



Regulus Therapeutics Reports First Quarter 2021 Financial Results and Recent Updates

May 13, 2021

Regulus Therapeutics Demonstrates Target Engagement in First-Ever Study of RGLS4326 in Patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD) Second Cohort Underway with Data Expected Mid-2021

SAN DIEGO, May 13, 2021 /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 reported financial results for the first quarter ended March 31, 2021 and provided a corporate update.



"We are excited about the data we recently announced from the first cohort of our phase 1b clinical trial of RGLS4326 for the treatment of patients with ADPKD where we saw mean increases of greater than 50% and 20% in Polycystin 1 (PC1) and Polycystin 2 (PC2), respectively. PC1 and PC2 are the products of the PKD1 and PKD2 genes, and are depressed in patients with this disease. The trends for both suggest that with continued therapy, higher levels of these proteins may be attainable and less frequent dosing required. Additionally, RGLS4326 was well tolerated by all nine patients with no serious adverse events reported", stated Jay Hagan, CEO of Regulus. "Data from the first cohort provides the safety and pharmacokinetic data needed to complete the modeled safety margins. We plan to submit these data to FDA this summer in the context of our discussions regarding the remaining partial clinical hold requirements."

Program Updates

RGLS4326 for ADPKD: In February 2021, the Company completed enrollment in the first cohort of a Phase 1b clinical study for RGLS4326 in patients with ADPKD (The "Phase 1b"). The Phase 1b is an adaptive design, open-label, multiple dose study in up to three cohorts of patients with ADPKD. The study is designed to evaluate the safety, pharmacokinetics, and changes in levels of PC1 and PC2 in patients with ADPKD administered RGLS4326 every other week for a total of four doses. The dose level for the first cohort is 1 mg/kg of RGLS4326 and the dose level for the second cohort is 0.3 mg/kg. The third and final cohort will be dosed at a level to be determined based on the results of the first two cohorts. In May 2021, the Company announced top-line results from the first cohort of patients with ADPKD in its ongoing Phase 1b clinical trial of RGLS4326.

In the first cohort, nine patients were enrolled and received 1 mg/kg of RGLS4326 subcutaneously every other week for four doses. Safety, pharmacokinetics, and certain disease related biomarkers were evaluated through the course of the study. The biomarkers included: PC1 and PC2, kidney injury marker 1 (KIM-1), neutrophil gelatinase-associated lipocalin (NGAL), as well as urea and creatinine and were chosen to evaluate changes in disease related measures.

Measured levels of PC1 and PC2 increased greater than 50% and 20%, respectively by the end of study compared to baseline levels. Regulus believes these initial data demonstrate that RGLS4326 engages the target miR-17 leading to increased expression of the PKD1 and PKD2 genes and the resultant increases in measured polycystin levels. Measured levels of PC1 and PC2 have been shown to inversely correlate with disease severity and are believed to be directly linked to the underlying genetic drivers of the disease. The overall trend in polycystin showed increasing levels of both PC1 and PC2 over time with a sustained effect suggesting less frequent dosing could be utilized. Importantly, at the time of the analysis, patient mutational status was not known and may further contribute to understanding differences in response rates. Approximately 85% of patients with

ADPKD are reported to have a mutation in the PKD1 gene, while the remaining 15% have a mutation in the PKD2 gene. Additionally, the PKD1 gene has one predicted binding site for miR-17 while the PKD2 gene has two predicted binding sites for miR-17, potentially contributing to different response rates between the biomarkers.

RGLS4326 was well tolerated by all nine patients with no serious adverse events reported. All reported adverse events were mild and generally transient in nature.

Overall, the pharmacokinetic profile of RGLS4326 in patients with ADPKD was similar to that observed in a prior healthy volunteer study. Concentrations of RGLS4326 in plasma were greater in patients (C_{max} ~ 3 ug/mL) relative to healthy volunteers (C_{max} ~ 2 ug/mL), suggesting a lower dose in patients could achieve the desired exposure in the kidney, the target organ of interest.

Data from this first cohort is planned to be submitted for presentation at PKD Connect in June 2021 and at Kidney Week, the American Society of Nephrology annual meeting being held in November 2021.

Corporate Highlights

Lease Agreement for New Corporate Headquarters Executed and Relocation Completed: In February 2021, we entered into a lease agreement (the "New Lease") for 13,438 square feet located at 4224 Campus Point Court, Suite 210, San Diego, California, 92121, which is to be used as our new principal offices and laboratory for research and development. The move into the space leased under the New Lease was completed in April 2021. Concurrently with the New Lease, we assigned the lease to the space that had served as our previous corporate headquarters, and have no remaining obligations associated with the previous corporate headquarters lease after April 2021.

Financial Results

Cash Position: As of March 31, 2021, Regulus had \$31.6 million in cash and cash equivalents.

Research and Development (R&D) Expenses: Research and development expenses were \$3.3 million for the three months ended March 31, 2021, compared to \$3.1 million for the same period in 2020. These amounts reflect internal and external costs associated with advancing our clinical and preclinical pipeline.

General and Administrative (G&A) Expenses: General and administrative expenses were \$2.5 million for the three months ended March 31, 2021, compared to \$2.4 million for the same period in 2020. These amounts reflect personnel-related and ongoing general business operating costs.

Net Loss: Net loss was \$6.0 million, or \$0.08 per share (basic and diluted), for the three months ended March 31, 2021, compared to \$5.9 million, or \$0.25 per share (basic and diluted), for the same period in 2020.

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 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. The Company will use information from the Phase 1 clinical studies, including the first cohort of the Phase 1b together with information from the recently completed additional nonclinical studies generated in 2020, in its plan to address the second set of requirements outlined in the Partial Clinical Hold letter to support studies of extended duration. Regulus plans to discuss its approach to addressing the remaining Partial Clinical Hold requirements with FDA in mid-2021. RGLS4326 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 clinical activities concerning the RGLS4326 program, including the preliminary biomarker, pharmacokinetic and safety data resulting from the first cohort of patients from the ongoing clinical study, the sufficiency of the data required to recommence clinical studies for extended duration dosing, the timing of the Company's interactions with FDA regarding the clinical hold and the timing and 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 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.

Regulus Therapeutics Inc.

**Selected Financial Information
Condensed Statement of Operations
(In thousands, except share and per share data)**

	Three months ended March 31,	
	2021	2020
Revenues:		
Revenue under strategic alliances	\$ -	\$ 6
Operating expenses:		
Research and development	3,320	3,119
General and administrative	<u>2,478</u>	<u>2,422</u>
Total operating expenses	<u>5,798</u>	<u>5,541</u>
Loss from operations	(5,798)	(5,535)
Other expense, net	<u>(215)</u>	<u>(410)</u>
Loss before income taxes	(6,013)	(5,945)
Income tax benefit	-	8
Net loss	<u>\$ (6,013)</u>	<u>\$ (5,937)</u>
Net loss per share, basic and diluted	<u>\$ (0.08)</u>	<u>\$ (0.25)</u>
Weighted average shares used to compute basic and diluted net loss per share:	<u>71,290,918</u>	<u>24,064,373</u>

	March 31, 2021	December 31, 2020
Cash and cash equivalents	\$ 31,597	\$ 31,087
Total assets	39,841	37,604
Term loan, less debt issuance costs	4,657	4,652
Stockholders' equity	27,111	26,026

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