

Regulus, Alnylam, and Isis Announce First microRNA Patent Grant in Japan from Tuschl III Patent Series

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– Tuschl III Patent Exclusively Licensed from Max Planck –

CARLSBAD, Calif. & CAMBRIDGE, Mass.--(BUSINESS WIRE)--Sep. 17, 2009-- Regulus Therapeutics Inc., Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), and Isis Pharmaceuticals, Inc. (Nasdaq: ISIS), announced today that the Japan Patent Office (JPO) has notified the Max Planck Society of its intent to grant a patent from the Tuschl III patent series (JP Application Number 2003-532675). This patent series pertains to the discovery of over 120 novel mammalian microRNAs, including miR-122, which is a leading pre-clinical program at Regulus. The grant of this first Tuschl III patent in Japan extends the scope of this patent estate, which has already yielded patents in the U.S. (U.S. Patent No. 7,232,806) and in Australia (Australian Patent No. 2002 347 035).

The Tuschl III patent series stems from groundbreaking research (Lagos-Quintana *et al.*, (2001) *Science* 294, 853-858) performed by Alnylam founder and Regulus scientific advisory board member Dr. Thomas Tuschl, Associate Professor of RNA Molecular Biology at The Rockefeller University, while at the Max Planck Society. The Tuschl III patent series is exclusively held by Regulus for microRNA therapeutics through license agreements amongst Max Planck, Alnylam, and Isis.

“Regulus is advancing a whole new frontier of pharmaceutical research through the discovery of microRNA therapeutics, which have the potential to affect broad disease pathways as opposed to single gene targets,” said Kleanthis G. Xanthopoulos, Ph.D., President and Chief Executive Officer of Regulus Therapeutics. “Through our partnerships with Alnylam, Isis, and our relationships with leading academic institutions such as the Max Planck, we have built a dominant intellectual property estate for the development of microRNA therapeutics. This is first in the Tuschl III series to grant in Japan, and we expect more to come from this important and early patent series.”

“We are pleased with the continued recognition of the pioneering contributions of Professor Tuschl’s work performed at the Max Planck,” said Dr. Joern Erselius, Managing Director, Max Planck-Innovation GmbH. “The Tuschl III patent series describes an important set of discoveries for the advancement of microRNA therapeutics. With Regulus, we have an ideal partner for the development of this seminal research into a promising new approach for medicine.”

The newly granted claims of the Tuschl III patent cover miR-122, a liver-specific microRNA that has subsequently been shown to facilitate replication of hepatitis C virus (HCV) infection. The claims cover single-stranded and double-stranded antisense compounds complementary to miR-122, as well as precursors and analogs of miR-122.

Regulus is advancing microRNA therapeutics targeting miR-122, among others. Pre-clinical studies suggest that miR-122 is essential for the replication of HCV (Jopling *et al.* (2005) *Science* 309, 1577-81) and that creating an inhibitor to miR-122 may define a novel therapeutic strategy for the treatment of HCV infection.

About microRNAs

microRNAs are small, non-coding RNAs that regulate a large number of human genes; there are more than 700 microRNAs in the human genome that play a role in controlling expression of over one-third of all human genes. Abnormal expression and genetic mutation of microRNAs have been linked to numerous diseases including cancer, cardiovascular disease, metabolic disease, autoimmunity, and viral infection, among others. In 2005, Alnylam scientists and collaborators at The Rockefeller University were the first to describe antagomirs, which are part of a larger class of microRNA inhibitors known as anti-miRs (Krutzfeldt *et al.*, (2005) *Nature* 438, 685-689). Anti-miRs were created to selectively inhibit microRNAs expressed in a broad range of tissues and to have pharmacological properties required for microRNA-based therapeutics. This research has created new drug discovery strategies focused on antagonizing microRNAs.

About Regulus Therapeutics Inc.

Regulus Therapeutics Inc. is a biopharmaceutical company aiming to discover, develop, and commercialize microRNA-based therapeutics. Regulus aspires to translate one of the most important new discoveries in biology into a novel approach for innovative medicines and to build the leading microRNA company. Regulus was established by Alnylam Pharmaceuticals (Nasdaq: ALNY) and Isis Pharmaceuticals (Nasdaq: ISIS) in September of 2007, and benefits substantially from their RNA therapeutic drug discovery expertise, unique and established oligonucleotide-based technologies, and a broad and dominant intellectual property estate specific to microRNA-based therapeutics. Regulus’ patent estate includes over 600 patents and more than 300 pending patent applications pertaining primarily to chemical modifications of oligonucleotides targeting microRNA for therapeutic applications. In addition, through its numerous collaborations with academic researchers, Regulus continues to expand its knowledge on the biological role of therapeutically relevant microRNAs. In April 2008, Regulus formed a major alliance with GlaxoSmithKline to explore microRNA therapeutics for immuno-inflammatory diseases. Regulus is headquartered in Carlsbad, California. For more information, visit www.regulusrx.com.

About Alnylam Pharmaceuticals

Alnylam is a biopharmaceutical company developing novel therapeutics based on RNA interference, or RNAi. The company is applying its therapeutic expertise in RNAi to address significant medical needs, many of which cannot effectively be addressed with small molecules or antibodies, the current major classes of drugs. Alnylam is leading the translation of RNAi as a new class of innovative medicines with peer-reviewed research efforts published in the world’s top scientific journals including *Nature*, *Nature Medicine*, and *Cell*. The company is leveraging these capabilities to build a broad pipeline of RNAi therapeutics; its most advanced program is in Phase II human clinical trials for the treatment of respiratory syncytial virus (RSV) infection and is partnered with Cubist and Kyowa Hakko Kirin. In addition, the company is developing RNAi therapeutics for the treatment of a wide range of disease areas, including liver cancers, TTR amyloidosis, hypercholesterolemia, and Huntington’s disease. The company’s leadership position in fundamental patents, technology, and know-how relating to RNAi has enabled it to form major alliances with leading companies including Medtronic, Novartis, Biogen Idec, Roche, Takeda, Kyowa Hakko Kirin, and Cubist. To reflect its outlook for key scientific, clinical, and business initiatives, Alnylam established “RNAi 2010” in January 2008 which includes the company’s plan to significantly expand the scope of delivery solutions for RNAi therapeutics, have four or more programs in clinical development, and to form four or more new major business collaborations, all by the end of 2010.

Alnylam and Isis are joint owners of Regulus Therapeutics Inc., a company focused on the discovery, development, and commercialization of microRNA-based therapeutics. Founded in 2002, Alnylam maintains headquarters in Cambridge, Massachusetts. For more information, please visit www.alnylam.com.

About Isis Pharmaceuticals, Inc.

Isis is exploiting its expertise in RNA to discover and develop novel drugs for its product pipeline and for its partners. The Company has successfully commercialized the world's first antisense drug and has 19 drugs in development. Isis' drug development programs are focused on treating cardiovascular, metabolic and severe neurodegenerative diseases and cancer. Isis' partners are developing antisense drugs invented by Isis to treat a wide variety of diseases. Isis and Alnylam Pharmaceuticals are joint owners of Regulus Therapeutics Inc., a company focused on the discovery, development and commercialization of microRNA therapeutics. Isis also has made significant innovations beyond human therapeutics resulting in products that other companies, including Abbott, are commercializing. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of over 1,600 issued patents worldwide. Additional information about Isis is available at www.isispharm.com.

Forward-Looking Statements

This press release includes forward-looking statements regarding the future therapeutic and commercial potential of Regulus', Alnylam's, and Isis' business plans, technologies and intellectual property related to microRNA therapeutics being discovered and developed by Regulus. Any statement describing Regulus', Alnylam's, and Isis' goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as such parties' goals. 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 parties' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause their 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 the management of each such party, these statements are based only on facts and factors currently known by Regulus', Alnylam's, and Isis' as the case may be. 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, 2008, and their most recent quarterly reports on Form 10-Q which are on file with the SEC. Copies of these and other documents are available from Alnylam or Isis.

Source: Regulus Therapeutics Inc. and Alnylam Pharmaceuticals, Inc. and Isis Pharmaceuticals, Inc.

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