Regulus Therapeutics Reports Fourth Quarter and Year-End 2023 Financial Results and Recent Updates

Positive topline data from the second cohort of patients in Phase 1b Multiple-Ascending Dose (MAD) Clinical Trial of RGLS8429 for the Treatment of Autosomal Dominant Polycystic Kidney Disease (ADPKD)

Oversubscribed $100 million private placement; expected to extend cash runway into H1 2026

Completed enrollment of the third cohort of patients in the MAD study; Data anticipated mid-2024

Completed Type D Meeting with FDA to Discuss Pathway for Accelerated Approval of RGLS8429

SAN DIEGO, March 21, 2024 /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 fourth quarter and year ended December 31, 2023, and provided a corporate update.

"2023 was a productive year for Regulus, and the growing momentum in our Phase 1b MAD study of RGLS8429 is further emphasized by our announcement of key milestones and data readouts, including the recent positive topline data from the second cohort of patients. In the topline data, we saw evidence of a mechanistic dose response at a 2 mg/kg dose level based on urinary polycystin levels and in particular their potential correlation with improvements in kidney volume and function" said Jay Hagan, CEO of Regulus. "Thanks to the strong data we've seen to date and the ongoing support of our shareholders, we completed an oversubscribed $100 million private placement this month, which is expected to extend our cash runway into the first half of 2026. We look forward to a busy 2024, including sharing top-line data from our third cohort, expected in mid-2024, and the initiation of our fourth and final cohort of the MAD study next quarter."

Program Updates

RGLS8429 for ADPKD: In March 2024, the Company shared positive topline data from the second cohort of patients in the Phase 1b MAD study of RGLS8429 for the treatment of ADPKD. In the second cohort, 14 patients were randomized 3:1 to receive either 2 mg/kg of RGLS8429 or placebo every other week for three months. RGLS8429 was well tolerated with no safety findings of concern. Greater biological activity of RGLS8429 was observed at 2 mg/kg based on urinary polycystin levels compared to 1mg/kg and placebo, which was most evident after 3 months of dosing. Exploratory results of imaging-based biomarkers were encouraging with 3 patients with the highest increases in PC1 and PC2 having reductions in height-adjusted total kidney volume (htTKV) >4%, with corresponding reductions in total kidney cyst volume (TKCV). These data suggest that targeting miR-17 may have a potential impact on htTKV and TKCV in patients with ADPKD, which the Company will further explore at higher doses in cohorts 3 and 4.

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 is evaluating RGLS8429 treatment across three different weight-based dose levels, including measuring changes in urinary polycystins 1 and 2 (PC1 and PC2), htTKV, cyst architecture, and overall kidney function.

In November 2023, Regulus announced it had dosed the first patient in the third cohort of the Phase 1b MAD study. This cohort is receiving 3 mg/kg of RGLS8429 or placebo every other week for three months. In January, the Company announced that it had completed enrollment in cohort 3 with top-line data expected in mid-2024.

In late 2023, Regulus amended the protocol for the Phase 1b MAD study to include a fourth cohort that will receive an open label fixed dose of 300 mg of RGLS8429 that will provide higher exposure in a larger number of patients based on anticipated body weight in order to compare biomarker and safety data to the weight-based dosing, with initiation of screening planned for Q2 2024. Based on the results from the second cohort, the Company plans to amend the protocol to increase the sample size to up to 30 patients in cohort 4.

In December 2023, the Company held a successful Type D meeting with the U.S. Food and Drug Administration (FDA) to discuss the accelerated approval pathway. The meeting was constructive and confirmed the potential for an accelerated approval pathway based on a single pivotal Phase 2 study of RGLS8429 for the treatment of ADPKD. The FDA has adopted an accelerated approval pathway for ADPKD based on a single pivotal trial demonstrating statistically significant reduction in TKV growth compared to placebo, with completion of a post approval Phase 3 trial as a post-marketing requirement, demonstrating a statistically significant improvement in estimated glomerular filtration rate (eGFR) compared to placebo.

Corporate Highlights

Closed Oversubscribed $100 Million Private Placement: On March 12, 2024, the Company announced that it entered into a definitive securities purchase agreement in connection with a private placement to certain institutional and other accredited investors. The financing included participation from new and existing institutional investors, including Adage Capital Partners L.P., Deep Track Capital, the Federated Hermes Kaufmann Funds, New Enterprise Associates (NEA), Octagon Capital, RA Capital Management, and Vivo Capital.

Financial Results

Cash and Cash Equivalents: As of December 31, 2023, Regulus had $23.8 million in cash and cash equivalents. Combined with the $100 million private placement equity financing in March, the Company expects its cash runway to extend into H1 2026.

Research and Development (R&D) Expenses: Research and development expenses were $5.8 million and $21.2 million for

the fourth quarter and year ended December 31, 2023, respectively, compared to $4.7 million and $18.4 million for the same periods in 2022, respectively.

General and Administrative (G&A) Expenses: General and administrative expenses were $2.5 million and $10.0 million for the fourth quarter and year ended December 31, 2023, respectively, compared to $2.2 million and $9.8 million for the same periods in 2022, respectively.

Net Loss: Net loss was $8.1 million, or $0.40 per share (basic and diluted), and $30.0 million, or $1.58 per share (basic and diluted), for the fourth quarter and year ended December 31, 2023, compared to $6.8 million, or $0.40 per share (basic and diluted), and $28.3 million, or $1.86 per share (basic and diluted), for the same periods in 2022.

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 the Phase 1b MAD study Regulus announced both top line data from the first cohort of patients in September 2023 and from the second cohort of patients in March 2024. After review of all available safety data from the second cohort, Regulus has advanced to the third cohort where dosing has begun, and patients are receiving 3 mg/kg of RGLS8429 or placebo every other week for three months. Regulus announced completion of enrollment in the third cohort in January 2024 with top-line data anticipated in mid-2024.

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, the expected timing for initiating clinical studies, potentially achieving therapeutic efficacy and the potential to address the underlying genetic causes of ADPKD, the expected timing for reporting data, the timing and future occurrence of other preclinical and clinical activities the potential accelerated approval pathway, the expected length of our cash runway and other statements relating to future events or conditions. 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, the approach we are taking to discover and develop drugs is novel and may never lead to marketable products, preliminary or initial results may not be indicative of future results, preclinical and clinical studies may not be successful, risks related to regulatory review and approval, risks related to our reliance on third-party collaborators and other third parties, risks related to intellectual property, 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 our need for additional capital. 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 for the fourth quarter and year ending December 31, 2023. 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	Year ended

	December 31,		December 31,	
	2023	2022	2023	2022
Operating expenses:				
Research and development	5,762	4,713	21,152	18,410
General and administrative	2,538	2,219	9,957	9,829
Total operating expenses	8,300	6,932	31,109	28,239
Loss from operations	(8,300)	(6,932)	(31,109)	(28,239)
Other income (expense), net	239	137	1,073	(83)
Loss before income taxes	(8,061)	(6,795)	(30,036)	(28,322)
Income tax expense	-	-	(1)	(1)
Net loss	$ (8,061)	$ (6,795)	$ (30,037)	$ (28,323)
Net loss per share, basic and diluted	$ (0.40)	$ (0.40)	$ (1.58)	$ (1.86)
Weighted average shares used to compute basic and diluted net loss per share:	20,222,111	16,839,700	18,960,401	15,259,958

	December 31, 2023	December 31, 2022
Cash, cash equivalents and short-term investments	$ 23,767	$ 39,160
Total assets	30,750	46,716
Term loan, less debt issuance costs	1,334	4,511
Stockholders' equity	21,187	33,291

SOURCE Regulus Therapeutics Inc.

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