



Sanofi-Aventis and Regulus Therapeutics Form Major Strategic Alliance on microRNA Therapeutics

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- Largest microRNA therapeutics alliance to date, valued at potentially over \$750 million including a \$25 million upfront, a \$10 million future equity investment subject to mutual agreement on company valuation, and a three-year option worth \$50 million for a broader technology alliance -

- Focused on developing microRNA-based medicines toward four targets -

- Structured as multi-year collaboration intended to advance several investigational new drugs into clinical development -

CARLSBAD, Calif., Jun 22, 2010 (BUSINESS WIRE) --Regulus Therapeutics Inc. and sanofi-aventis (EURONEXT: SAN and NYSE: SNY) announced today that they have entered into a global, strategic alliance to discover, develop, and commercialize microRNA therapeutics. The alliance represents the largest microRNA partnership formed to date, valued at potentially over \$750 million, and includes a \$25 million upfront fee, a \$10 million future equity investment subject to mutual agreement on company valuation, and annual research support for three years with the option to extend two additional years. The alliance will initially focus on the therapeutic area of fibrosis. Regulus and sanofi-aventis will collaborate on up to four microRNA targets, including Regulus' lead fibrosis program targeting microRNA-21. sanofi-aventis also receives an option for a broader technology alliance that provides Regulus certain rights to participate in development and commercialization of resulting products. If exercised, this three-year option is worth an additional \$50 million to Regulus.

[microRNAs](#) are a new class of small non-coding RNAs that regulate gene expression by interfering with translation or stability of target messenger RNA transcripts. Endogenous microRNAs regulate the expression of over one-third of all human genes, and the association of microRNA dysfunction with disease phenotypes has given rise to an entirely new class of pharmaceutically relevant targets. In preclinical studies, Regulus has demonstrated that modulating microRNAs can effectively regulate disease pathways and produce therapeutically beneficial effects.

"This new partnership continues to illustrate sanofi-aventis' commitment to develop innovative therapies," declared Marc Cluzel, M.D., Ph.D., Executive Vice-President, Research & Development, sanofi-aventis. "microRNAs are believed to be extremely important in human development and physiology. Together with Regulus we will develop therapeutics which could potentially open a new paradigm in the treatment of major diseases and could offer an attractive new therapeutic approach for patients."

"Regulus is very pleased to form this landmark alliance with sanofi-aventis, a leading visionary company developing important new medicines," said Kleanthis Xanthopoulos, Ph.D., President and Chief Executive Officer of Regulus. "The significant support from sanofi-aventis in this new alliance will strengthen our efforts as we continue to build the leading microRNA therapeutics company through our commitment to scientific excellence and advancement of our pipeline of innovative new medicines. Indeed, this landmark alliance will significantly extend our capabilities and resources to lead the discovery and development of microRNA therapeutics."

Anlylam Pharmaceuticals (Nasdaq: ALNY) and Isis Pharmaceuticals (Nasdaq: ISIS) formed Regulus in 2007, with each company currently owning approximately 50% of the preferred stock.

About the Regulus and sanofi-aventis Collaboration

Regulus and sanofi-aventis have entered into a strategic alliance on microRNA therapeutics. The alliance is initially focused on the therapeutic area of fibrosis. Regulus has granted sanofi-aventis four worldwide, exclusive licenses to discover, develop, and commercialize microRNA therapeutics, including Regulus' leading fibrosis program targeting microRNA-21. Regulus receives from sanofi-aventis an upfront fee of \$25 million, a future equity investment of \$10 million subject to mutual agreement on company valuation, and annual research funding for three years with the option to extend for two additional one-year periods. Regulus also could receive preclinical milestones as well as development and sales milestones for collaboration targets. In addition, Regulus is eligible to receive royalties on microRNA therapeutic products commercialized by sanofi-aventis. sanofi-aventis will support 100% of the costs of clinical development and commercialization of each program. In addition, Regulus has granted sanofi-aventis an option to enter into a technology alliance worth up to \$50 million that could provide sanofi-aventis with access to Regulus' microRNA platform and a limited number of product licenses. Assuming exercise of the technology alliance option, Regulus has certain opt-in rights to participate in the development and commercialization of future sanofi-aventis clinical microRNA programs. In addition, Regulus is eligible to receive milestone payments and royalties on microRNA therapeutic products developed and commercialized under the technology alliance option.

The alliance is valued at potentially over \$750 million in consideration of upfront payments, equity investment, research funding,

and potential preclinical, clinical and commercial milestone payments for multiple products if all products are successfully commercialized. Regulus will pay approximately \$4 million of the initial funding to its licensors, the majority of which will be to Isis and Alnylam. Isis and Alnylam could also receive additional payments based on future success-based milestone payments earned during the alliance.

About microRNAs

The discovery of [microRNA](#) in humans is one of the most exciting scientific breakthroughs in the last decade. microRNAs are small RNA molecules, typically 20 to 25 nucleotides in length that do not encode proteins but instead regulate gene expression. Nearly 700 microRNAs have been identified in the human genome, and more than one-third of all human genes are believed to be regulated by microRNAs. As a single microRNA can regulate entire networks of genes, these new molecules are considered the master regulators of the 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 the possibility of a novel class of therapeutics and 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 new medicines based on microRNAs. Regulus is targeting microRNAs as a new class of therapeutics by working with a broad network of academic collaborators and leveraging oligonucleotide drug discovery and development expertise from its founding companies Alnylam Pharmaceuticals (*Nasdaq:ALNY*) and Isis Pharmaceuticals (*Nasdaq:ISIS*). Regulus is advancing microRNA therapeutics towards the clinic in several areas including hepatitis C infection, cardiovascular disease, fibrosis, oncology, immuno-inflammatory diseases, and metabolic diseases. 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 2008, Regulus entered into a major alliance with GlaxoSmithKline to discover and develop microRNA therapeutics for immuno-inflammatory diseases. In 2010, Regulus entered into a new collaboration with GlaxoSmithKline to develop and commercialize microRNA therapeutics targeting microRNA-122 for the treatment of Hepatitis C Viral infection. For more information, visit <http://www.regulusrx.com>.

About sanofi-aventis

Sanofi-aventis, a leading global pharmaceutical company, discovers, develops and distributes therapeutic solutions to improve the lives of everyone. Sanofi-aventis is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY). For more information, please visit: www.sanofi-aventis.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 for the treatment of a wide range of disease areas, including respiratory syncytial virus (RSV), liver cancers, TTR-mediated amyloidosis (ATTR), hypercholesterolemia, and Huntington's disease. In addition, Alnylam formed Alnylam Biotherapeutics, a division of the company focused on the development of RNAi technologies for application in manufacturing processes for biotherapeutic products, including recombinant proteins and monoclonal antibodies. 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. 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 IsisPharmaceuticals, 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 22 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 Isis', Alnylam's and Regulus' business plans, technologies and intellectual property related to microRNA therapeutics being discovered and developed by Regulus, including statements regarding expectations around the newly formed alliance between Regulus and sanofi-aventis, the therapeutic potential of targeting microRNA-21 and the potential for future payments to Isis and Alnylam under this alliance. Any statement describing Isis', Alnylam's or 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 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 Isis, Alnylam or Regulus, 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', Isis', and Alnylam's programs are described in additional detail in each of Isis' and Alnylam's annual report on Form 10-K for the year ended December 31, 2009 and their most recent quarterly report on Form 10-Q, which are on file with the SEC. Copies of these and other documents are available from either Isis or Alnylam.



SOURCE: Regulus Therapeutics Inc.

Regulus Therapeutics

Zachary Zimmerman, Ph.D., 760-268-6811

busdev@regulus.com

or

Russo Partners

Heidi Chokeir (Media), Ph.D., 619-528-2217