

Regulus Provides Strategic Update and Reports Fourth Quarter and Year-End 2013 Financial Results and Recent Highlights

- *Achieved All Goals on 'Road to the Clinic'; Launched 'Clinical Map Initiative'*-
- *Regulatory Approval Received for Phase I Clinical Study of RG-101* -
- *Strengthened Focus on Orphan Diseases and Oncology* -
- *Exceeded YE 2013 Guidance with \$114.0M in Cash* -

LA JOLLA, Calif., Feb. 27, 2014 /PRNewswire/ -- [Regulus Therapeutics Inc.](#) (NASDAQ:RGLS), a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs, today provided an update on its corporate strategy and reported financial results for the fourth quarter and year ended December 31, 2013, including a summary of recent corporate highlights.

Corporate Strategy Update:

Achieved All Goals on 'Road to the Clinic' and Launches 'Clinical Map Initiative'

- Regulus announced today that it has achieved all goals under its 'Road to the Clinic' Strategy:
 - Regulus has nominated two microRNA candidates for clinical development, RG-101, a GalNAc-conjugated anti-miR targeting miR-122 for the treatment of chronic hepatitis C virus infection ("HCV"), and RG-012, an anti-miR targeting microRNA-21 ("miR-21") for the treatment of Alport Syndrome, a life-threatening kidney disease driven by genetic mutations with no approved therapy;
 - Regulus has received regulatory approval to initiate the Phase I clinical study of RG-101; and
 - Regulus exceeded its previously issued cash guidance, ending 2013 with \$114.0 million in cash, cash equivalents and short-term investments.
- Regulus also announced today its 'Clinical Map Initiative', which outlines certain corporate goals to advance its microRNA therapeutics pipeline over the next several years:
 - Demonstrate human proof-of-concept results in the Phase I clinical study of RG-101 for the treatment of HCV by the end of 2014;
 - Initiate a Phase I clinical study of RG-012 for the treatment of Alport Syndrome in the first half of 2015;
 - Nominate a third microRNA candidate for clinical development by the end of 2014; and
 - Maintain a strong financial position and end 2014 with at least \$75.0 million in cash, cash equivalents and short-term investments.

"In 2013, we demonstrated significant progress toward our goal of building a leading biopharmaceutical company dedicated to discovering and developing a new and major class of medicines targeting microRNAs. Today, we are pleased to have achieved our goals on the 'Road to the Clinic' and transition into a clinical-stage company with the launch of our 'Clinical Map Initiative,'" said Kleanthis G. Xanthopoulos, Ph.D., President and CEO of Regulus. "We believe that 2014 will be another exciting year for Regulus. We expect to commence dosing in our Phase I clinical trial of RG-101, advance RG-012 toward clinical development, potentially nominate a third candidate for clinical development and maintain a strong financial position to support these goals. Importantly, we look forward to our first human proof-of-concept study with RG-101 in HCV patients. If positive, these results will go a long way toward validating our technology platform and approach to treating disease. Overall, we are pleased with our achievements and we look forward to building a meaningful clinical portfolio based on microRNA therapeutics."

Recent Pipeline Highlights

- **Regulatory Approval Received for Phase I Clinical Study of RG-101.**
 - In November 2013 at the American Association for the Study of Liver Diseases (AASLD) meeting, Regulus presented data evaluating RG-101 for *in vitro* and *in vivo* potency, pharmacokinetic/pharmacodynamics, toxicology and safety pharmacology and inhibition of HCV replication. In addition, Regulus has also tested RG-101 for efficacy in a human chimeric liver mouse model infected with HCV genotypes 1a and 3a. In this model, up to a 2 log reduction in HCV viral load titer was observed in both genotypes after a single dose of RG-101. The duration of action observed for RG-101 supports the potential for a once-a-month dosing regimen. To date, RG-101 has demonstrated an excellent preclinical safety profile and has been well tolerated.
 - The Phase I clinical study of RG-101 will have four parts: (i) a single ascending-dose study in healthy volunteer subjects; (ii) a multiple-ascending dose study in healthy volunteer subjects; (iii) a single-dose drug-drug interaction study of RG-101 in combination with an approved oral direct-acting

antiviral ("DAA") in healthy volunteer subjects; and (iv) a single-dose study in HCV patients to assess the safety and viral load reduction, which is designed to demonstrate human proof-of-concept. The primary objective of the Phase I clinical study of RG-101 is to evaluate safety and tolerability and the secondary objectives are to evaluate pharmacokinetics, viral load reduction and any impact an oral DAA may have on the pharmacokinetics of RG-101. Up to approximately 100 healthy volunteer subjects and HCV patients are planned to be enrolled in the Phase I study, which is being conducted in the Netherlands, and dosing is expected to commence in the near term.

- **Strengthened Focus on Orphan Diseases and Oncology Indications.**

- **Nominated RG-012 as Clinical Development Candidate for the Treatment of Alport Syndrome.** In November 2013 at the American Society of Nephrology (ASN) Kidney Week meeting, Regulus presented data demonstrating that RG-012 is a potent inhibitor of miR-21 in both *in vitro* and *in vivo* preclinical models and that subcutaneous administration of RG-012 has significantly decreased the rate of renal fibrosis and increased the lifespan of the mice up to 50%. RG-012 has been well tolerated to date with a favorable pharmacokinetic profile that supports the potential for a once/week dosing regimen. Regulus expects to initiate a natural history of disease study in the third quarter of 2014 and to initiate a Phase I clinical study of RG-012 for the treatment of Alport Syndrome in the first half of 2015.
- **Renewed Strategic Alliance with Sanofi; Received Additional \$10 Million Equity Investment.** Regulus renewed its strategic alliance with Sanofi to discover, develop, and commercialize microRNA therapeutics to focus on specific orphan disease and oncology targets. Regulus will lead development of its RG-012 program for the treatment of Alport Syndrome, its program targeting miR-21 in oncology and its program targeting microRNA-221/microRNA-222 for the treatment of hepatocellular carcinoma. Regulus is responsible for advancing the clinical candidates in these programs to proof-of-concept. Sanofi will have the exclusive option, exercisable after proof-of-concept, to take over further development and commercialization of each microRNA therapeutic program. If Sanofi chooses to exercise its option on any program, Sanofi will reimburse Regulus for a significant portion of its preclinical and clinical development costs and will pay Regulus an option exercise fee. Regulus is eligible to receive development and commercialization milestone payments and will have an option to co-promote in the United States or receive royalty payments in the mid 10% to 20% range on any of these programs.
- **Discovery Efforts Continued to Support Therapeutic Pipeline.** Regulus continued to pursue several additional undisclosed microRNA targets, namely for orphan disease and oncology indications, with the goal of potentially nominating a third candidate for clinical development by the end of 2014.

- **AstraZeneca Collaboration to Focus on miR-103/107, miR-19 and Replacement Target for miR-33 Program.**

- Under its collaboration with AstraZeneca to discover and develop microRNA therapeutics for cardiovascular diseases, metabolic diseases and oncology, Regulus announced today that the ongoing efforts on two of the collaboration programs are targeting microRNA-103/107 for the treatment of metabolic diseases and microRNA-19 for oncology indications, a target selected by AstraZeneca in October 2013. Additionally, Regulus announced today that the companies have agreed to terminate the program targeting microRNA-33 ("miR-33") for the treatment of atherosclerosis as a collaboration target. AstraZeneca has a contractual right to substitute a new target for miR-33.

"Our scientific accomplishments in 2013 have advanced our therapeutic pipeline in a meaningful way and have prepared us to enter the clinic," said Neil W. Gibson, Ph.D., Chief Scientific Officer of Regulus. "Additionally, we are pleased to have strengthened our focus on orphan diseases and oncology indications and we look forward to expanding our clinical portfolio in the coming year."

Recent Corporate Highlights

- **Expanded microRNA Biomarkers Platform and Established Regulus *micro Markers*™ R&D Division.** The division utilizes a clinically-validated, highly reproducible, proprietary technology platform to identify microRNAs as potential biomarkers for disease. In 2012, Regulus formed a research collaboration with Biogen Idec focused on the discovery of microRNAs as biomarkers for multiple sclerosis and has entered into an arrangement with another leading, commercial-stage pharmaceutical company to explore microRNAs as biomarkers for specific patient populations.
- **Attracted Key Talent.** Regulus strengthened its executive management team with the addition of David Szekeres as Chief Business Officer and General Counsel. Additionally, Martin Beaulieu, Ph.D. joined Regulus as head of the Regulus *microMarkers*™ division.

Fourth Quarter and Year-End 2013 Financial Results and 2014 Financial Outlook

Regulus completed 2013 with \$114.0 million in cash, cash equivalents and short-term investments, compared to \$98.1 million as of December 31, 2012.

Regulus reported a net loss of \$1.9 million and \$18.7 million for the quarter and year ended December 31, 2013, respectively, compared to \$6.9 million and \$17.4 million for the same periods in 2012.

Basic and diluted net loss per share was \$0.05 and \$0.11 for the quarter ended December 31, 2013, respectively, compared to basic and diluted net loss per share of \$0.22 for the same period in 2012. Basic and diluted net loss per share was \$0.49 for the year ended December 31, 2013, compared to basic and diluted net loss per share of \$2.12 for 2012. Comparability of net loss per share for the periods presented is impacted by the initial public offering and concurrent common stock issuances in October 2012 and the public offering of common stock in July 2013.

Regulus reported revenue of \$5.5 million for the quarter ended December 31, 2013, compared to \$3.2 million for the same period in 2012. Revenue for the quarter ended December 31, 2013 included \$4.5 million from the Sanofi collaboration and license agreement and \$1.0 million from other strategic alliances and collaborations, including approximately \$0.3 million in research milestones. The increase in revenues in the fourth quarter 2013 compared to the same period in 2012 was primarily due to the incremental recognition of \$3.3 million from the change in Regulus' estimated period of performance for the research term within the Sanofi collaboration and license agreement, which extended through the end of the option period in early 2014. Revenues were \$19.6 million for the year ended December 31, 2013 compared to \$12.7 million in 2012. Revenues for the year ended December 31, 2013 included approximately \$15.4 million from the Sanofi collaboration and license agreement and \$4.2 million from other strategic alliances and collaborations. Revenue during these periods consisted primarily of amortization of upfront payments received from Regulus' strategic alliances and collaborations, which is recognized over the estimated period of performance.

Research and development expenses were \$8.2 million and \$29.9 million for the quarter and year ended December 31, 2013, compared to \$5.6 million and \$20.3 million for the same periods in 2012. These increases were substantially attributable to IND-enabling activities for RG-101 and other programs in 2013. Regulus expects its research and development expenses to continue to increase to the extent it commences clinical studies and initiates additional IND-enabling activities.

General and administrative expenses were \$1.9 million and \$7.4 million for the quarter and year ended December 31, 2013, compared to \$1.9 million and \$4.9 million for the same periods in 2012. The increase in 2013 was primarily attributable to operating costs associated with the growth of the company and incremental costs associated with being a public reporting company.

Net loss in the quarter ended December 31, 2013 included a non-cash gain of \$2.6 million from the change in value of the amended and restated convertible promissory note originally issued to GlaxoSmithKline plc in 2010, with such change in value attributable to a decrease in value of Regulus common stock during the quarter. Net loss in the quarter ended December 31, 2012 included a non-cash charge of \$2.6 million, with such change in value attributable to an increase in value of common stock of the Company during the quarter. For the years ended December 31, 2013 and 2012, total net non-cash charges associated with the convertible promissory note were \$1.1 million and \$4.7 million, respectively.

Regulus expects to finish 2014 with at least \$75.0 million in cash, cash equivalents and short-term investments, which includes the \$10.0 million common stock purchase made by its strategic alliance partner Sanofi in February 2014.

Conference Call & Webcast Information

Regulus will host a conference call and webcast at 5:00 p.m. Eastern Standard Time today to discuss its fourth quarter and year-end 2013 financial results, recent company highlights and its expectations for 2014. A live webcast of the call will be available online at www.regulusrx.com. To access the call, please dial (877) 257-8599 (domestic) or (970) 315-0459 (international) and refer to conference ID 2177234. To access the telephone replay of the call, dial (855) 859-2056 (domestic) or (404) 537-3406 (international), passcode 2177234. The webcast and telephone replay will be archived on the company's website following the call.

About Regulus

Regulus Therapeutics Inc. (*NASDAQ:RGLS*) is a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs. Regulus is uniquely positioned to leverage a mature therapeutic platform that harnesses the oligonucleotide drug discovery and development expertise of Alnylam Pharmaceuticals, Inc. and Isis Pharmaceuticals, Inc., which founded the company. Regulus has a well-balanced microRNA therapeutic pipeline entering clinical development, an emerging microRNA biomarkers platform to support its therapeutic programs, and a rich intellectual property estate to retain its leadership in the microRNA

field. Regulus intends to focus its proprietary efforts on developing microRNA therapeutics for oncology indications and orphan diseases and is currently advancing several programs toward clinical development in oncology, fibrosis and metabolic diseases. Specifically, Regulus is developing RG-012, an anti-miR targeting microRNA-21 for the treatment of Alport Syndrome, a life-threatening kidney disease driven by genetic mutations with no approved therapy, and RG-101, a GalNAc-conjugated anti-miR targeting microRNA-122 for the treatment of chronic hepatitis C virus infection. Regulus' commitment to innovation and its leadership in the microRNA field have enabled the formation of strategic alliances with AstraZeneca, GlaxoSmithKline and Sanofi. In addition, the Company has established Regulus microMarkers™, a research and development division focused on identifying microRNAs as biomarkers of human disease, which is designed to support its therapeutic pipeline, collaborators and strategic partners.

For more information, please visit <http://www.regulusrx.com>.

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 financial estimates (including Regulus' projected cash at the end of 2014), the projected sufficiency of Regulus' capital position for future periods, the expected ability of Regulus to undertake certain activities and accomplish certain goals (including with respect to development and other activities related to RG-012 and RG-101 and with respect to the nomination of a third microRNA candidate for clinical development), the projected timeline of clinical development activities, and expectations regarding future therapeutic and commercial potential of Regulus' business plans, technologies and intellectual property related to microRNA therapeutics being discovered and developed by Regulus. 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. These and other risks concerning Regulus' financial position and programs 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 December 31,		Year ended December 31,	
	2013	2012	2013	2012
Revenues:				
Revenue under strategic alliances	\$ 5,454	\$ 3,238	\$ 19,569	\$ 12,700
Total revenues	5,454	3,238	19,569	12,700
Operating expenses:				
Research and development	8,232	5,607	29,942	20,342
General and administrative	1,884	1,934	7,429	4,932

Total operating expenses	10,116	7,541	37,371	25,274
Loss from operations	(4,662)	(4,303)	(17,802)	(12,574)
Other income (expense), net	2,716	(2,555)	(889)	(4,844)
Loss before income taxes	(1,946)	(6,858)	(18,691)	(17,418)
Income tax (benefit) expense	(19)	18	(23)	(10)
Net loss	\$ (1,927)	\$ (6,876)	\$ (18,668)	\$ (17,408)

Net loss per share:

Basic	\$ (0.05)	\$ (0.22)	\$ (0.49)	\$ (2.12)
Diluted	\$ (0.11)	\$ (0.22)	\$ (0.49)	\$ (2.12)

Weighted average shares used to compute net loss per share:

Basic	41,779,422	31,907,152	38,479,447	8,212,538
Diluted	43,191,081	31,907,152	38,479,447	8,212,538

**Regulus Therapeutics Inc.
Condensed Balance Sheets
(In thousands)**

	December 31, 2013	December 31, 2012
Assets		
Cash, cash equivalents and short-term investments	\$ 114,005	\$ 98,100
Other current assets	3,177	829
Non-current assets	5,883	4,589
Total assets	\$ 123,065	\$ 103,518
Liabilities and stockholders' equity		
Current liabilities	\$ 5,482	\$ 2,317
Total deferred revenue	11,388	28,207
Convertible notes payable, at fair value	11,279	10,134
Other long-term obligations liabilities	1,459	767
Stockholders' equity	93,457	62,093

Total liabilities and stockholders' equity	\$	123,065	\$	103,518
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SOURCE Regulus Therapeutics Inc.

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<https://ir.regulusrx.com/2014-02-27-Regulus-Provides-Strategic-Update-and-Reports-Fourth-Quarter-and-Year-End-2013-Financial-Results-and-Recent-Highlights>