Regulus Announces New Publication Showing Potential Therapeutic Benefit of Targeting microRNA-21 in Fibrosis

-New study published in Science Translational Medicine demonstrates microRNA-21 contributes to fibrogenesis in the kidney

-Regulus, in partnership with Sanofi, developing novel anti-fibrotic therapies targeting microRNAs

LA JOLLA, Calif., Feb. 16, 2012 /PRNewswire/ -- Regulus Therapeutics Inc., a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs, today announced that new preclinical data investigating the role of microRNA-21 (miR-21) in the treatment of kidney fibrosis has been published in the journal *Science Translational Medicine*. Regulus' lead program for fibrosis targets miR-21, which is up-regulated in fibrotic tissues of humans. Previous preclinical studies by Regulus scientists and collaborators have shown that therapeutic oligonucleotides targeting miR-21 (anti-miR-21) can decrease fibrosis in preclinical models by reducing the expression of extracellular matrix proteins. Despite the current burden of fibrosis-related human disease, there are few therapies that can specifically treat this devastating disease.

"We are pleased with the published results demonstrating that targeting miR-21 with proprietary anti-miR oligonucleotides is effective at preventing kidney fibrosis in preclinical models," said Neil W. Gibson, Ph.D., Regulus' Chief Scientific Officer. "We plan to select an anti-miR-21 development candidate this year for advancement into the clinic in the near future and are excited about the potential to bring this innovative treatment to patients with fibrotic diseases."

"Expression of miR-21 was found to be increased in fibrotic kidney samples from animal models and human patient samples. Genetic deletion of miR-21 in preclinical models protected kidneys from fibrosis and treatment with anti-miRs targeting miR-21 also blocked fibrosis in preclinical models," said Dr. Duffield, M.D., Ph.D. Associate Professor of Medicine, in the Division of Nephrology, at the University of Washington. "Taken together, these data suggest that anti-miR-21 could have a therapeutic benefit in patients with chronic kidney disease."

In the published study, Regulus and its collaborators from the University of Washington investigated the role of miR-21 in kidney fibrosis. Genetic deletion of miR-21 in mice resulted in no overt abnormality, however, these miR-21 knock out mice suffered less fibrosis in response to kidney injury, which was pheno-copied in wild-type mice treated with anti-miR-21 oligonucleotides. Analysis of gene expression profiles identified groups of genes involved in metabolic pathways that were up-regulated in the absence of miR-21, in particular genes involved in lipid metabolism and enhanced oxygen radical production. Systemic administration of anti-miR-21 effectively reversed the deleterious effects of miR-21 in kidney injuries. These animal studies demonstrate that miR-21 contributes to fibrogenesis and epithelial injury in the kidney in two mouse models and is a candidate target for anti-fibrotic therapies.

The journal article titled, "MicroRNA 21 Promotes Fibrosis of the Kidney by Silencing Metabolic Pathways," is now available in *Science Translational Medicine* and on the publications page of the Regulus website at www.regulusrx.com.

About Fibrosis

Fibrosis is the harmful build-up of excessive fibrous tissue leading to scarring and ultimately the loss of organ function. Fibrosis can affect any tissue and organ system, and is most common in the heart, liver, lung, peritoneum, and kidney. The fibrotic scar tissue is made up of extracellular matrix proteins such as type I collagen, proteoglycans and fibronectin. Regulus has identified several microRNAs that are dysregulated in fibrosis. Results from this new preclinical study demonstrate that miR-21 contributed to fibrogenesis and is a candidate target for anti-fibrotic therapies.

About microRNAs

The discovery of microRNA 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 700 microRNAs have been identified in the human genome, and over one-third 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. microRNAs have been shown to play an integral role in numerous biological processes, including the immune response, cell-cycle control, metabolism, viral replication, stem cell differentiation and human development. Most microRNAs are conserved across multiple species, indicating the evolutionary importance of these molecules as modulators of critical biological pathways. Indeed, microRNA expression, or function, has been shown to be significantly altered in many disease states, including cancer,

heart failure and viral infections. Targeting microRNAs with anti-miRs, antisense oligonucleotide inhibitors of microRNAs, or miR-mimics, double-stranded oligonucleotides to replace microRNA function opens potential for a novel class of therapeutics and offers a unique approach to treating disease by modulating entire biological pathways.

About Regulus Therapeutics, Inc.

Regulus Therapeutics is a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs. Regulus is using a mature therapeutic platform based on technology that has been developed over 20 years and tested in more than 5,000 humans. The company works with a broad network of academic collaborators and leverages the oligonucleotide drug discovery and development expertise of its founding companies, Alnylam Pharmaceuticals (*NASDAQ:ALNY*) and Isis Pharmaceuticals (*NASDAQ:ISIS*). Regulus is advancing microRNA therapeutics toward clinical development in several areas, including fibrosis, hepatitis C, immuno-inflammatory diseases, metabolic diseases and oncology. Regulus' intellectual property estate contains both the fundamental and core patents in the field and includes over 600 patents and more than 300 pending patent applications pertaining primarily to chemical modifications of oligonucleotides targeting microRNAs for therapeutic applications. In April 2008, Regulus formed a major alliance with GlaxoSmithKline to discover and develop microRNA therapeutics for immuno-inflammatory diseases. In February 2010, Regulus and GlaxoSmithKline entered into a new collaboration to develop and commercialize microRNA therapeutics targeting microRNA-122 for the treatment of hepatitis C infection. In June 2010, Regulus and sanofi-aventis entered into the largest-to-date strategic alliance for the development of microRNA therapeutics with an initial focus on fibrosis.

For more information, please visit http://www.regulusrx.com. Regulus is also on YouTube at http://www.youtube.com/user/RegulusRx#p/f and on Twitter at www.twitter.com/regulusrx .

Forward-Looking Statements

This press release includes forward-looking statements regarding the future therapeutic and commercial potential of Regulus' business plans, technologies and intellectual property related to microRNA therapeutics being discovered and developed by Regulus, including statements regarding the therapeutic potential of targeting microRNA -21 for treating fibrosis and kidney injury. Any statement describing Regulus' goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in 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 products. Such forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause the results to differ materially from those expressed or implied by such forward-looking statements. Although these forward-looking statements reflect the good faith judgment of Regulus' management, these statements are based only on facts and factors currently known by Regulus. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Regulus', Alnylam's, and Isis' programs are described in additional detail in Alnylam's and Isis' annual reports on Form 10-K for the year ended December 31, 2010, and its most recent quarterly report on Form 10-Q. Copies of these and other documents are available from Alnylam or Isis.

SOURCE Regulus Therapeutics Inc.

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