-line results from the 4 mg/kg cohort and additional results from the 2 mg/kg cohort in a completed clinical study evaluating RG-101, a wholly-owned, GalNac-conjugated anti-miR targeting microRNA-122 ("miR-122"), for the treatment of hepatitis C virus infection ("HCV"). Treatment with a single subcutaneous dose of 4 mg/kg of RG-101 as monotherapy resulted in significant and sustained viral load reductions in all patients, including difficult to treat genotypes, various liver fibrosis status and those who have experienced viral relapse after a prior IFN-containing regimen. To date, RG-101 continues to have a favorable safety profile with no serious adverse events or discontinuations reported in the treated HCV patients.

Top-line results from the 4 mg/kg dose cohort:

In the 4 mg/kg dose cohort, 16 HCV patients were enrolled: 14 patients, 12 naive and 2 patients who experienced viral relapse after a prior IFN-containing regimen, received a single subcutaneous dose of 4 mg/kg of RG-101 as monotherapy, and 2 patients received placebo.

- In the 14 treated HCV patients, there was a mean viral load reduction of 4.8 $\log_{10}$ at day 29 (range -5.8 to -3.0); and
- 9 out of 14 patients had HCV RNA levels below the limit of quantification (< 15 IU/ml) ("BLOQ") at day 57 and these patients will be followed up to six months to investigate the potential for viral cures following the single administration of 4 mg/kg of RG-101.

Extended follow-up results from the 2 mg/kg dose cohort:

In October 2014, Regulus reported interim efficacy and safety results and its first human proof of concept results from the 2 mg/kg cohort of the completed study evaluating RG-101 for the treatment of HCV.

- At day 85, 4 out of 14 treated patients with varied genotypes, liver fibrosis status and treatment history were Target Not Detected ("TND"); 2 of the treated patients that were BLOQ at day 57 relapsed shortly thereafter; and
- Due to the longevity of the viral responses demonstrated, the protocol is being amended to add an additional year of follow up to investigate the potential for viral cures with one single administration of RG-101.

Summary of 2 mg/kg and 4 mg/kg dose cohort results:

Treatment with a single subcutaneous dose of either 2 mg/kg or 4 mg/kg of RG-101 as monotherapy has resulted in significant and sustained viral load reductions in all patients including difficult to treat genotypes, various liver fibrosis status and those who have experienced viral relapse after a prior IFN-containing regimen. At day 57, 15 out of 28 patients treated with one single administration of either 2 mg/kg or 4 mg/kg of RG-101 had HCV RNA levels BLOQ and 12 out of these 15 treated patients were TND.

"The profile of RG-101 has been significantly enhanced with these top-line data, making it an ideal pan-genotypic asset to investigate further in combination with all classes of oral agents to shorten the duration of treatment, increase patient compliance and maintain viral response, and also as monotherapy in certain underserved HCV populations," said Kleanthis G. Xanthopoulos, Ph.D., President and CEO of Regulus. "With the promising data reported today, our confidence in our ability to treat diseases with microRNA therapeutics is higher than ever and we look forward to continuing to execute our 'Clinical Map Initiative' goals for RG-101 and our microRNA therapeutics pipeline."

"We continue to be pleased with the clinical results demonstrated with RG-101 and have a much more robust data set to inform our dual-track clinical development plans for Phase II," said Paul Grint, M.D., Chief Medical Officer of Regulus. "We have filed our pre-IND briefing book with the U.S. Food and Drug Administration and are working to file a Clinical Trial Application to conduct monotherapy and combination studies in multiple countries. In the second quarter of 2015, we look forward to initiating these studies and reporting full results from the completed study."

"These results demonstrate a significant breakthrough in the treatment of HCV," said Hendrik W. Reesink, M.D., Ph.D., Associate Professor in the Department of Gastroenterology and Hepatology at the Academic Medical Center in The Netherlands. "These landmark studies were conducted with a high level of novelty and practical clinical importance. All twenty-eight patients treated with one administration of RG-101 responded and more than 50% had HCV RNA levels below the lower limit of quantification at day 57. I look forward to seeing RG-101 rapidly advance in Phase II to test its utility in combination with oral agents and possibly as monotherapy."

Conference Call & Webcast Information

Regulus will host a conference call and webcast at 8:00 a.m. Eastern Standard Time today to discuss the RG-101 results. A slide presentation will also be available on Regulus' website, www.regulusrx.com to accompany the live webcast. To access the call, please dial (877) 257-8599 (domestic) or (970) 315-0459 (international) and refer to conference ID 80841144. To access the telephone replay of the call, dial (855) 859-2056 (domestic) or (404) 537-3406 (international), passcode ID 80841144. The webcast and telephone replay will be archived on the company's website for ninety days following the call.

About RG-101 for HCV

RG-101 is Regulus' wholly-owned, GalNAc-conjugated anti-miR targeting miR-122 for the treatment of HCV. Regulus has evaluated RG-101 in a completed clinical study conducted in the Netherlands. 58 healthy volunteers and 32 HCV patients with multiple genotypes, liver fibrosis status and treatment history were enrolled in the four part study: (i) a single ascending-dose study in which healthy volunteer subjects received a single subcutaneous dose of RG-101, 0.5 mg/kg, 1 mg/kg, 2 mg/kg, 4 mg/kg and 8 mg/kg or placebo; (ii) a multiple-ascending dose study in which healthy volunteer subjects received a monthly single subcutaneous dose for four months of RG-101 or placebo; (iii) a single-dose drug-drug interaction study in which healthy volunteer subjects received a single subcutaneous dose of RG-101 in combination with simeprevir (OLYSIO™), an approved direct acting antiviral; and (iv) a single-dose study in which HCV patients received either a single subcutaneous dose of RG-101 or placebo at two doses, 2 mg/kg of RG-101 (the first dose cohort) or 4 mg/kg of RG-101 (the second dose cohort), to assess the safety and viral load reduction. Dosing in part IV is complete and extended follow up is ongoing. The primary objective is to evaluate safety and tolerability and the secondary objectives are to evaluate pharmacokinetics, viral load reduction and any impact an oral direct acting antiviral, such as simeprevir (OLYSIO™), may have on the pharmacokinetics of RG-101.

Today, Regulus reported additional results from the above study and plans to report full study results in the second quarter of 2015.

About microRNAs

The discovery of microRNAs in humans during the last decade is one of the most exciting scientific breakthroughs in recent history. microRNAs are small RNA molecules, typically 20 to 25 nucleotides in length, that do not encode proteins but instead regulate gene expression. More than 500 microRNAs have been identified in the human genome, and over two-thirds of all human genes are believed to be regulated by microRNAs. A single microRNA can regulate entire networks of genes. As such, these molecules are considered master regulators of the human genome. microRNA expression, or function, has been shown to be significantly altered or dysregulated in many disease states, including oncology, fibrosis, metabolic diseases, immune-inflammatory diseases and HCV. Targeting microRNAs with anti-miRs, chemically modified, single-stranded oligonucleotides, offers a unique approach to treating disease by modulating entire biological pathways and may become a new and major class of drugs with broad therapeutic application.

Hepatitis C Virus Infection (HCV)

Hepatitis C is a result of a hepatocyte specific infection induced by the virus known as HCV. Chronic HCV may lead to significant liver disease, including chronic active hepatitis, cirrhosis, and hepatocellular carcinoma. Up to 185 million people are chronically infected with HCV worldwide, and more than 350,000 people die from HCV annually. The CDC estimates that there

are currently approximately 3.2 million persons infected with HCV in the United States. HCV shows significant genetic variation in worldwide populations due to its frequent rates of mutation and rapid evolution. There are six genotypes of HCV, with several subtypes within each genotype, which vary in prevalence across the different regions of the world. The response to treatment varies from individual to individual underscoring the inadequacy of existing therapies and highlights the need for combination therapies that not only target the virus but endogenous host factors as well, such as microRNA-122. Regulus believes that its' miR-122 antagonist, RG-101, may be a useful agent in emerging combination regimens to address difficult-to-treat genotypes and to potentially expand upon the current therapies available to clinicians treating HCV patients.

'Clinical Map Initiative' Goals for RG-101

Regulus' 'Clinical Map Initiative' outlines certain corporate goals to advance its microRNA therapeutics pipeline over the next several years. To rapidly advance RG-101, Regulus is pursuing a Phase II dual-track clinical development strategy (i) to investigate RG-101 in combination with oral agents to potentially shorten treatment durations, optimize clinical outcomes and potentially improve responses in certain underserved HCV patient populations; and (ii) to investigate RG-101 further as a single agent to determine whether HCV viral cures are achievable with monotherapy treatment (single or multiple doses of RG-101). In the near term, Regulus expects to file both a Clinical Trial Application and an Investigational New Drug application for RG-101 with the goal to initiate the above described studies in Europe and the United States in the second quarter of 2015.

About Regulus

Regulus Therapeutics Inc. (*NASDAQ:RGLS*) is a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs. Regulus has leveraged its oligonucleotide drug discovery and development expertise to develop a well-balanced microRNA therapeutics pipeline complemented by a maturing microMarkers^{SM} biomarkers platform and a rich intellectual property estate to retain its domain dominant leadership in the microRNA field. Under its 'Clinical Map Initiative', Regulus is developing RG-101, a GalNAc-conjugated anti-miR targeting microRNA-122 for the treatment of chronic hepatitis C virus infection, and RG-012, an anti-miR targeting microRNA-21 for the treatment of Alport syndrome, a life-threatening kidney disease driven by genetic mutations with no approved therapy. Regulus is also advancing several programs toward clinical development in orphan disease indications, oncology and fibrosis. Regulus' commitment to innovation has resulted in multiple peer-reviewed publications in notable scientific journals and has resulted in the formation of strategic alliances with AstraZeneca and Sanofi and a research collaboration with Biogen Idec focused on microRNA biomarkers. Regulus maintains its corporate headquarters in La Jolla, CA. For more information, please visit http://www.regulusrx.com.

Forward-Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including the expected ability of Regulus to undertake certain activities and accomplish certain goals with respect to RG-101, the projected timeline of clinical development activities related to RG-101, and expectations regarding future therapeutic and commercial potential with respect to RG-101. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Words such as "believes," "anticipates," "plans," "expects," "intends," "will," "goal," "potential" and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Regulus' current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, risks associated with the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. These and other risks concerning Regulus are described in additional detail in Regulus' filings with the Securities and Exchange Commission. All forward-looking statements contained in this press release speak only as of the date on which they were made. Regulus undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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