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Tiny LNA-based compounds inhibit entire disease-associated microRNA families

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A study published online in this week's *Nature Genetics* demonstrates that tiny Locked Nucleic Acid (LNA)-based compounds developed by Santaris Pharma A/S can inhibit entire disease-associated microRNA families. This provides a potential new approach for treating a variety of diseases including cancer, viral infections, cardiovascular and muscle diseases.

Santaris Pharma A/S, a clinical-stage biopharmaceutical company focused on the research and development of mRNA and microRNA targeted therapies, developed the tiny LNA-based compounds, which are 8-mer LNA oligonucleotides, using its proprietary LNA Drug Platform. The high affinity and target specificity of tiny LNA-based compounds enabled functional inhibition of both single microRNAs and entire microRNA families in a range of tissues in vivo without off-target effects.

MicroRNAs have emerged as an important class of small regulatory RNAs encoded in the genome. They act to control the expression of sets of genes and entire pathways and are thus thought of as master regulators of gene expression associated with many diseases. Because they dictate the expression of fundamental regulatory pathways, microRNAs represent potential drug targets in the treatment of many disease processes.

"Using tiny LNA-based compounds to successfully inhibit entire disease-associated microRNA families provides a new range of opportunities to

develop novel microRNA-targeted drugs for both in-house drug discovery programs, as well as with our partners," said Henrik Ørum, Ph.D., Vice President and Chief Scientific Officer of Santaris Pharma A/S. "The versatility of our proprietary LNA Drug Platform has the potential to develop new modalities to target a broad range of diseases, including cardiometabolic disorders, infectious and inflammatory diseases, and cancer by targeting microRNAs, entire microRNA families or messengerRNAs."

The study published in Nature Genetics was carried out by Santaris Pharma A/S scientists and collaborators at Cold Spring Harbor Laboratory, New York. In this study, scientists demonstrated that tiny LNA-based compounds inhibited both single microRNAs and entire microRNA families in cultured cells, as well as in vivo in several mice tissues and in a mouse breast tumor model. The tiny LNA-based compounds were well tolerated by the mice and could be delivered without the use of complex delivery vehicles.

The Santaris Pharma A/S LNA Drug Platform is the only RNA technology with both mRNA and microRNA targeted drugs in clinical trials, demonstrating the broad utility of the proprietary platform. In September 2010, Santaris Pharma A/S successfully advanced miravirsen, a lead microRNA drug candidate targeting miR-122, into Phase 2 studies for the treatment of patients infected with the Hepatitis C virus. In addition, Santaris Pharma A/S is advancing two mRNA-targeted drugs, SPC5001 targeting PCSK9 and SPC4955 targeting apoB, for the treatment of high cholesterol into Phase 1 in the first half of 2011.

Santaris Pharma A/S also has a robust product pipeline with its partners consisting of mRNA and microRNA drug discovery and development collaborations. These include partnerships with Pfizer, Inc. (delivery of lead candidates against up to 20 targets), miRagen Therapeutics (cardiovascular diseases), Shire plc (rare genetic disorders),

GlaxoSmithKline (four viral disease drug candidates) and Enzon Pharmaceuticals (eight cancer targets successfully delivered – three are now in Phase 1 clinical studies).

More information: Obad, dos Santos, Petri, Heidenblad, Broom, Ruse, Fu, Lindow, Stenvang, Straarup, Hansen, Koch, Pappin, Hannon and Kauppinen. 2011. Silencing of microRNA families by seed-targeting tiny LNAs. *Nature Genetics* DOI:10.1038/ng.786

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