

## **Regulus Therapeutics Forms Strategic Alliance for Discovery, Development and Commercialization of microRNA Therapeutics with AstraZeneca**

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### **Focused on three exclusive microRNA targets**

LA JOLLA, Calif., Aug. 14, 2012 /PRNewswire/ -- Regulus Therapeutics Inc., a biopharmaceutical company leading the discovery and development of innovative medicines targeting microRNAs, announced today that it has entered into a strategic alliance with AstraZeneca to discover, develop, and commercialize microRNA therapeutics for three exclusive targets which are currently in pre-clinical development. These targets are focused on cardiovascular and metabolic diseases and oncology.

Under the terms of the agreement, AstraZeneca will make a \$28M payment which includes an equity investment and an upfront payment to Regulus.

Regulus and AstraZeneca will collaborate on three microRNA targets, which include Regulus' lead cardiovascular/metabolic disease program targeting microRNA-33 for the treatment of atherosclerosis.

Regulus will lead preclinical development and, if successful, could receive pre-clinical milestone payments. AstraZeneca will lead and fund the clinical development and commercialization of these programs.

In addition, Regulus could also receive clinical milestones based on the successful development of microRNA therapies in each target area. Regulus is also eligible to receive significant launch and commercial milestone payments and royalties contingent on the successful commercialization of microRNA therapeutic products by AstraZeneca.

Gunnar Olsson, Vice President and Head of AstraZeneca's Cardiovascular & Gastrointestinal Innovative Medicines Unit, said: "MicroRNA therapeutics have the potential to open up innovative and important treatment options for patients and AstraZeneca is pleased to collaborate with Regulus in this new and exciting area. Through this collaboration we will marry Regulus' expertise in the microRNA field with our own internal drug development experience with the goal of bringing new treatment options to patients with atherosclerosis-related disease, metabolic disturbances, cancer and potentially other therapeutic areas of interest to AstraZeneca."

"Regulus is pleased to form another significant strategic alliance on microRNA therapeutics," said Kleantlis G. Xanthopoulos, Ph.D., President and Chief Executive Officer of Regulus Therapeutics Inc. "AstraZeneca is a global, innovation-driven company that we believe can greatly aid our efforts to advance microRNA therapeutics to the clinic and the market. The entire field of RNA therapeutics has been rapidly advancing, reaching significant milestones recently. We are committed to realize the broad utility of these new RNA-based medicines to treat human disease in the future. "

Neil W. Gibson, Ph.D., Chief Scientific Officer of Regulus Therapeutics Inc., added, "We wanted to partner our microRNA-33 program with AstraZeneca due to their excellent track record on developing and commercializing drugs in cardiovascular and metabolic diseases and their commitment to the RNA therapeutic field. We look forward to growing our strategic relationship with AstraZeneca with additional targets to develop important first-in-class medicines."

#### **About microRNA-33 for Atherosclerosis**

Atherosclerosis is the build-up of plaque that occurs when cholesterol and inflammatory cells accumulate in blood vessels. These plaques can rupture, leading to slowing or blockage of blood flow and ultimately resulting in a heart attack or stroke. Scientific research has shown a strong correlation between high cholesterol levels and cardiovascular disease which, according to the Centers for Disease Control, is the leading cause of death in the United States.

Regulus' lead program for atherosclerosis targets microRNA-33, which has a unique mechanism of action for the management of cholesterol levels. The inhibition of microRNA-33 with our anti-miRs promotes reverse cholesterol transport, or RCT, which is the efflux of cholesterol from specific cholesterol-laden inflammatory cells called macrophages in atherosclerotic plaques. Treatment with anti-microRNA-33 in an atherosclerotic mouse model led to reduction in arterial plaque size by 35% (Rayner et al., *J Clin Invest.* 2011) and treatment in non-human primates increased circulating levels of HDL-C by 50%. By enhancing

RCT, anti-miR-33 differs from other emerging therapeutic strategies that focus only on raising HDL-C in circulation.

## **About microRNAs**

The discovery of [microRNAs](#) 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 500 microRNAs have been identified in the human genome, and over one-third of all human genes are believed to be regulated by microRNAs. microRNA expression, or function, has been shown to be significantly altered or dysregulated in many disease states, including oncology, fibrosis and metabolic diseases. In preclinical studies, Regulus has demonstrated that modulating microRNAs can effectively regulate disease pathways and produce therapeutically beneficial effects.

## **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. 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 oncology, fibrosis, hepatitis C and metabolic diseases. Regulus has formed strategic alliances with AstraZeneca, GlaxoSmithKline and Sanofi.

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](http://www.twitter.com/regulusrx).

## **About AstraZeneca**

AstraZeneca is a global, innovation-driven biopharmaceutical business with a primary focus on the discovery, development and commercialization of prescription medicines for gastrointestinal, cardiovascular, neuroscience, respiratory and inflammation, oncology and infectious disease. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information please visit: [www.astrazeneca.com](http://www.astrazeneca.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 relationship between Regulus and AstraZeneca. 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 drugs. 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', 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, 2011 and its most recent quarterly report 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.