Regulus and Sanofi Present New Data Enhancing the Preclinical Profile of RG-012, an Anti-miR Targeting microRNA-21 for the Treatment of Renal Dysfunction in Alport Syndrome Patients, at ASN's Kidney Week 2014 Meeting

- Treatment with RG-012 Protects Kidney Function and Demonstrates Additive Therapeutic Effect with Emerging Standard of Care in Preclinical Model of Alport Syndrome -

LA JOLLA, Calif., Nov. 15, 2014 /PRNewswire/ -- Regulus Therapeutics Inc. (NASDAQ: RGLS), a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs, today announced that positive new preclinical data was presented on RG-012 for the treatment of renal dysfunction in Alport syndrome patients at the American Society of Nephrology's (ASN) Kidney Week 2014 meeting being held November 11-16, 2014 in Philadelphia, PA. Alport syndrome is a life-threatening, genetic kidney disease with no approved therapy, and currently, ACE (angiotensin-converting enzyme) inhibitors are emerging as standard of care to treat proteinuria, an indicator of chronic kidney disease (CKD) in these patients. Studies have shown that miR-21 plays a role in the progression of Alport syndrome and is up-regulated in mouse disease models, other renal fibrosis models and human CKD patients. These findings, and the new preclinical data presented at the ASN meeting, provide additional evidence that RG-012 may provide therapeutic benefit in the treatment of Alport syndrome.

In an oral presentation titled "Anti-miR-21 as a Potential Novel Therapy for Both Early and Late Stages of Alport Syndrome", Regulus' strategic alliance partner, Genzyme, a Sanofi company, presented new data demonstrating that treatment with RG-012 in a mouse model of disease improves renal function, protects against kidney damage and extents the lifespan of the mice when treatment begins at both early and late stages of the disease by reversing multiple dysregulated pathways. Further, combination studies were performed with RG-012 and ramipril, Sanofi's ACE inhibitor, a kidney protectant, to assess the therapeutic utility of adding a microRNA therapeutic to this emerging standard of care. In these preclinical studies, treatment with RG-012 was shown to protect kidney function better than ramipril alone and an additive therapeutic effect was observed in combination with ramipril.

"These data enhance the preclinical profile of RG-012 and provide us with further confidence in the potential to treat disease with microRNA therapeutics," said Neil W. Gibson, Ph.D., Chief Scientific Officer of Regulus. "Currently, we are enrolling Alport syndrome patients in ATHENA, our global natural history of disease study, and expect to initiate a Phase I study in healthy volunteers in the first half of 2015 and a Phase II proof-of-concept study thereafter."

About Alport Syndrome

Alport syndrome is an inherited form of kidney disease caused by mutations in the type IV collagen genes (Col4A3, Col4A4 and Col4A5). Type IV collagen is important for maintaining the integrity of the glomerular basement membrane (GBM), a vital component in the kidney structure and filtration process. The genetic mutation in the collagen gene results in increased fibrosis, or thickening, in the GBM. Alport syndrome patients experience a progressive loss of kidney function, which may lead to chronic kidney disease, end stage renal disease requiring dialysis or kidney transplantation, or may even lead to death. Alport syndrome can also cause hearing loss and eye abnormalities during late childhood or early adolescence. ACE (angiotensin-converting enzyme) inhibitors are emerging as standard of care in patients with Alport syndrome used to treat proteinuria, or abnormal amounts of protein in the urine, an indicator of chronic kidney disease. Alport syndrome represents a high unmet medical need with no approved therapy.

About RG-012 for the Treatment of Renal Dysfunction in Alport Syndrome Patients

Currently, there is little known information on exactly how Alport syndrome progresses, although miR-21 is known to play a role in the disease progression. miR-21 is up-regulated in Col4A3 deficient mouse models of Alport syndrome, other renal fibrosis models and human CKD patients. The role of miR-21 has been validated through genetic knock-out models and anti-miRs targeting miR-21 have reduced the severity of fibrosis in two distinct preclinical rodent models. Regulus is developing RG-012, a single stranded, chemically modified oligonucleotide that binds to and inhibits the function of miR-21 to treat renal dysfunction in Alport syndrome patients. In preclinical studies, RG-012 has demonstrated potent inhibition of miR-21 *in vitro* and *in vivo,* a decrease in the rate of progression of renal fibrosis, an increase in the lifespan of the mice by up to fifty percent, and an additive benefit in combination with an emerging standard of care therapy.

Regulus is currently enrolling patients in its ATHENA natural history of disease study to gather information about the changes in renal function over time in patients with Alport syndrome. Data from the ATHENA study will provide the clinical basis for the design of a Phase II study to monitor the therapeutic effect of RG-012 on the

decline in renal function and time to end-stage renal disease in Alport syndrome patients. Under the 'Clinical Map Initiative', Regulus expects to initiate a Phase I study in the first half of 2015 and a Phase II proof-of-concept study thereafter. Further, RG-012 has been granted orphan drug designation from the U.S. FDA as a therapeutic for the treatment of Alport syndrome.

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'

Regulus' 'Clinical Map Initiative' outlines certain corporate goals to advance its microRNA therapeutics pipeline over the next several years. Under this initiative, Regulus is developing RG-101, a wholly-owned GalNAc-conjugated anti-miR targeting microRNA-122 for the treatment of HCV and RG-012, an anti-miR targeting microRNA-21 for the treatment of Alport syndrome, a life-threatening genetic kidney disease with no approved therapy, and expects to nominate a third candidate for clinical development in the first half of 2015. Regulus plans to rapidly advance RG-101 into a Phase II combination study in HCV patients, which is planned to commence in the second quarter of 2015. Regulus also plans to initiate a Phase I clinical study of RG-012 in the first half of 2015 and a Phase II proof-of-concept study in Alport syndrome patients thereafter.

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 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 oncology, fibrosis and metabolic diseases. 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^{SM}, 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-012, the projected timeline of clinical development activities related to RG-012, and expectations regarding future therapeutic and commercial potential with respect to RG-012. 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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