Regulus Therapeutics Expands Worldwide Patent Coverage on microRNA-122 to Treat Hepatitis C Virus (HCV) Infection

-The Australia Patent Office Joins the U.S. and European Patent Offices in Granting Claims for Inhibiting microRNA-122 to Reduce Viral Load-

LA JOLLA, Calif., Nov. 2, 2011 /PRNewswire/ -- Regulus Therapeutics Inc., a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs, today announced that the Australian Patent Office has recently granted claims in the 'Sarnow' patent series for microRNA-122 (miR-122) therapy in the treatment of hepatitis C viral (HCV) infections. The granted claims in Australia extend the reach of the Sarnow patent estate that already covers the use of an anti-miR inhibitor of miR-122 for the treatment of HCV in the United States and Europe. The Sarnow patent series, owned by Stanford University, has been exclusively licensed to Regulus and covers any compound that targets miR-122 for the treatment of HCV in the United States, Europe, and Australia.

Regulus controls a comprehensive and dominant patent estate related to microRNA therapeutics, including miR-122 therapeutic agents. Specifically for miR-122, Regulus controls the following:

- The 'Sarnow' patent estate claiming the use of anti-miR-122 to treat HCV infection, as a single therapeutic agent or in combination with other HCV therapeutic agents (US Patent No. 7,307,067; US Patent No. 7,838,504; EP Patent No. 1 747 023; and Australian Patent Application No. 2005240118 recently accepted for grant);
- The 'Esau' patent claiming the use of anti-miRs targeting miR-122 as inhibitory agents (US Patent No. 7,683,036);
- The 'Tuschl III' patent claiming compositions of matter for miR-122 and complementary oligonucleotides (US Patent No. 7,232,806);
- The 'Manoharan' patent claiming antagomirs, including antagomirs targeting miR-122 (US Patent No. 7,582,744); and
- A Regulus-owned European patent claiming the use of miR-122 antagonists for reducing cholesterol (EP 1 931 782).

"We are pleased with the recent allowance of miR-122 claims in Australia following issuances in Europe and the United States. This further exemplifies Regulus' leading intellectual property portfolio in the field of microRNA therapeutics. Recent clinical data in the field has demonstrated that inhibiting miR-122 with an oligonucleotide is safe, well tolerated, and able to reduce viral titers. That data, in combination with Regulus' data demonstrating potent inhibition with a proprietary anti-miR having favorable pharmacokinetic properties, supports the development of anti-miR-122 for the treatment of HCV in combination with other anti-virals," said Kleanthis G. Xanthopoulos, Ph.D., President and Chief Executive Officer of Regulus Therapeutics. "The HCV landscape has undergone a tremendous amount of transformation with the recent emergence of new direct-acting antivirals. Anti-miR-122 is attractively positioned because it targets a host factor that is essential for viral replication and therefore may be resistant to viral mutation and escape."

miR-122 is a liver-expressed microRNA that has been shown to be a critical endogenous "host factor" for the replication of HCV, and anti-miRs targeting miR-122 have been shown to block HCV infection (Jopling *et al.* (2005) *Science* 309, 1577-81). In earlier work, scientists at Alnylam Pharmaceuticals and Isis Pharmaceuticals (Regulus' co-founders) demonstrated the ability to antagonize miR-122 *in vivo* using chemically modified single-stranded anti-miR oligonucleotides. Data from multiple preclinical studies have shown a robust HCV antiviral effect following inhibition of miR-122. In February 2010, Regulus and GlaxoSmithKline entered into a new collaboration to develop and commercialize microRNA therapeutics targeting microRNA-122 for the treatment of hepatitis C infection.

Regulus is advancing multiple other microRNA therapeutic programs to the clinic in the areas of fibrosis, immuno-inflammatory disease, metabolic disease, and oncology.

About microRNAs

The discovery of microRNA 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 700 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. microRNAs have been shown to play an integral role in numerous biological processes, including the immune response, cell-cycle control, metabolism, viral replication, stem cell differentiation and human development. Most microRNAs are conserved across multiple species, indicating the evolutionary importance of these molecules as modulators of critical biological pathways. Indeed, microRNA expression, or function, has been shown to be significantly altered in many disease states, including cancer, heart failure and viral infections. Targeting microRNAs with anti-miRs, antisense oligonucleotide inhibitors of microRNAs, or miR-mimics, double-stranded oligonucleotides to replace microRNA function opens potential for a novel class of therapeutics and offers a unique approach to treating disease by modulating entire biological pathways. To learn more about microRNAs, please visit http://www.regulusrx.com/microrna/microrna-explained.php.

About Regulus Therapeutics, Inc.

Regulus Therapeutics is a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs. Regulus is using a mature therapeutic platform based on technology that has been developed over 20 years and tested in more than 5,000 humans. The company works with a broad network of academic collaborators and leverages the oligonucleotide drug discovery and development expertise of its founding companies, Alnylam Pharmaceuticals (*NASDAQ: ALNY*) and Isis Pharmaceuticals (*NASDAQ: ISIS*). Regulus is advancing microRNA therapeutics toward clinical development in several areas, including fibrosis, hepatitis C, immuno-inflammatory diseases, metabolic diseases and oncology. Regulus' intellectual property estate contains both the fundamental and core patents in the field and includes over 600 patents and more than 300 pending patent applications pertaining primarily to chemical modifications of oligonucleotides targeting microRNAs for therapeutic applications. In April 2008, Regulus formed a major alliance with GlaxoSmithKline to discover and develop microRNA therapeutics for immuno-inflammatory diseases. In February 2010, Regulus and GlaxoSmithKline entered into a new collaboration to develop and commercialize microRNA therapeutics targeting microRNA-122 for the treatment of hepatitis C infection. In June 2010, Regulus and Sanofi entered into the largest-to-date strategic alliance for the development of microRNA therapeutics with an initial focus on fibrosis.

For more information, please visit http://www.regulusrx.com. Regulus is also on YouTube at http://www.youtube.com/user/RegulusRx#p/f and on Twitter at www.twitter.com/regulusrx.

Forward-Looking Statements

This press release includes forward-looking statements regarding the future therapeutic and commercial potential of Regulus' business plans, technologies and intellectual property related to microRNA therapeutics being discovered and developed by Regulus, including statements regarding the therapeutic potential of targeting miR-122. Any statement describing Regulus' goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in 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 products. Such forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause the results to differ materially from those expressed or implied by such forward-looking statements. Although these forward-looking statements reflect the good faith judgment of Regulus' management, these statements are based only on facts and factors currently known by Regulus. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Regulus', Alnylam's, and Isis' programs are described in additional detail in Alnylam's and Isis' annual reports on Form 10-K for the year ended December 31, 2010, and its most recent quarterly report on Form 10-Q. Copies of these and other documents are available from Alnylam or Isis.

SOURCE Regulus Therapeutics Inc.

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