

Regulus Therapeutics Reports Second Quarter 2020 Financial Results and Recent Updates

Completion of Dosing in Phase 1 Multiple Ascending Dose Study ("MAD") of RGLS4326 in Healthy Volunteers for Autosomal Dominant Polycystic Kidney Disease ("ADPKD")

FDA Orphan Designation of RGLS4326 for ADPKD

Appointment of Denis Drygin, Ph.D., as Chief Scientific Officer

LA JOLLA, Calif., Aug. 13, 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 reported financial results for the second quarter ended June 30, 2020 and provided a corporate update.

"We are pleased with the progress of our ADPKD program and the completion of dosing of the MAD clinical study for RGLS4326 in healthy volunteers," said Jay Hagan, CEO of Regulus. "We plan to initiate a Phase 1b study in patients with ADPKD to evaluate short-term treatment of RGLS4326 for safety, tolerability, pharmacokinetics, and changes in biomarkers of the disease. We have also recently completed additional non-clinical studies needed to address some of the FDA requirements to support studies of extended duration."

Second Quarter 2020 Corporate Highlights and Recent Updates

Appointment of Chief Scientific Officer: In August, Dr. Denis Drygin joined Regulus as its Chief Scientific Officer.

Program Updates

- **RGLS4326 for Autosomal Dominant Polycystic Kidney Disease:** In July 2020, the Company completed dosing in the MAD clinical study for RGLS4326 in healthy volunteers. The Phase 1 MAD study is a randomized, double blind, placebo-controlled clinical trial evaluating three different dose levels of RGLS4326 for safety, tolerability, and pharmacokinetic properties. Top-line results showed that RGLS4326 is well-tolerated with no serious adverse events reported. Preliminary results suggest plasma exposure is dose proportional. In July 2020, the FDA granted Orphan Drug Designation to RGLS4326 for ADPKD.

The Company plans to initiate a Phase 1b open-label, short-term multiple dose study in patients with ADPKD in the second half of 2020. The study will evaluate RGLS4326 for safety, pharmacokinetics, and changes in levels of polycystin 1 (PC1) and polycystin 2 (PC2). Patients with ADPKD, due to the mutation in the PKD gene, have been reported to have low levels of PC1 and PC2. This study is designed to evaluate whether different dose levels of RGLS4326 can increase levels of PC1 and PC2 in ADPKD patients.

- **Advancement of Hepatitis B virus (HBV) Program:** The Company has identified several microRNA targets that serve as host factors for the hepatitis B virus (HBV). Our lead compound directed to one of the host microRNAs has demonstrated nanomolar potency against HBV DNA replication and more than 95% reduction in Hepatitis B surface antigen in *in vitro* studies. Additionally, we have demonstrated reduction of HBV DNA, surface antigen and pgRNA in an *in vivo* efficacy model. We believe that targeting a host factor in the liver represents a unique mechanism of action for treatment of the virus compared to other programs in development and holds the potential for achieving a functional cure. We have nominated a development candidate and plan to commence IND-enabling activities.
- **Additional Research Updates:** Cell therapies have been approved to treat a variety of hematological malignancies. Targeting solid tumors, however, has proven challenging for cell therapies due to the immune-suppressive effect of the tumor microenvironment (TME). The Company believes that ex vivo modulation of microRNA may enable cell therapy approaches to overcome the effects of the TME and address other challenges faced by cell therapies. The Company has demonstrated that targeting microRNA ex vivo can improve certain characteristics of engineered cells including an improved in vitro expansion, effector function, cytokine production, as well as resistance to exhaustion induced by tonic signaling. The Company is pursuing multiple applications of microRNA technology in a variety of cell therapies.

Second Quarter 2020 Financial Results

Cash Position: As of June 30, 2020, Regulus had \$23.4 million in cash and cash equivalents.

Research and Development (R&D) Expenses: Research and development expenses were \$4.2 million and \$7.4 million for the three and six months ended June 30, 2020, respectively, compared to \$1.8 million and \$7.8 million for the three and six months ended June 30, 2019, respectively. The aggregate increase for the three months ended June 30, 2020, as compared to the three months ended June 30, 2019, was driven by an increase in external development expenses, primarily attributable to the FDA lifting the partial clinical hold on the MAD study in December 2019 and completion of the dosing for the Phase 1 of the MAD study in July 2020. The aggregate decrease for the six months ended June 30, 2020, as compared to the six months ended June 30, 2019, was driven by a reduction in personnel and internal expenses, partially offset by an increase in external development expenses attributable to recommencement and completion of the dosing of the MAD study in July 2020.

General and Administrative (G&A) Expenses: General and administrative expenses were \$2.3 million and \$4.7 million for the three and six months ended June 30, 2020, respectively, compared to \$2.9 million and \$6.4 million for the three and six months ended June 30, 2019, respectively. These amounts reflect personnel-related and ongoing general business operating costs. The decreases for the three and six months ended June 30, 2020, as compared to the three and six months ended June 30, 2019, are primarily attributable to continued cost reduction efforts subsequent to our corporate restructurings.

Revenue: Revenue was zero and less than \$0.1 million for the three and six months ended June 30, 2020, respectively, compared to less than \$0.1 million and \$6.8 million for the three and six months ended June 30, 2019, respectively. Revenue recognized for the six months ended June 30, 2019 was attributable to the upfront payments received under the 2018 Sanofi Amendment related to the transfer of the RG-012 program to Sanofi.

Net Loss: Net loss was \$6.9 million, or \$0.23 per share (basic and diluted), and \$12.9 million, or \$0.48 per share (basic and diluted), for the three and six months ended June 30, 2020, respectively, compared to \$5.0 million, or \$0.30 per share (basic and diluted), and \$8.3 million, or \$0.61 per share (basic and diluted), for the same periods in 2019.

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 Company recently completed the multiple ascending dose study of RGLS4326 in healthy volunteers. Administration of RGLS4326 was well-tolerated with no serious adverse events reported. The Company is initiating a Phase 1b study in patients with ADPKD to evaluate short-term treatment of RGLS4326 for safety, tolerability, pharmacokinetics, and changes in biomarkers of the disease. The RGLS4326 IND is currently on a Partial Clinical Hold for treatment of extended duration beyond the current Phase 1b study until the second set of requirements outlined by FDA 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.

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.

Regulus Therapeutics Inc.

Selected Financial Information

Condensed Statement of Operations

(In thousands, except share and per share data)

	Three months ended June 30,		Six months ended June 30,	
	2020	2019	2020	2019
Revenues:				
Revenue under strategic alliances	\$ -	\$ 18	\$ 6	\$ 6,796
Operating expenses:				
Research and development	4,242	1,836	7,360	7,819
General and administrative	2,254	2,850	4,676	6,383
Total operating expenses	6,496	4,686	12,036	14,202
Loss from operations	(6,496)	(4,668)	(12,030)	(7,406)
Other expense, net	(451)	(347)	(862)	(869)
Loss before income taxes	(6,947)	(5,015)	(12,892)	(8,275)
Income tax expense (benefit)	-	(1)	8	(1)
Net loss	\$ (6,947)	\$ (5,016)	\$ (12,884)	\$ (8,276)
Net loss per share, basic and diluted	\$ (0.23)	\$ (0.30)	\$ (0.48)	\$ (0.61)
Weighted average shares used to compute basic and diluted net loss per share:	29,801,974	16,705,587	26,933,173	13,560,183

June 30,
2020 December 31,
2019

(Unaudited)

Cash and cash equivalents	\$ 23,419	\$ 34,121
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Total assets	29,782	42,081
Term loan, less debt issuance costs	14,642	14,631
Stockholders' equity	8,584	20,015

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