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Regulus Announces Pipeline Updates and Advancements

Phase II RG-012 HERA and Renal Biopsy studies for Alport syndrome move forward
Discontinuing clinical development of RG-101
Pre-clinical pipeline progresses

LA JOLLA, Calif., June 12, 2017 /PRNewswire/ -- Regulus Therapeutics Inc. (NASDAQ: RGLS), a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs, today announced updates to its pre-clinical and clinical development programs.

"We are squarely focused on taking the steps necessary to advance our pipeline and continue building shareholder value. To that end, we recognize that we must be disciplined in our investment choices and focus our resources and capital on our most promising discovery and development programs, including the application of important development, regulatory and commercial considerations," said Jay Hagan, President and Chief Executive Officer of Regulus. "MicroRNA therapeutics have the potential to become an important new class of drugs with broad therapeutic application. Regulus' focus will be in diseases with significant unmet medical need in organs to which we have been able to preferentially deliver oligonucleotide therapeutics effectively, such as the liver and kidney."

RG-012 for Alport syndrome: Initiation of the Phase II clinical programs for RG-012 for the treatment of Alport syndrome is on track as planned. Important changes to the Phase II study design have been incorporated with the goal to accelerate patient enrollment, improve statistical power, and potentially achieve proof of mechanism data by the end of 2017. HERA, the Phase II randomized (1:1), double-blinded, placebo-controlled study evaluating the safety and efficacy of RG-012 in Alport syndrome patients, has been modified to increase enrollment to 40 patients to improve its statistical power. Dose frequency has also been adjusted to once every other week. The separate renal biopsy study will evaluate RG-012 renal tissue pharmacokinetics, target engagement and downstream effects on genomic disease biomarkers. Data from the renal biopsy study is anticipated by year-end and interim data from HERA is anticipated mid-2018.

RG-101 (anti-miR122) for HCV: The Company announced today that it plans to discontinue clinical development of RG-101 upon completion of the one remaining clinical study, which is expected to occur in July 2017. Comprehensive pre-clinical investigation and thorough evaluation of the clinical data from RG-101 has led to the identification of a bilirubin transport mechanism as the likely cause for the cases of hyperbilirubinemia in the RG-101 program. We believe that a combination of factors including inhibition of conjugated bilirubin transport by RG-101, impaired baseline bilirubin transport in HCV patients and the preferential uptake of RG-101 by hepatocytes contributed to this mechanism. Additional patient specific contributing factors cannot be excluded. Applying the learnings from the RG-101 program, alternative compounds targeting miR-122 have been identified that maintain potent HCV antiviral activity while lacking inhibition of the bilirubin transporter. These compounds have the potential for rapid clinical proof-of-concept of a novel, markedly shortened treatment regimen for HCV and will be considered for further development pending an updated global commercial market assessment for HCV.

RGLS4326 (anti-miR-17) for autosomal dominant polycystic kidney disease (**ADPKD):** The IND for RGLS4326 is on

track for filing by year end 2017. IND enabling toxicology, repeat pharmacology and manufacturing work have been completed as scheduled to support regulatory submissions. Data from the pre-clinical program have been recently published in *Nature Communications* and support the rationale for targeting miR-17 for the treatment of ADPKD, an orphan indication with no treatment options affecting approximately 600,000 people in the United States.

RGLS5040 (anti-miR-27) for cholestatic disease: RGLS5040, an unconjugated inhibitor of microRNA27, has been discontinued based on a positioning of the compound with respect to the competitive landscape coupled with the results from repeat pharmacology studies as part of IND-enabling work. The Company continues to work on developing highly effective therapeutics for genetic forms of cholestatic disease as part of its overall research activities targeting unmet diseases of the liver and kidney.

"With the focus of our efforts on the most promising programs in our portfolio and the opportunity to explore additional novel clinical applications of miRNA targeted therapeutics, I am more excited than ever about the opportunity to deliver game-changing therapeutics for patients with great unmet medical need," said Dr. Timothy Wright, Regulus' Chief R&D Officer.

Separately, AstraZeneca informed the Company that it intends to terminate the clinical development program for AZD4076 (RG-125) for the treatment of NASH in Type 2 Diabetes/Pre-diabetes. Pursuant to the terms of the licensing agreement, AstraZeneca's rights with respect to AZD4076(RG-125) will revert to Regulus when the termination becomes effective in twelve months. AZD4076(RG-125) was jointly identified and selected as a clinical candidate in April 2015 by AstraZeneca under the companies' strategic alliance to discover, develop and commercialize microRNA therapeutics.

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 rich intellectual property estate to retain its leadership in the microRNA field. Regulus is advancing several programs in renal, hepatic and central nervous systems diseases. 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-101 or 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.

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