

Regulus Announces Strategic Update and Corporate Restructuring

Efforts Aimed at Extending Cash Runway to mid-2019

LA JOLLA, Calif., July 5, 2018 /PRNewswire/ -- [Regulus Therapeutics Inc.](#) (Nasdaq: RGLS), a biopharmaceutical company focused on the discovery and development of innovative medicines targeting microRNAs, today announced a strategic update and corporate restructuring. With the goal of extending its cash runway, Regulus has taken the following steps: recruitment activities for the RG-012 clinical program in Alport syndrome have been paused while discussions with Sanofi to potentially restructure the partnership are ongoing; preclinical research efforts will be focused on its Hepatitis B virus (HBV) programs; and a workforce reduction of approximately 60% is being implemented. These actions are anticipated to yield over \$20 million of annualized savings, which are intended to extend the Company's cash runway into mid-2019.

The Company also announced that it has voluntarily paused the Phase 1 multiple ascending dose (MAD) study for RGLS4326 due to unexpected observations in its 27-week mouse chronic toxicity study, which was designed to support the Phase 2 proof-of-concept study in Autosomal Dominant Polycystic Kidney Disease (ADPKD) previously planned to start in mid-2019. The observations in the mouse chronic toxicity study were unexpected, given the favorable safety profile of RGLS4326 in previous non-GLP and GLP toxicity studies at the same or similar doses supporting the Investigational New Drug application (IND) and Phase 1 program. In consultation with FDA, the Company has initiated investigative studies and is planning a new 27-week mouse chronic toxicity study with certain changes that are believed to address the unexpected findings. The 40-week non-human primate chronic toxicity study continues with no significant findings to date. Importantly, RGLS4326 has been generally safe and well-tolerated in the Phase 1 single ascending dose (SAD) and MAD studies to date.

"I am very disappointed that we need to take these drastic steps to preserve our capital, especially given the significant contributions by our dedicated employees to the progress made toward unlocking the potential of targeting microRNAs," said Jay Hagan, Regulus' President and Chief Executive Officer. "In the near-term, we will concentrate our efforts on investigating the unexpected mouse toxicity findings in our RGLS4326 program, advancing our HBV programs, and looking for additional ways to improve shareholder value."

Pipeline Update

RG-012 for the treatment of Alport syndrome: The Company also announced today that preliminary results from the first patients through the renal biopsy study are encouraging with kidney tissue concentrations achieved that would be predictive of therapeutic benefit based on animal disease models. In addition, modulation of the target, miR-21, was observed.

Preclinical Programs: The Company has determined that advancing its preclinical programs targeting HBV represents the most attractive opportunity in its pipeline for investment, affecting an estimated 350 million people worldwide. Regulus has identified multiple microRNA targets that serve as host factors for the virus. Targeting host factors with GalNAc-conjugated oligonucleotides directed to the liver represents a potentially attractive approach to treating the disease. Regulus and others have already demonstrated effective delivery to the liver with this technology, and Regulus has demonstrated human proof-of-concept (POC) with this approach previously with a program targeting the Hepatitis C Virus. The Company currently expects to file an IND for the HBV program in H2 2019, with the potential of achieving human POC in a Phase 1 study.

Regulus will seek to partner the balance of its preclinical programs, which include glioblastoma multiforme, NASH, and immunology.

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 RG-012, RGLS4326, or its Hepatitis B Virus program), Regulus' estimated cash runway and anticipated cost savings associated with its planned reduction in

workforce, 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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