

Regulus Announces Preliminary Results of Planned Interim Data Analysis of RGLS4326 in New Mouse Chronic Toxicity Study

*No Adverse or Other Significant Findings to Date Across All Dose Groups Tested
Data Package to Be Submitted to FDA to Support Potential Resumption of Phase 1 Clinical Study*

LA JOLLA, Calif., Jan. 4, 2019 /PRNewswire/ -- [Regulus Therapeutics Inc.](#) (Nasdaq: RGLS), a biopharmaceutical company focused on the discovery and development of innovative medicines targeting microRNAs, today announced the preliminary results of a planned interim data analysis from the new mouse chronic toxicity study of RGLS4326 in development for the treatment of Autosomal Dominant Polycystic Kidney Disease, or ADPKD.

As previously reported by the Company in July 2018, and in consultation with FDA, the Company voluntarily paused its ongoing Phase 1 Multiple Ascending Dose ("MAD") study of RGLS4326 in healthy volunteers due to unexpected observations in the 27-week mouse chronic toxicity study. The Company terminated that mouse study prematurely at week 14. The study was run in parallel to the Phase 1 program to enable initiation of the Phase 2 program in ADPKD patients upon completion of the Phase 1 MAD study. The observations from the mouse chronic toxicity study were unexpected given the favorable safety profile of RGLS4326 in previous 7-week non-GLP and GLP toxicity studies in both mice and non-human primates required for Phase 1 testing, which had no significant findings across similar dose levels and frequencies. Based upon the Company's investigation and the results announced today, the Company believes the unexpected observations from the previously terminated study were likely a result of technical issues at the contract research organization ("CRO").

In September 2018, the Company announced the initiation of a new 27-week mouse chronic toxicity study, incorporating several changes intended to address the unexpected observations in the previous mouse chronic toxicity study. Certain key changes included the use of a different CRO to conduct the study and the use of a new batch of RGLS4326.

The planned interim analysis of this study after 13 weeks of dosing has shown no adverse or other significant findings across the range of doses tested and is intended to support re-initiation of the Phase 1 MAD study after consultation with FDA. RGLS4326 has also been generally well-tolerated in the Phase 1 Single Ascending Dose ("SAD") and MAD studies in human subjects to date.

The Company plans to submit a comprehensive data package for RGLS4326 to FDA that will include the results from the planned 13-week interim analysis of the ongoing repeat mouse chronic toxicity study, as well as results from additional investigations, analytical testing, additional data from the previously terminated mouse chronic toxicity study, data from the completed Phase 1 SAD study and data from the first cohort of the Phase 1 MAD study. The Company anticipates engagement with FDA in the coming weeks to discuss the resolution of the voluntary pause in human dosing and the plan to resume the Phase 1 MAD study.

"I am proud of the team at Regulus and the data package they have assembled on RGLS4326," said Jay Hagan, President and Chief Executive Officer of Regulus. "I am pleased with the investigative work and encouraged by the results of the planned interim analysis from this new mouse chronic toxicity study. We look forward to engaging with FDA to discuss this submission and the potential path forward to resuming the clinical activities for this important program."

About Autosomal Dominant Polycystic Kidney Disease (ADPKD)

ADPKD, caused by the mutations in the PKD1 or PKD2 genes, is among the most common human monogenic disorders and a leading genetic cause of end-stage renal disease. The clinical hallmark of this disease is the development of multiple fluid filled cysts primarily in the kidneys and to a lesser extent in the liver and other organs. Excessive kidney tubule derived cyst cell proliferation, a central pathological feature, fuels the expansion of cysts, ultimately causing end-stage renal disease in approximately 50% of ADPKD patients by age 60. Approximately 1 in 1,000 people bear a mutation in either PKD1 or PKD2 genes worldwide.

About RGLS4326

RGLS4326 is a novel oligonucleotide designed to inhibit miR-17 and designed to preferentially target the kidney. Preclinical studies with RGLS4326 have demonstrated direct regulation of PKD1 and PKD2 in human ADPKD cyst cells, a reduction in kidney cyst formation, improved kidney weight/body weight ratio, decreased cyst cell proliferation, and preserved kidney function in mouse models of ADPKD.

About Regulus

Regulus Therapeutics Inc. (Nasdaq: RGLS) is a biopharmaceutical company focused on the discovery and development of innovative medicines targeting microRNAs. Regulus has leveraged its oligonucleotide drug discovery and development expertise to develop a pipeline complemented by a rich intellectual property estate in the microRNA field. 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 RGLS4326 and its ability to recommence human clinical trials), the projected timeline of clinical development activities, the anticipated engagement with the FDA regarding the Regulus' RGLS4326 program and the timing thereof, 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 current shutdown of the U.S. Government, which may delay or otherwise inhibit Regulus' ability to engage with FDA on matters relating to RGLS4326; and 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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