Regulus to Present Additional Preclinical Data Supporting RG-012 as a Novel microRNA Therapeutic in Development for Alport Syndrome at ASN's Kidney Week 2015

RG-012 Shown to Directly Inhibit microRNA-21, Demonstrates Favorable Preclinical Profile Supporting Proof of Mechanism and Clinical Development

LA JOLLA, Calif., Oct. 5, 2015 /PRNewswire/ -- Regulus Therapeutics Inc. (NASDAQ:RGLS), a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs (miR), will present new preclinical data regarding RG-012, a single stranded, chemically modified oligonucleotide that binds to and inhibits the function of microRNA-21 ("miR-21"), at the American Society of Nephrology's (ASN) Kidney Week 2015 meeting being held November 3-8, 2015 in San Diego, CA. RG-012 is being developed by Regulus in a strategic alliance with Genzyme, a Sanofi company, for the treatment of Alport syndrome, a life-threatening genetic kidney disease with no approved therapy.

November 7, 2015, 10am-12pm: Novel Methodology for Assessing Inhibition of MicroRNA-21 by RG-012, a MicroRNA Therapeutic in Development for the Treatment of Kidney Dysfunction in Patients with Alport Syndrome

- The novel methodology allows for the direct measurement of microRNA inhibition by determining the displacement of a microRNA from actively translating polysome complexes;
- In both the liver and kidneys of Col4A3 deficient mice, a model that closely mimics Alport syndrome in humans, RG-012 demonstrated dose-dependent displacement of miR-21 from actively translating polysome complexes, and subsequent derepression of messenger RNA targets; and
- These results provide further support for the clinical development of RG-012.

November 7, 2015, 10am-12pm: Nonclinical Pharmacokinetics and Toxicokinetics of RG-012, an Inhibitor of MicroRNA-21 Being Investigated for Treatment of Alport Syndrome

- RG-012 was characterized by rapid absorption and slow tissue elimination after subcutaneous administrations (half-life in the liver and kidney of approximately two to three weeks);
- RG-012 exhibited little to no potential to inhibit or induce CYP450 enzymes in vitro, reducing concerns of any potential drug-drug interactions; and
- These favorable preclinical pharmacokinetic and toxicokinetic properties supported initial clinical testing of RG-012 in healthy volunteers and support planned evaluations in patients with Alport syndrome.

November 6, 2015, 10am-12pm: Discovery of Urine MicroRNA Biomarkers in a Pre-Clinical Model of Alport Nephropathy

- Regulus profiled microRNAs in urine, serum and kidney tissue of a wild type control and a preclinical model of Alport nephropathy in order to identify microRNA biomarkers with the ability to reflect disease progression;
- Regulus identified several urine microRNAs with highly significant differential expression in Col4A3 deficient mouse when compared to wild type mice; and
- These data suggest that analysis of urine may be favorable for the development of non-invasive microRNA based tests.

"We are pleased to be making several presentations on our RG-012 program during this year's Kidney Week meeting that we believe further demonstrate the compound's novel mechanism and therapeutic potential to treat patients with Alport Syndrome," said Paul Grint, M.D., President and Chief Executive Officer of Regulus. "There are few treatment options for patients with this devastating and debilitating disease and we look forward to advancing RG-012 in clinical development."

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. In June 2015, Regulus initiated dosing in a first-in-human Phase I clinical study to evaluate the safety, tolerability and pharmacokinetics of subcutaneous dosing of RG-012 in healthy volunteers. In addition to the Phase I clinical study, Regulus is currently enrolling Alport syndrome patients in a natural history of disease study called ATHENA. With this study, which has thirteen clinical sites worldwide, Regulus aims to learn more 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.

About RG-012 and 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 thickening in the GBM and impairment of glomerular filtration. Alport syndrome patients experience a progressive loss of kidney function, which ultimately leads to 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.

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 for the treatment of Alport syndrome. 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 Col4A3 deficient mice by up to fifty percent, and an additive benefit in combination with an emerging standard of care therapy. Further, RG-012 has received orphan drug status from the U.S. Food and Drug Administration and European Commission as a therapeutic in development 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 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 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. In addition, RG-125, a GalNAc-conjugated anti-miR targeting microRNA-103/107 for the treatment of NASH in patients with type 2 diabetes/pre-diabetes, has been selected for clinical development. 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 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 statements associated with 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), 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.

Logo - http://photos.prnewswire.com/prnh/20150130/172637LOGO

SOURCE Regulus Therapeutics Inc.

For further information: Investor Relations, Amy Conrad, Senior Director, Investor Relations and Corporate Communications, Regulus Therapeutics Inc., 858-202-6321, aconrad@regulusrx.com; or Media, Liz Bryan, Spectrum Science, lbryan@spectrumscience.com, 202-955-6222 x2526
