

Regulus Therapeutics Announces First Patient Dosed in Phase 1b Clinical Trial of RGLS4326 for the Treatment of Patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD)

LA JOLLA, Calif., Oct. 15, 2020 /PRNewswire/ -- [Regulus Therapeutics Inc.](#) (Nasdaq: RGLS), a biopharmaceutical company focused on the discovery and development of innovative medicines targeting microRNAs (the "Company" or "Regulus"), today announced initiation of dosing in its Phase 1b clinical study of RGLS4326 in patients with ADPKD.

The Phase 1b is an adaptive design, open-label, multiple dose study in up to three cohorts of patients with ADPKD and will evaluate administration of RGLS4326 for safety, pharmacokinetics, and changes in levels of polycystin 1 (PC1) and polycystin 2 (PC2). Patients with ADPKD, due to a mutation in the PKD genes, have been reported to have low levels of PC1 and PC2, the proteins encoded by the PKD1 and PKD2 genes, respectively. This study is designed to assess whether different dose levels of RGLS4326 can increase levels of PC1 and PC2 in ADPKD patients. The first cohort is expected to enroll up to nine patients who will receive RGLS4326 every two weeks over a six week period. The Company anticipates availability of results from the first cohort by the end of Q1 2021.

The Company plans to use the data from this first cohort of patients with ADPKD, together with the data from the multiple ascending dose and the single ascending dose studies in healthy volunteers as well as the recently completed nonclinical studies, to obtain feedback from the U.S. Food & Drug Administration ("FDA") on the acceptability of the Company's approach to addressing the second set of FDA requirements to support studies of extended duration in patients.

"We are excited to evaluate this potentially disease modifying investigational drug in patients with ADPKD," said Jay Hagan, CEO of Regulus. "This Phase 1b study will provide important data on safety, pharmacokinetics, and biomarkers of ADPKD which we plan to use in our approach to address the remaining partial clinical hold requirements."

For more information about the clinical trial design, please visit www.clinicaltrials.gov (NCT04536688).

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*, reduction of cyst growth in human *in vitro* ADPKD models, and attenuation of cyst proliferation and improvement of kidney function in mouse models of ADPKD. The RGLS4326 IND is currently on a Partial Clinical Hold for treatment of extended duration by FDA until the second set of requirements outlined by the agency have been satisfactorily addressed. Information from the Phase 1 clinical studies, together with information from the recently completed additional nonclinical studies, will be used to address the second set of requirements to support studies of extended duration. RGLS4326 has received orphan drug designation from FDA in July 2020.

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.

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, the

sufficiency of the data resulting from the ongoing or planned preclinical studies required to recommence clinical studies for extended duration dosing 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. In addition, while Regulus expects the COVID-19 pandemic to adversely affect its business operations and financial results, the extent of the impact on Regulus' ability to achieve its preclinical and clinical development objectives and the value of and market for its common stock, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate duration of the pandemic, travel restrictions, quarantines, social distancing and business closure requirements in the U.S. and in other countries, and the effectiveness of actions taken globally to contain and treat the disease. 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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