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## Regulus Therapeutics Selected for Fierce 15 Top Biotech Companies

**CAMBRIDGE, Mass. and CARLSBAD, Calif., June 24, 2008** – 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 (miRNA) therapeutics, announced today that it has been named to the annual FierceBiotech “Fierce 15” list, designating it as one of the top privately held biotech companies of 2008. “Spawned by two powerhouses in the RNA-targeted therapeutics field – Isis and Alnylam Pharmaceuticals – Regulus got started at an advanced stage in the microRNA field,” said John Carroll, Editor of FierceBiotech. “The company was quick to capitalize on its hefty IP with an up to \$600 million pact with GlaxoSmithKline. Anyone tracking microRNA drug development should pay close attention.” “Regulus is honored to be recognized by FierceBiotech as a ‘Fierce 15’ chosen from among so many innovative companies in our industry,” said Kleanthis G. Xanthopoulos, Ph.D., President and Chief Executive Officer of Regulus. “With our broad and dominant intellectual property position, expertise in microRNAs, world-class Scientific Advisory Board and the support of Isis and Alnylam, we are positioned to quickly translate the therapeutic potential of microRNAs into new treatment options for many diseases, including oncology, viral infections and inflammatory diseases.”

### About “Fierce 15”

The editors of FierceBiotech evaluate hundreds of privately held firms based on company vision, revenue potential, quality of deals, strength of technology, partnerships, and competitive market position each year. The Fierce 15 celebrates the spirit of being “fierce” – championing innovation and creativity, even in the face of intense competition. Regulus Therapeutics was determined to be one of the “fiercest,” proven by the Company’s creativity and innovations in the industry.

### About miRNAs

miRNAs 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. miRNA therapeutics represent a new approach for the treatment of a wide range of human diseases. The inappropriate absence or presence of specific miRNAs in various cells has been shown to be associated with specific human diseases including cancer, viral infection, metabolic disorders and inflammatory disease. Targeting miRNAs 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 miRNA therapeutics. Regulus aspires to translate one of the most important new discoveries in biology into a novel new approach for innovative medicine and to build the leading miRNA company. Created as a joint venture by Alnylam Pharmaceuticals and Isis Pharmaceuticals, Regulus benefits from oligonucleotide drug discovery expertise, an established technology, and a broad intellectual property estate created and consolidated by its parent companies for the development and commercialization of miRNA therapeutics. Regulus’ patent estate includes over 600 patents and more than 300 pending patent applications, pertaining primarily to chemical modifications of oligonucleotides targeting miRNA for therapeutic applications. In addition, Regulus has collaborations with academic researchers to build on the company’s understanding of more than 60 miRNAs. In April 2008, Regulus formed a major alliance with GlaxoSmithKline to explore miRNA therapeutics for inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease. Regulus, founded in September 2007, maintains facilities in Carlsbad, California. For more information, visit [www.regulusrx.com](http://www.regulusrx.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. Ibis Biosciences, Inc., Isis’ majority-owned subsidiary, is developing and commercializing the Ibis T5000™ 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](http://www.isispharm.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 a wide range of disease areas, including hypercholesterolemia, liver cancers, 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, and Kyowa Hakko Kogyo. To reflect its outlook for key scientific, clinical, and business initiatives, Alnylam has established "*RNAi 2010*" 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 is a joint owner of Regulus Therapeutics LLC, a joint venture focused on the discovery, development, and commercialization of microRNA therapeutics. Founded in 2002, Alnylam maintains headquarters in Cambridge, Massachusetts. For more information, visit [www.alnylam.com](http://www.alnylam.com).

## **Forward-Looking Statement**

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. 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, 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 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 Isis', Alnylam's and Regulus' programs are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2007, and its quarterly report on Form 10-Q for the quarter ended March 31, 2008 and in Alnylam's annual report on Form 10-K for the year ended December 31, 2007, and its quarterly report on Form 10-Q for the quarter ended March 31, 2008, which are on file with the SEC. Copies of these and other documents are available from Isis or Alnylam.