Regulus Initiates ATHENA Natural History of Disease Study in Alport Syndrome Patients

-ATHENA to Shed Light on Rare, Life-Threatening Kidney Disease -
-Results Will Advance and Inform Clinical Development of RG-012, a microRNA Therapeutic for the Treatment of Renal Dysfunction in Alport Syndrome Patients -

LA JOLLA, Calif., Sept. 18, 2014 /PRNewswire/ -- Regulus Therapeutics Inc. (NASDAQ: RGLS), a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs, announced today it has initiated its ATHENA natural history of disease study in patients with Alport syndrome, a life-threatening genetic kidney disease with no approved therapy. The ATHENA study is designed to characterize the natural decline of renal function markers such as Glomerular Filtration Rate ("GFR"), creatinine, proteinuria and beta-2 microglobulin, in Alport syndrome patients over time. Over the course of two years, Regulus aims to enroll up to 120 Alport syndrome patients who are 16 years and older with a GFR between 30-75ml/min at planned clinical sites in the United States, Australia, Canada and Europe.

The data collected from the ATHENA study will provide much needed information about the changes in renal function over time in Alport syndrome patients, which will inform future clinical development plans of Regulus' RG-012, a single stranded, chemically modified oligonucleotide that binds to and inhibits the function of microRNA-21 ("miR-21"), currently in development to treat renal dysfunction in Alport syndrome patients.

"Orphan diseases like Alport syndrome are poorly or incompletely understood and we believe that conducting a natural history study is an essential element to facilitate efficient clinical development. In the ATHENA study, we anticipate that prospectively measuring changes in GFR and other renal biomarkers should 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 patients with Alport syndrome," said Paul Grint, M.D., Chief Medical Officer of Regulus. "The data from ATHENA will be important to the Alport syndrome patient community and Regulus' future success in treating the disease with RG-012, a key program under our 'Clinical Map Initiative'."

About Alport Syndrome

Alport syndrome is a life-threatening, genetic kidney disease that impacts the body's ability to create a specific type of collagen highly expressed in the kidney. This specific type of collagen is important for maintaining the integrity of the glomerular basement membrane, a vital component in the kidney structure and filtration process. In Alport syndrome patients, multiple mutations have been identified in the collagen genes. The impact of the genetic mutation in the collagen genes results in increased fibrosis in the glomerular basement membrane, progressive loss of kidney function leading to chronic kidney disease, end-stage renal disease requiring dialysis or kidney transplantation, or may even lead to death. Alport syndrome patients often experience hearing loss and eye abnormalities, although the major clinical concern is the loss of kidney function. Alport syndrome represents a significant unmet medical need and has no approved therapy.

About RG-012 for the Treatment of Alport Syndrome

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 renal dysfunction in Alport syndrome patients. In animal models of kidney fibrosis and Alport syndrome, Regulus has discovered that miR-21 is highly overexpressed and anti-miRs targeting miR-21 have been shown to reduce the severity of fibrosis. 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 mice by up to fifty percent, and a favorable pharmacokinetic profile that supports the potential for a once per week dosing regimen.

In July 2014, RG-012 received orphan drug designation from the U.S. Food & Drug Administration as a therapeutic for the treatment of Alport syndrome. In September 2014, Regulus initiated ATHENA, a natural history of disease study to gather greater information about the progression of Alport syndrome, particularly the rate of decline in renal function in Alport syndrome patients over time. Regulus expects to initiate a Phase I clinical study of RG-012 for the treatment of Alport syndrome in the first half of 2015 and a Phase II proof-of-concept study thereafter.

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 in the Phase I clinical study of RG-101 for the treatment of HCV by the end of 2014, 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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For further information: Investor Relations Contact: Amy Conrad, Senior Director, Investor Relations and Corporate Communications, Regulus Therapeutics Inc., 858-202-6321, aconrad@regulusrx.com, or Media Contact: Liz Bryan, Spectrum Science, lbryan@spectrumscience.com, 202-955-6222 x2526
