A Single Subcutaneous Dose of 2mg/kg of RG-101, Regulus' Wholly-Owned, GalNac-Conjugated anti-miR Targeting microRNA-122, Demonstrates 4.1 log10 Mean Viral Load Reduction as Monotherapy at Day 29 in Patients with Varied HCV Genotypes and Treatment History

- Interim Results from Ongoing Study Demonstrate Human Proof-of-Concept and Underscore the Value of Regulus' microRNA Platform -

- Conference Call Today at 8:30 a.m. EDT to Discuss Results -

LA JOLLA, Calif., Oct. 22, 2014 /PRNewswire/ -- Regulus Therapeutics Inc. (NASDAQ:RGLS), a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs, today announced that it has demonstrated human proof-of-concept with a microRNA therapeutic from an ongoing 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"). Interim results from the ongoing clinical study demonstrate that treatment with a single subcutaneous dose of 2 mg/kg of RG-101 as monotherapy resulted in significant and sustained reductions in HCV RNA in a varied group of patients, including difficult to treat genotypes and patients who experienced viral relapse after a prior IFN-containing regimen. Additionally, RG-101 was safe and well tolerated and has demonstrated a very favorable pharmacokinetic profile to date, which may allow for combination with oral direct-acting antiviral ("DAA") agents to treat HCV.

Interim results from the ongoing clinical study are summarized below:

In the first dose cohort of part IV of the ongoing study, 16 HCV patients were enrolled with multiple genotypes, 10 GT1s, 5 GT3s, and 1 GT4. 14 patients, 8 naïve and 6 patients who experienced viral relapse after a prior IFN-containing regimen, received a single subcutaneous dose of 2 mg/kg of RG-101 as monotherapy while 2 patients received placebo.

- In the 14 HCV treated patients, there was a mean viral load reduction of 4.1 $\log_{10}$ at day 29 (range -5.8 $\log_{10}$ to -2.3 $\log_{10}$).
- 6 out of 14 patients had HCV RNA levels below the limit of quantification at day 29 and the 3 patients from this group who have reached day 57 still have HCV RNA levels below the limit of quantification.
- Viral load reduction occurs within the first 96 hours and virologic response is not influenced by IL-28 genotype.
- Due to the long-lasting and sustained virologic effect seen, the ongoing study protocol has been amended to follow patients for up to six months after dosing to evaluate the possibility for certain patients to achieve viral cure after a single dose of RG-101.
- There were no drug-drug interactions from part III of the ongoing study in which RG-101 was combined with simeprevir (OLYSIO™), an approved oral DAA (protease inhibitor), and the combination had no effect on the pharmacokinetic profile of RG-101 or simeprevir (OLYSIO™).
- RG-101 is safe and well tolerated with no serious adverse events reported to date.

"We are very excited to have demonstrated our first human proof-of-concept results with a microRNA therapeutic from the ongoing study of RG-101, which is a significant milestone in Regulus' history, and represents a key achievement under our 'Clinical Map Initiative'," said Kleanthis G. Xanthopoulos, Ph.D., President and Chief Executive Officer of Regulus. "We believe these interim data are exceptional and provide strong evidence to support the rapid advancement of RG-101 into future clinical studies, while presenting a clear opportunity for a potentially disruptive therapy to the current HCV treatment paradigm."

"RG-101 is the first microRNA therapeutic in clinical development to combine the most advanced RNA technologies from three leading RNA therapeutics companies; chemistry 2.5 from Isis, GalNAc conjugate from Alnylam, and Regulus' unique and proprietary chemistry including the novel linker that facilitates the release of the parent oligonucleotide after hepatocyte uptake," said Neil W. Gibson, Ph.D., Chief Scientific Officer. "We believe the innovative design of RG-101 has led to achievement of our first human proof-of-concept results, and hope these findings will advance the growth of our microRNA therapeutics pipeline."

"We are very pleased and encouraged with the interim results and believe these findings strongly support the rapid advancement of RG-101 into Phase II development," said Paul Grint, M.D., Regulus' Chief Medical Officer. "Currently, we plan to file an Investigational New Drug Application with the U.S. Food and Drug Administration in the first quarter of 2015 and plan to initiate a Phase II DAA combination study of RG-101 in HCV patients in the second quarter of 2015. In addition, we look forward to reporting additional data from the ongoing study in the first half of next year."

"The efficacy and sustained viral response seen with a single dose of RG-101 is very promising and it was encouraging to see response across a diversity of genotypes and treatment experience in this clinical trial. Additionally, all patients in the first cohort on active therapy demonstrated a viral response to RG-101, which is also very encouraging," said Dr. Eric Lawitz, M.D., Vice President, Scientific and Research Development, The Texas Liver Institute, and Clinical Professor of Medicine, University of Texas Health Science Center in San Antonio. "These findings suggest the clinical benefit of utilizing a unique mechanism of action to potentially treat difficult patient populations. There may be an opportunity to improve upon the current real world compliance issues with therapies such as RG-101 that may be administered subcutaneously by a clinician. I look forward to seeing RG-101 advance into future clinical trials."

Conference Call & Webcast Information

Regulus will host a conference call and webcast at 8:30 a.m. Eastern Daylight Time today to discuss its interim results from the ongoing clinical study of RG-101 for the treatment of HCV. A live webcast of the call will be available online at www.regulusrx.com. To access the call, please dial (877) 257-8599 (domestic) or (970) 315-0459 (international) and refer to conference ID 24374685. To access the telephone replay of the call, dial (855) 859-2056 (domestic) or (404) 537-3406 (international), passcode ID 24374685. 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 a wholly-owned, GalNAc-conjugated anti-miR targeting miR-122 for the treatment of HCV. Regulus is currently evaluating RG-101 in an ongoing study being conducted in the Netherlands. The study has the following four parts: (I) a single ascending-dose study in which healthy volunteer subjects receive 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 receive 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 receive a single subcutaneous dose of RG-101 in combination with simeprevir, an approved DAA; and (IV) a single-dose study in which HCV patients receive 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. 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 DAA, such as simeprevir, may have on the pharmacokinetics of RG-101. Up to 100 healthy volunteer subjects and HCV patients with multiple HCV genotypes and treatment history are planned to be enrolled.

Today, Regulus reported interim results from the above study and plans to report additional results from the ongoing study in 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 800 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.

About 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 170 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.

Update to the 'Clinical Map Initiative'

Launched in February 2014, Regulus' 'Clinical Map Initiative' outlines certain corporate goals to advance its microRNA therapeutics pipeline over the next several years. In October 2014, Regulus demonstrated human proof-of-concept with a microRNA therapeutic, RG-101, a wholly-owned, GalNac-conjugated anti-miR targeting microRNA-122 for the treatment of HCV. The company plans to rapidly advance RG-101 in clinical development and expects to initiate a Phase II DAA combination study in HCV patients in the second quarter of 2015. In addition, Regulus expects to initiate a Phase I clinical study of RG-012 for the treatment of Alport syndrome, nominate a third microRNA candidate for clinical development by the end of 2014, and maintain a strong financial position and end 2014 with at least $75.0 million in cash, cash equivalents and short-term investments.

About Regulus

Regulus Therapeutics Inc. (*NASDAQ:RGLS*) is a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs. Regulus is uniquely positioned to leverage a mature therapeutic platform that harnesses the oligonucleotide drug discovery and development expertise of Alnylam Pharmaceuticals, Inc. and Isis Pharmaceuticals, Inc., which founded the company. Regulus has a well-balanced microRNA therapeutics pipeline entering clinical development, an emerging microRNA biomarkers platform to support its therapeutic programs, and a rich intellectual property estate to retain its leadership in the microRNA field. Regulus intends to focus its proprietary efforts on developing microRNA therapeutics for oncology indications and orphan diseases and is currently advancing several programs toward clinical development in oncology, fibrosis and metabolic diseases. Specifically, Regulus is developing 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, and RG-101, a GalNAc-conjugated anti-miR targeting microRNA-122 for the treatment of chronic hepatitis C virus infection. Regulus' commitment to innovation and its leadership in the microRNA field have enabled the formation of strategic alliances with AstraZeneca and Sanofi and a research collaboration with Biogen Idec focused on microRNA biomarkers. In addition, the Company has established Regulus microMarkers™, a division focused on identifying microRNAs as biomarkers of human disease, which is designed to support its therapeutic pipeline, collaborators and strategic partners.

For more information, please visit http://www.regulusrx.com.

Forward-Looking Statements

Statements contained in this presentation 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 presentation 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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