Regulus Therapeutics Announces RGLS4326 Program Update

Data Requirements Defined To Reinitiate Multiple Ascending Dose And Chronic Dose Studies With RGLS4326
Single Ascending Dose Studies With RGLS4326 May Be Pursued

LA JOLLA, Calif., July 23, 2019 /PRNewswire/ -- Regulus Therapeutics Inc . (Nasdaq: RGLS), a biopharmaceutical company focused on the discovery and development of innovative medicines targeting microRNAs, today announced a program update for RGLS4326 for the treatment of Autosomal Dominant Polycystic Kidney Disease (ADPKD). The Company has been working with the United States Food and Drug Administration (FDA) since July 2018, when Regulus voluntarily paused the Phase 1 clinical program due to unexpected findings in the mouse chronic toxicity study being run in parallel with the Phase 1 program. In consultation with FDA, Regulus provided the interim analyses from a new mouse chronic toxicity study and the non-human primate (NHP) chronic toxicity study and supporting information to enable re-initiation of the Multiple Ascending Dose (MAD) study. After review of the requested submission, FDA notified the Company of additional nonclinical data requirements and placed the IND on a partial clinical hold, formalizing the specific requirements to reinitiate the MAD study and further proceed into chronic dosing in ADPKD patients.

The additional data requirements have been outlined in two parts. In order to resume the MAD study, FDA has requested the final reports from the chronic toxicity studies in both mice and NHP and satisfactory related analyses to ensure subjects can be safely dosed. Additional data and analyses from new nonclinical studies, planned to be generated over the next several quarters, will be required for chronic dosing, and may also be used to support the resumption of the MAD study.

Regulus is allowed to proceed with additional Single Ascending Dose (SAD) clinical studies as part of the process to gather additional supporting information to guide the future development of the program. The Company previously announced that it had completed both the SAD study in healthy volunteers up to the planned highest dose, as well as the first dose level of the MAD study in healthy volunteers. Clinical data generated to date showed that RGLS4326 administration was generally well-tolerated with no serious adverse events for all doses tested.

"We appreciate the productive dialog with FDA throughout this process," stated Jay Hagan, CEO of Regulus. "They have provided clear requirements that we believe we can address with data anticipated in the next several months from ongoing studies, augmented by data to be generated from additional studies that we expect to be completed early next year."

About ADPKD

ADPKD, caused by the mutations in the PKD1 or PKD2 genes, is among the most common human monogenic disorders and a leading cause of end-stage renal disease. The disease is characterized by the development of multiple fluid filled cysts primarily in the kidneys, and to a lesser extent in the liver and other organs. Excessive kidney cyst cell proliferation, a central pathological feature, ultimately leads to end-stage renal disease in approximately 50% of ADPKD patients by age 60.

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 maintains its corporate headquarters in La Jolla, CA.

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 completion of preclinical and clinical activities concerning the RGLS4326 program, including statements regarding the sufficiency of the data resulting from the ongoing or planned preclinical studies required to recommence the clinical studies and the timing of preclinical and clinical activities. 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, and feedback from the FDA. These and other risks 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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