Regulus Presents New Preclinical Data on Multiple Programs and Provides Portfolio Overview at 10th Annual Oligonucleotide Therapeutics Society (OTS) Meeting

-New Preclinical Results Increase Mechanistic Understanding of Targeting miR-103/107 for Metabolic Disorders and miR-21 for Renal Dysfunction in Alport Syndrome Patients-
-'Clinical Map Initiative' on Track; Human Proof-of-Concept Results for RG-101 in HCV Patients to Be Reported in Near Term-

LA JOLLA, Calif., Oct. 14, 2014 /PRNewswire/ -- Regulus Therapeutics Inc. (*NASDAQ:RGLS*), a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs, today announced that it will present new preclinical data on multiple programs and an overview of its clinical portfolio at the 10th Annual Oligonucleotide Therapeutics Society ("OTS") meeting being held October 12-October 15, 2014 at the Hilton San Diego Resort and Spa.

"Regulus is pleased to be making several presentations at this important meeting focused on the development of oligonucleotide therapeutics," said Neil W. Gibson, Ph.D., Regulus' Chief Scientific Officer. "As evidenced by these presentations, we continue to advance our science and mature our clinical and preclinical microRNA therapeutics programs in a meaningful way."

Regulus will present the following posters during the OTS meeting on multiple preclinical programs:

- In a poster titled "Anti-Diabetic Activity of miR-103/107 Anti-miRs", Regulus scientists will present preclinical data further demonstrating the potential benefit of a microRNA therapeutic for the treatment of metabolic disorders. In diabetic mouse models, subcutaneous administration of an anti-miR-103/107 once or twice weekly improved insulin sensitivity and glucose excursion, and mediated improvements in glucose homeostasis in a diet-induced obesity model and in a hyperinsulinemic-euglycemic clamp setting. These observations were accompanied by significant changes in adipocyte size. Regulus and its strategic alliance partner, AstraZeneca, continue to advance the miR-103/107 program for the treatment of metabolic disorders; and
- In a poster titled "Inhibition of miR-21 with RG-012 Improves Renal Function and Survival in Multiple Strains of Col4A3 Deficient Mice", Regulus scientists, in collaboration with its strategic alliance partner Sanofi, will present new preclinical data demonstrating that weekly subcutaneous delivery of RG-012 has shown to provide both glomerular and tubule protection in the kidneys of Col4A3 deficient mice in an Alport syndrome model.

The OTS posters are available on Regulus' website at http://www.regulusrx.com.

In addition, Dr. Gibson will give an oral presentation titled "The Treatment of Human Disease via Inhibition of microRNAs: RG-101 and RG-012" on Wednesday, October 15, 2014 from 3:45pm PST-4:15pm PST. Dr. Gibson will provide an overview of Regulus' microRNA therapeutics portfolio, including a summary of the preclinical data that supports the current clinical development of RG-101, a GalNAc conjugated anti-miR targeting microRNA-122 ("miR-122") for the treatment of chronic hepatitis C virus infection ("HCV"), and a summary of RG-012, an anti-miR targeting microRNA-21 for the treatment of renal dysfunction in Alport syndrome patients. In the near term, Regulus expects to report preliminary results from the ongoing study of RG-101, including interim human proof-of-concept results in HCV patients from the first cohort of part IV of the study.

About RG-101 for HCV

RG-101 is a wholly-owned, GalNAc-conjugated anti-miR targeting miR-122 for the treatment of HCV. In preclinical studies, Regulus has observed significant HCV viral load reduction in a human chimeric liver mouse model infected with genotypes 1a and 3a, a long duration of action for RG-101 which supports the potential for a once-a-month dosing regimen, and a favorable preclinical safety profile in which RG-101 has been well tolerated.

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 oral direct-acting antiviral ("DAA"); and (IV) a single-dose study in which HCV patients receive either a single subcutaneous dose of RG-101, 2 mg/kg (the first dose cohort) or 4 mg/kg (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.

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 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. Regulus expects to report human proof-of-concept results for RG-101 in HCV patients in the near term, initiate a Phase I clinical study of RG-012 for the treatment of Alport syndrome in the first half of 2015, 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, GlaxoSmithKline 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 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 financial estimates (including Regulus' projected cash at the end of 2014), the projected sufficiency of Regulus' capital position for future periods, the expected ability of Regulus to undertake certain activities and accomplish certain goals (including with respect to development and other activities related to RG-012 and RG-101 and with respect to the nomination of a third microRNA candidate for clinical development), the projected timeline of clinical development activities, and expectations regarding future therapeutic and commercial potential of Regulus' business plans, technologies and intellectual property related to microRNA therapeutics and biomarkers 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' financial position and programs 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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