

Regulus Therapeutics Reports Third Quarter 2020 Financial Results and Recent Updates

First Patient Dosed in Phase 1b Clinical Trial of RGLS4326 for the Treatment of Patients with Autosomal Dominant Polycystic Kidney Disease ("ADPKD")
Restructuring of Sanofi and Oxford Agreements
Receipt of \$5 Million Milestone and Material Payments from Sanofi and Proceeds Used to Repay Debt Principal with Oxford LLC
Achievement of Interim Enrollment Milestone Under Collaboration with Sanofi

LA JOLLA, Calif., Nov. 5, 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 third quarter ended September 30, 2020 and provided a corporate update.

"We are pleased with the progress on our ADPKD program with the recent announcement of dosing of the first patient in the Phase 1b clinical trial of RGLS4326 in patients with ADPKD", stated Jay Hagan, CEO of Regulus. "Next year is shaping up to be an important one for Regulus, with data from the first cohort anticipated by end of Q1 2021. We also achieved \$10 million in milestones from our collaboration with Sanofi enabling us to reduce our outstanding debt to \$4.7 million and extend the interest-only period through the end of 2021."

Third Quarter 2020 Corporate Highlights and Recent Updates

Amendment of Sanofi Collaboration Agreement and Achievement of Milestones: In August 2020, the Company entered into an amendment with Sanofi concerning the receipt of potential milestones from Sanofi for its development of miR-21 programs. Under the terms of the amendment with Sanofi, the Company was eligible to receive \$4 million upon the completion of transfer and verification of certain materials valued at an additional \$1 million sold to Sanofi. In addition to this payment of \$5 million received, the Company achieved a \$5 million interim enrollment milestone and is eligible to receive an additional \$25 million upon the successful achievement of a development milestone related to the Phase 2 HERA study.

Term Loan Amendments and Reduction in Principal: In August 2020, and concurrently with the Sanofi amendment, the Company amended its term loan agreement with Oxford LLC, under which the Company is eligible for up to an additional seven months of interest only payments in the event the Company pays down \$10 million in loan principal before April 30, 2021. In September and October 2020, the Company made payments totaling \$5 million to Oxford and plans to make an additional \$5 million payment to Oxford before the end of 2020, thus triggering the additional interest only period. These payments will reduce the remaining principal due under the term loan to approximately \$4.7 million. Remaining principal and accrued interest payments will commence on January 1, 2022.

Program Updates

- **RGLS4326 for ADPKD:** In October 2020, the Company dosed the first patient in a Phase 1b clinical study for 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 planned 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.
- **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. The Company believes 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. The Company has nominated a development candidate and plans 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 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.

Third Quarter 2020 Financial Results

Cash Position: As of September 30, 2020, Regulus had \$17.8 million in cash and cash equivalents.

Revenue: Revenue was \$5.0 million for the three and nine months ended September 30, 2020, respectively, compared to less than \$0.1 million and \$6.8 million for the three and nine months ended September 30, 2019, respectively. Revenue recognized for the three and nine months ended September 30, 2020 was attributable to the completion of transfer and verification of certain materials to Sanofi under the August 2020 amendment. Revenue recognized for the nine months ended September 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.

Research and Development (R&D) Expenses: Research and development expenses were \$4.0 million and \$11.4 million for the three and nine months ended September 30, 2020, respectively, compared to \$2.4 million and \$10.3 million for the three and nine months ended September 30, 2019, respectively. The aggregate increase for the three months ended September 30, 2020, as compared to the three months ended September 30, 2019, was driven by an increase in internal development expenses, primarily attributable to FDA lifting the partial hold on the MAD study in December 2019 and completion of the dosing for the Phase 1 of the MAD study in July 2020, as well as start-up activities leading up to the first patient dosing in our RGLS4326 Phase 1b study in October 2020. The aggregate increase for the nine months ended September 30, 2020, as compared to the nine months ended September 30, 2019, was driven by an increase in external development expenses, attributable to RGLS4326 MAD and Phase 1b study activities, partially offset by a reduction in personnel and internal expenses.

General and Administrative (G&A) Expenses: General and administrative expenses were \$2.1 million and \$6.7 million for the three and nine months ended September 30, 2020, compared to \$2.6 million and \$9.0 million for the three and nine months ended September 30, 2019. These amounts reflect personnel-related and ongoing general business operating costs. The decreases for the three and nine months ended September 30, 2020, as compared to the three and nine months ended September 30, 2019, are primarily attributable to continued cost reduction efforts subsequent to our corporate restructurings.

Net Loss: Net loss was \$1.5 million, or \$0.04 per share (basic and diluted), and \$14.4 million, or \$0.47 per share (basic and diluted), for the three and nine months ended September 30, 2020, respectively, compared to \$5.4 million, or \$0.26 per share (basic and diluted), and \$13.7 million, or \$0.86 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 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 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 concerning the HBV and cell therapies programs. 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 September 30,		Nine months ended September 30,	
	2020	2019	2020	2019
Revenues:				
Revenue under strategic alliances	\$ 5,000	\$ 18	\$ 5,006	\$ 6,814
Operating expenses:				
Research and development	4,036	2,440	11,396	10,259
General and administrative	2,059	2,571	6,736	8,954
Total operating expenses	6,095	5,011	18,132	19,213
Loss from operations	(1,095)	(4,993)	(13,126)	(12,399)
Other expense, net	(428)	(430)	(1,289)	(1,299)
Loss before income taxes	(1,523)	(5,423)	(14,415)	(13,698)
Income tax (expense) benefit	(1)	-	7	(1)
Net loss	\$ (1,524)	\$ (5,423)	\$ (14,408)	\$ (13,699)
Net loss per share, basic and diluted				
	\$ (0.04)	\$ (0.26)	\$ (0.47)	\$ (0.86)
Weighted average shares used to compute basic and diluted net loss per share:	38,137,281	20,849,083	30,695,137	16,016,515

	September 30, 2020		December 31, 2019	
	(Unaudited)			
Cash and cash equivalents	\$	17,843	\$	34,121
Total assets		27,343		42,081
Term loan, less debt issuance costs		13,647		14,631
Stockholders' equity		7,754		20,015

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