Regulus Announces Patent Grant from U.S. Patent Office in Sarnow Patent Estate on microRNA Therapeutics for the Treatment of HCV

- New Method of Use Claims Strengthen Patent Estate Covering microRNA-122 Inhibitors for the Treatment of HCV Infection -

LA JOLLA, Calif., June 25, 2014 /PRNewswire/ -- Regulus Therapeutics Inc. (NASDAQ: RGLS), a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs, today announced that the U.S. Patent and Trademark Office ("USPTO") has granted a patent in the company's exclusively licensed 'Sarnow' patent estate, for claims related to targeting microRNA-122 ("miR-122") for the treatment of HCV in combination with other anti-viral therapies. The Sarnow patent estate, owned by Stanford University and exclusively licensed to Regulus, has produced patents in Europe, Japan and the United States covering the use of a broad class of anti-miR inhibitors of miR-122 for the treatment of HCV as monotherapy or in combination with other anti-viral therapies. Regulus' lead asset, RG-101, a GalNAc-conjugated anti-miR that targets miR-122, is being evaluated in a Phase I clinical study for the treatment of HCV. Regulus expects to demonstrate human proof-of-concept results from Part IV of the Phase I study by the end of 2014. If favorable, these results may positively advance Regulus' microRNA technology platform and provide clinical support for its unique approach to treating disease.

"We are pleased with the newly granted miR-122 claims in the US, which represent the fourth U.S. patent to grant within the Sarnow patent estate," said David L. Szekeres, Chief Business Officer and General Counsel of Regulus. "In the United States and abroad, we continue to strengthen Regulus' already comprehensive patent estate relating to miR-122 compositions-of-matter and methods of use, which we believe is an important component for the commercialization of therapies targeting the host factor miR-122 to treat HCV infection."

The recently granted claims add to Regulus' already robust patent estate relating to miR-122-specific compositions-of-matter and methods of use, which includes:

- The Sarnow patent estate claiming methods related to the treatment of HCV infection using anti-miR-122 oligonucleotides, either as a monotherapy or in combination with other antiviral therapies (including US Patent No. 7,307,067, US Patent No. 7,838,504, US Patent No. 8,217,020, US Patent No. 8,759,312, European Patent No. 1747023; Japan Patent No. 4,943,322; allowed Australia Application No. 2005240118; also pending in Canada and Israel);

- Regulus-owned US Patent No. 7,683,036 claiming methods of inhibiting miR-122 activity using fully modified anti-miR-122 oligonucleotides and US Patent No. 8,546,350 claiming methods of inhibiting miR-122 activity using various types of modified anti-miR-122 oligonucleotides;

- US Patent No. 7,232,806, Japan Patent No. 4,371,812, Australia Patent No. 2002347035, and Israel Patent No. 161100, exclusively licensed to Regulus for therapeutic uses, claiming broad anti-miR-122 compositions-of-matter (also pending in Europe and Canada); and

- Regulus-owned European Patent No. 1931782, Australia Patent No. 2006284855, and Japan Patent No. 5523705 claiming uses of a broad class of anti-miR-122 oligonucleotides to lower cholesterol levels (also pending in US and Canada).

About Regulus' Intellectual Property Estate

Regulus believes that it has a leading intellectual property position and substantial know-how relating to the development and commercialization of microRNA therapeutics, composed of approximately 200 patents and patent applications that the company owns or has in-licensed from academic institutions and third parties including its founding companies, Alnylam Pharmaceuticals, Inc. and Isis Pharmaceuticals, Inc., related to microRNA and microRNA drug products. Regulus also has access to approximately 850 patents and patent applications exclusively related to RNA technologies, including patents and patent applications relating to chemical modification of oligonucleotides that are useful for the development of microRNA therapeutics.

About microRNAs and RG-101 for the Treatment of HCV

The discovery of microRNAs in humans during the last decade is one of the most exciting scientific breakthroughs in recent history. microRNAs are small RNA molecules, typically 20 to 25 nucleotides in length, that do not encode proteins but instead regulate gene expression. More than 800 microRNAs have been identified in the human genome, and over one-third of all human genes are believed to be regulated by microRNAs. A single microRNA can regulate entire networks of genes. As such, these molecules are considered

master regulators of the human genome. microRNA expression, or function, has been shown to be significantly altered or dysregulated in many disease states, including oncology, fibrosis, metabolic diseases, immune-inflammatory diseases and HCV. Targeting microRNAs with anti-miRs, chemically modified, single-stranded oligonucleotides, offers a unique approach to treating disease by modulating entire biological pathways and may become a new and major class of drugs with broad therapeutic application.

microRNA-122 ("miR-122") is the most abundant microRNA in hepatocytes and is a critical host factor for survival and replication of all know HCV genotypes, and anti-miRs targeting miR-122 have been shown to block HCV infection. RG-101 is a novel anti-miR-122 oligonucleotide therapeutic that is effectively targeted to hepatocytes for the treatment of HCV through conjugation to GalNAc, a carbohydrate-based chemistry approach for asialoglycoprotein receptor-mediated delivery of oligonucleotides to hepatocyte cells of the liver. Utilizing the GalNAc conjugate chemistry has significantly improved the potency of the active oligonucleotide of RG-101 by achieving targeted delivery of the oligonucleotide to the infected hepatocytes. In preclinical studies, Regulus has observed significant HCV viral load reduction in a human chimeric liver mouse model infected with genotypes 1a and 3a, a long duration of action for RG-101 which supports the potential for a once-a-month dosing regimen, and a favorable preclinical safety profile in which RG-101 has been well tolerated.

Currently, RG-101 is being evaluated in a four-part Phase I clinical study: (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. 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. By the end of 2014, Regulus expects to demonstrate human proof-of-concept results from Part IV of the Phase I study of RG-101, which is a key corporate goal under the company's 'Clinical Map Initiative'.

About the 'Clinical Map Initiative'

Launched in February 2014, Regulus' 'Clinical Map Initiative' outlines certain corporate goals to advance its microRNA therapeutics pipeline over the next several years. Regulus expects to 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.

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 therapeutics 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 and a research collaboration with Biogen Idec focused on microRNA biomarkers. 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 and biomarkers 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.

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