Regulus Commences Dosing RG-101 in Healthy Volunteers in Phase I Study

- Study Designed to Demonstrate Human Proof-of-Concept Results by YE 2014 -

LA JOLLA, Calif., March 5, 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 commenced dosing RG-101, a GalNAc-conjugated anti-miR targeting microRNA-122 ("miR-122") in healthy volunteer subjects in a Phase I clinical study. The primary objective of the study is to evaluate safety and tolerability of RG-101 and the secondary objectives are to evaluate pharmacokinetics, viral load reduction and any impact an oral direct-acting antiviral may have on the pharmacokinetics of RG-101.

"We are very pleased to have dosed our first human subject, advancing Regulus into a clinical-stage company," said Neil W. Gibson, Ph.D., Chief Scientific Officer of Regulus. "We continue to be encouraged by the preclinical data seen to date and believe that RG-101 has the potential to be a best-in-class host factor agent, specifically due to its pan-genotypic properties, including demonstrated efficacy in the hard to treat HCV genotype 3, and the potential for a once monthly dosing regimen. We look forward to reporting data from the Phase I clinical study of RG-101 by the end of this year."

About the RG-101 Phase I Clinical Study

The Phase I clinical study of RG-101 will have four parts: (i) a single ascending-dose study in healthy volunteer subjects; (ii) a multiple-ascending dose study in healthy volunteer subjects; (iii) a single-dose drug-drug interaction study of RG-101 in combination with an approved oral direct-acting antiviral ("DAA") in healthy volunteer subjects; and (iv) a single-dose study in HCV patients to assess the safety and viral load reduction, which is designed to demonstrate human proof-of-concept. Up to approximately 100 healthy volunteer subjects and HCV patients are planned to be enrolled in the Phase I study, which is being conducted in the Netherlands.

About RG-101 for the Treatment of HCV

RG-101 is a key program in Regulus' 'Clinical Map Initiative', which outlines certain corporate goals to advance its microRNA therapeutics pipeline over the next several years. Under its 'Clinical Map Initiative', Regulus expects to demonstrate human proof of concept results in the Phase I clinical study of RG-101 by the end of 2014.

The most abundant microRNA in hepatocytes is miR-122 and is a critical host factor for survival and replication of all know HCV genotypes. RG-101 is a novel anti-miR-122 oligonucleotide therapeutic that is effectively targeted to hepatocytes for the treatment of HCV through conjugation to GalNAc, a carbohydrate-based chemistry approach for asialoglycoprotein receptor-mediated delivery of oligonucleotides to hepatocyte cells of the liver. Utilizing the GalNAc conjugate chemistry has significantly improved the potency of the active oligonucleotide of RG-101 by achieving targeted delivery of the oligonucleotide to the infected hepatocytes. Regulus has presented data evaluating RG-101 for *in vitro* and *in vivo* potency, pharmacokinetic/pharmacodynamics, toxicology and safety pharmacology and inhibition of HCV replication. Regulus has also tested RG-101 for efficacy in a human chimeric liver mouse model infected with HCV genotypes 1a and 3a. In this model, up to a 2 log reduction in HCV viral load titer was observed in both genotypes after a single dose of RG-101. The duration of action observed for RG-101 supports the potential for a once-a-month dosing regimen. To date, RG-101 has demonstrated an excellent preclinical safety profile and has been well tolerated.

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 therapeutic 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, GlaxoSmithKline and Sanofi. In addition, the Company has established Regulus microMarkers™, a research and development 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 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 statements associated with Regulus' expectations regarding future therapeutic and commercial potential of Regulus' business plans, including the belief that RG-101 is the best-in-class anti-HCV host factor agent and its expectations regarding future clinical studies, and technologies and intellectual property related to microRNA therapeutics being discovered and developed by Regulus. 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' programs are described in additional detail in Regulus' SEC filings. 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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