Regulus Therapeutics Advances to Cohort 2 of Phase 1b Multiple-Ascending Dose (MAD) Clinical Trial of RGLS8429 for the Treatment of Autosomal Dominant Polycystic Kidney Disease (ADPKD)

Blinded safety data observed so far are encouraging

SAN DIEGO, May 16, 2023 /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, after review of all available safety data, that it will advance to the second cohort of patients in the Phase 1b MAD study of RGSL8429 for the treatment of ADPKD.

"We are pleased to see our Phase 1b MAD trial continue to advance with the initiation of the second cohort of patients," said Jay Hagan, CEO of Regulus Therapeutics. "This is another important step in our quest to develop a novel treatment for ADPKD. We look forward to topline data from the first cohort around the end of the third quarter of this year."

The Phase 1b MAD study is a double-blind, placebo-controlled trial evaluating the safety, tolerability, pharmacokinetics and pharmacodynamics (PK/PD) of RGLS8429 in adult patients with ADPKD. The study will evaluate RGLS8429 treatment across three different dose levels, including measuring changes in polycystins, height-adjusted total kidney volume (htTKV), cyst architecture, and overall kidney function. The first cohort is being dosed at 1 mg/kg of RGLS8429 or placebo every other week for three months. No issues were identified in cohort 1 based on the review of all available blinded safety data clearing the way to advancement to cohort 2. The safety review incorporated available data from all 12 patients in the first cohort including several who had completed the dosing schedule. Patients in the second cohort will receive 2 mg/kg of RGLS8429 or placebo every other week for three months. The Company also recently completed the 27-week chronic toxicity study of RGLS8429 in mice. No RGLS8429-related toxicity, including CNS effects, was observed at any dose level up to the top dose of 300 mg/kg administered every other week.

More information about the MAD clinical trial is available at clinicaltrials.gov (NCT05521191).

About ADPKD

Autosomal Dominant Polycystic Kidney Disease (ADPKD), caused by 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. Approximately 160,000 individuals are diagnosed with the disease in the United States alone, with an estimated global prevalence of 4 to 7 million.

About RGLS8429

RGLS8429 is a novel, next generation oligonucleotide for the treatment of ADPKD designed to inhibit miR-17 and to preferentially target the kidney. Administration of RGLS8429 has shown robust data in preclinical models, where clear improvements in kidney function, size, and other measures of disease severity have been demonstrated along with a superior pharmacologic profile in preclinical studies compared to Regulus' first-generation compound, RGLS4326. Regulus announced completion of the Phase 1 SAD study in September 2022. The Phase 1 SAD study demonstrated that RGLS8429 has a favorable safety and PK profile. RGLS8429 was well-tolerated with no serious adverse events reported and plasma exposure was approximately linear across the four doses tested and is similar to the PK data from the first-generation compound. In April, Regulus announced completion of enrollment for the first cohort of patients in the Phase 1b MAD study and with the recent review of all available safety data, is advancing to the second cohort where patients will receive 2 mg/kg of RGLS8429 or placebo every other week for three months.

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 Company's RGLS8429 program, including the expected timing for initiating clinical studies, the expected timing for reporting topline data, the safety of RGLS8429 and the timing and future occurrence of other 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 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 filed annual report on Form 10-K. 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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