Regulus Therapeutics Announces Successful Completion of Pre-IND Meeting with FDA for RGLS8429

Company remains on track to submit IND and initiate Phase 1 study in second quarter 2022
Company to include evaluation of treatment impact on slowing cystic kidney expansion

SAN DIEGO, Jan. 20, 2022 /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 that the Company has completed a pre-investigational new drug (Pre-IND) meeting with the U.S. Food and Drug Administration (FDA). The purpose of the meeting was to obtain input from the FDA on pre-clinical, clinical and regulatory matters pertaining to the Company's next generation compound RGLS8429 as a potential treatment for Autosomal Dominant Polycystic Kidney Disease (ADPKD). The formal minutes from this meeting were received by the Company earlier this week.

The successful completion of this interaction with the FDA is an important milestone that provides regulatory clarity regarding Regulus' planned Phase 1 trial design. The agency provided overall agreement with the trial design and length of the Phase 1 study, including the proposed starting dose for RGLS8429, as well as sufficiency of the non-clinical package, with no commentary regarding its first-generation compound, RGLS4326 and any additional filing requirements. Based on the minutes, the Company is on track to submit an IND application in the second quarter of 2022 to obtain clearance for initiation of the Phase 1 clinical trial.

The Phase 1 study will consist of two parts. Part 1 will consist of a single-ascending dose (SAD) study in healthy volunteers to assess safety and tolerability of RGLS8429 and characterize the pharmacokinetics of RGLS8429. A total of 32 subjects will be randomized to RGLS8429 or placebo into one of four sequential cohorts. The proposed doses for the four cohorts are 1 mg/kg, 2 mg/kg, 4 mg/kg, and 6 mg/kg. Part 2 will be a multiple ascending dose (MAD) study in adult patients with ADPKD to assess safety and tolerability of RGLS8429, to characterize the pharmacokinetics of RGLS8429, and to evaluate the dose response of RGLS8429 treatment on disease parameters in ADPKD patients including levels of the disease biomarker, polycystin, cystic kidney volume (htTKV), and overall kidney function. A total of 36 subjects will be randomized to RGLS8429 or placebo into one of three sequential cohorts. The proposed doses for the three cohorts are 0.75 mg/kg, 1.5 mg/kg, and 3 mg/kg every other week for three months.

Regulus' updated clinical plans agreed to with FDA include extending dosing to three months in each cohort of ADPKD patients, inclusion of measurements of changes in htTKV by Magnetic Resonance Imaging (MRI), and testing higher doses of RGLS8429 than were tested with the first-generation compound. Height-adjusted total kidney volume (htTKV), a measure of cystic kidney volume, is a biomarker for disease severity and progression to kidney failure in patients with ADPKD. Increased htTKV has been found to occur prior to loss of kidney function, typically by years or decades, and retrospective evidence from published clinical studies has shown a correlation between reduction in TKV and reduction in the rate of decline in renal function.

"We are pleased with the clear and encouraging input we received from the FDA," said Jay Hagan, President and Chief Executive Officer of Regulus Therapeutics. "The FDA's feedback was informative and will be useful in finalizing the design of the Phase 1 study which now includes the opportunity to study the potential impact of our investigational product in patients longer. As we prepare for submission of the IND application, on track with our previous guidance, in the second quarter, we look forward to data from the healthy volunteer portion of the study in the second half of this year and data from patients with ADPKD in the first half of 2023. We are pleased to have strengthened our balance sheet through the successful completion of a $34.6 million private placement in November which enables us to conduct this more robust clinical study design."

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 San Diego, CA.

Forward-Looking Statements

Statements contained in this presentation 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 timing of the filing of the Investigation New Drug application and the planned clinical development activities concerning the Company's RGLS8429 program in ADPKD. 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 the risk additional toxicology data may be negative. 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, including under the "Risk Factors" heading of Regulus most recently quarterly report on Form 10-Q. 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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For further information: Investor Relations Contact: Cris Calsada, Chief Financial Officer, 858-202-6376, ccalsada@regulusrx.com; Media Contact: Sarah Sutton, Argot Partners, 212-600-1902, regulus@argotpartners.com

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