Regulus Advances Orphan Disease Portfolio with Nomination of RG-012 as Clinical Development Candidate for the Treatment of Alport Syndrome

-RG-012 is an anti-miR Targeting microRNA-21 for the Treatment of Alport Syndrome, a Life-Threatening, Genetic Kidney Disease with No Approved Therapy-
-Nomination Further Advances 'Road to the Clinic' Strategy-

LA JOLLA, Calif., Feb. 19, 2014 /PRNewswire/ -- Regulus Therapeutics Inc. (*NASDAQ:RGLS*), a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs, today announced that it has advanced its orphan disease portfolio with the nomination of its second microRNA candidate for clinical development, RG-012, an anti-miR targeting microRNA-21 ("miR-21") for the treatment of Alport Syndrome, a life-threatening, genetic kidney disease with no approved therapy.

"The nomination of RG-012 as our second microRNA candidate for clinical development is a significant achievement on our 'Road to the Clinic' strategy," said Kleanthis G. Xanthopoulos, Ph.D., President and CEO of Regulus. "This program underscores Regulus' focus on orphan disease indications and we look forward to rapidly advancing and expanding our clinical portfolio of meaningful microRNA therapeutics."

RG-012 has a very favorable preclinical profile to date which Regulus believes supports clinical studies in man. RG-012 is a potent inhibitor of miR-21 in both *in vitro* and *in vivo* preclinical models. Subcutaneous administration of RG-012 has significantly decreased the rate of renal fibrosis and increased the lifespan of the mice up to 50% in a mouse model of Alport Syndrome, which we believe is a good surrogate for the human disease. Regulus believes these preclinical survival results may translate to a similar increased lifespan in human patients. Moreover, RG-012 has been well tolerated to date with a favorable pharmacokinetic profile that supports the potential for a once/week dosing regimen.

Neil W. Gibson, Ph.D., Regulus' Chief Scientific Officer added, "We believe that RG-012 may become a transformative treatment for patients with Alport Syndrome, a life-threatening, genetic disease with significant unmet medical need. We are currently performing additional preclinical studies and finalizing development plans for RG-012 and expect to enter clinical development in the first half of 2015."

Regulus is responsible for advancing RG-012 to proof-of-concept. At that stage of development, Regulus' strategic alliance partner, Sanofi, has an exclusive option exercisable after proof-of-concept to assume all costs, responsibilities and obligations for further development and commercialization of RG-012. If Sanofi chooses to exercise its option on RG-012, 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.

Targeting miR-21 for the Treatment of Alport Syndrome

Alport Syndrome is a genetic condition caused by mutations in the COL4A3, COL4A4, and COL4A5 genes that is characterized by kidney disease, hearing loss, and eye abnormalities. The mutated genes provide instructions for making one component of a protein called type IV collagen. This protein plays an important role in the kidneys, specifically in structures called glomeruli. Glomeruli are clusters of specialized blood vessels that remove water and waste products from blood and create urine. The kidneys become less able to function as this condition progresses, resulting in end-stage renal disease. According to the National Institutes of Health, Alport Syndrome occurs in approximately 1 in 50,000 newborns and is an orphan disease with no approved therapy.

miR-21 is a 22-mer non-coding RNA that negatively regulates gene/networks and has been reported to be up-regulated in fibrotic kidney diseases in both animal models and human patients (Chau, B. N. et al. Sci Transl Med. 2012; Zhong X, et al. (2013) Diabetologia (2013). Preclinical studies have demonstrated that treatment with an anti-miR-21 significantly attenuates chronic kidney disease progression. Mechanistic understanding of inhibition of miR-21 leading to anti-fibrotic efficacy continues to emerge and Regulus believes that continued development of RG-012 for the treatment of Alport Syndrome will contribute to the evolving understanding of targeting miR-21 for fibrotic conditions.

About the 'Road to the Clinic' Strategy

Launched in February 2013, the 'Road to the Clinic' Strategy outlines certain corporate goals that seek to advance our microRNA therapeutic pipeline toward the clinic. Specifically, Regulus set the goal of nominating two microRNA candidates for clinical development. Regulus has nominated RG-101, a GalNAc-conjugated microRNA antagonist or anti-miR which targets miR-122 for the treatment of HCV, and RG-012, an anti-miR targeting miR-21 for the treatment of Alport Syndrome. Regulus believes its strong financial position supports

these stated goals and expects to end 2013 with approximately $110 million in cash, cash equivalents and short-term investments. Regulus plans to update its 'Road to the Clinic' strategy and cash guidance on its fourth quarter and year-end 2013 financial results webcast and conference 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. Regulus is also developing 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 Regulus' 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' programs are described in additional detail in Regulus' SEC filings. 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.

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