

Regulus Therapeutics Appoints Kleanthis G. Xanthopoulos, Ph.D. as President and Chief Executive Officer

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CAMBRIDGE, Mass. & CARLSBAD, Calif., Dec 03, 2007 (BUSINESS WIRE) -- Regulus Therapeutics LLC, a joint venture between Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY) and Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) formed to discover, develop and commercialize microRNA therapeutics, announced today the appointment of Kleanthis G. Xanthopoulos, Ph.D., as President and Chief Executive Officer. Dr. Xanthopoulos is the co-founder and former President and Chief Executive Officer of Anadys Pharmaceuticals, Inc.

"Kleanthis has had a distinguished and broadly recognized career as a leader in the life sciences industry," said John Maraganore, Ph.D., Chairman of Regulus, and President and Chief Executive Officer of Alnylam. "We expect his experience in building organizations from research to development stages will be instrumental as we build a leading company focused on advancing microRNA therapeutics."

"We are delighted that Kleanthis has joined Regulus," said Stanley Croke, M.D., Ph.D., Chairman and Chief Executive Officer of Isis. "He has the right combination of entrepreneurial spirit and scientific knowledge balanced with business expertise, to advance the efforts already underway at Regulus."

"MicroRNAs are an exciting new area of biology, and microRNA therapeutics represent a previously unexplored area of pharmaceuticals research that could lead to the emergence of novel high-impact drugs," said Kleanthis G. Xanthopoulos, Ph.D., President and Chief Executive Officer of Regulus. "Indeed, due to their mechanism of action, we believe microRNA therapeutics could have important implications for the treatment of a broad range of diseases including cancer, viral infection, and metabolic disorders. I am very excited to be joining Regulus at this time, as Isis and Alnylam have established a solid foundation of scientific and intellectual property leadership comprising an estate of more than 500 patents and decades of RNA-based research and development on which to build this leading biopharmaceutical company."

Before joining Regulus, Dr. Xanthopoulos was a managing director of Enterprise Partners Venture Capital. Prior to that, he was a co-founder and served as President and Chief Executive Officer and Director of Anadys Pharmaceuticals from its inception in May 2000 to November 2006. From 1997 to 2000 he held a variety of positions at Aurora Biosciences Corporation (now Vertex Pharmaceuticals Incorporated) including Vice President, Genomics & Molecular Biology. Dr. Xanthopoulos participated in The National Institutes of Health (NIH) Human Genome Project and was a Section Head of the National Human Genome Research Institute at NIH from 1995 to 1997. He was an Associate Professor of Molecular Biology at the Karolinska Nobel Medical Institute, Stockholm, Sweden from 1991 to 1995, and a Postdoctoral Research Fellow at The Rockefeller University from 1987 to 1990. An Onassis scholar, Dr. Xanthopoulos received his B.Sc. in Biology with honors from Aristotle University of Thessaloniki, Greece, and received both his M.Sc. in Microbiology and Ph.D. in Molecular Biology from the University of Stockholm, Sweden.

Dr. Xanthopoulos is a member of the board of directors of Anadys Pharmaceuticals, Odyssey Thera, Inc., and an executive board member of BIOCUM, Southern California's life science industry association, where he chairs the Capital Formation Committee.

About microRNAs

microRNAs are a recently discovered class of genetically encoded small RNAs, approximately 20 nucleotides in length, and are believed to regulate the expression of a large number of human genes. microRNA therapeutics represent a new approach for the treatment of a wide range of human diseases. The inappropriate absence or presence of specific microRNAs in various cells has been shown to be associated with specific human diseases including cancer, viral infection, and metabolic disorders. Targeting microRNAs with novel therapeutic agents could result in novel and broadly acting treatments for human diseases.

About Regulus

Regulus Therapeutics LLC is a biopharmaceutical company formed to discover, develop and commercialize microRNA therapeutics. The company was created as a joint venture between Alnylam Pharmaceuticals, a leader in RNAi therapeutics, and Isis Pharmaceuticals, a leader in antisense technologies and therapeutics. Isis and Alnylam scientists and collaborators were the first to discover microRNA antagonist strategies that work in vivo in animal studies (Krutzfeldt et al. *Nature* 438, 685-689 (2005); Esau et al. *Cell Metab.*, 3, 87-98 (2006)). Isis and Alnylam have also created and consolidated key intellectual property for the development and commercialization of microRNA therapeutics. The company, founded in 2007, maintains facilities 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. In addition, the company is developing RNAi therapeutics for the treatment of influenza, hypercholesterolemia, and liver cancers, among other diseases. 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, and Roche. The company, founded in 2002, maintains headquarters in Cambridge, Massachusetts. For more information, 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 18 drugs in development. Isis' drug development programs are focused on treating cardiovascular and metabolic diseases. Isis' partners are developing antisense drugs invented by Isis to treat a wide variety of diseases. Isis' wholly owned subsidiary, Isis' wholly owned subsidiary, is developing and commercializing the Ibis T5000(TM) Biosensor System, a revolutionary system to identify infectious organisms. Isis is a joint owner of Regulus Therapeutics LLC, a joint venture focused on the discovery, development and commercialization of microRNA therapeutics. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee

of over 1,500 issued patents worldwide. Additional information about Isis is available at www.isispharm.com.

Alnylam Forward-Looking Statements

Various statements in this release concerning Alnylam's future expectations, plans and prospects, including statements concerning the potential of microRNA therapeutics and the importance of Alnylam's intellectual property, know-how, and other technology in the discovery, development and commercialization of microRNA therapeutics, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including risks related to: Alnylam's approach to discover and develop novel drugs, which is unproven and may never lead to marketable products; obtaining, maintaining and protecting intellectual property; Alnylam's ability to enforce its patents against infringers and to defend its patent portfolio against challenges from third parties; Alnylam's ability to obtain additional funding to support its business activities; Alnylam's dependence on third parties for development, manufacture, marketing, sales and distribution of products; obtaining regulatory approval for products; competition from others using technology similar to Alnylam's and others developing products for similar uses; Alnylam's dependence on collaborators; and Alnylam's short operating history; as well as those risks more fully discussed in the "Risk Factors" section of its most recent quarterly report on Form 10-Q on file with the Securities and Exchange Commission. In addition, any forward-looking statements represent Alnylam's views only as of today and should not be relied upon as representing its views as of any subsequent date. Alnylam does not assume any obligation to update any forward-looking statements.

Isis Forward Looking Statements

This press release includes forward-looking statements regarding the future therapeutic and commercial potential of Isis' technologies and intellectual property related to microRNA therapeutics being discovered and developed by Regulus. Any statement describing 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 Isis' 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. Isis' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Isis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Isis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' programs are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2006, and its quarterly report on Form 10-Q for the quarter ended September 30, 2007, which are on file with the SEC. Copies of these and other documents are available from the Company.

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SOURCE: Regulus Therapeutics LLC

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