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Research Published in the New England Journal of Medicine Demonstrates Marked and Long-Lasting Antiviral Activity Against HCV for Santaris Pharma A/S' Miravirsen, the First MicroRNA-Targeted Drug to Enter Clinical Trials

-- Final Phase 2a results show dose-dependent, prolonged antiviral activity in Hepatitis C patients --

Hørsholm, Denmark/San Diego, California, March 27, 2013 — Santaris Pharma A/S, a clinical-stage biopharmaceutical company focused on the discovery and development of RNA-targeted therapies, today announced the publication of study results online in the *New England Journal of Medicine* (NEJM). The publication highlights the potential benefits of miravirsen, a host-targeted, pan-HCV genotype anti-viral agent and the first microRNA-targeted drug to enter clinical trials for the treatment of Hepatitis C virus (HCV). In the study, miravirsen, given as a four-week monotherapy treatment, provided robust dose-dependent antiviral activity with a mean reduction of 2 to 3 logs from baseline in HCV RNA (log10 IU/mL). The effect was sustained well beyond the end of therapy.

Clinical data from the Phase 2a study demonstrated the following:

- Miravirsen was safe, well tolerated and provided prolonged antiviral activity well after the last dose of miravirsen monotherapy (x5 weekly injections)
- There were no signs of viral resistance
- Adverse events were infrequent, mild and did not lead to study drug discontinuation
- There were no dose limiting toxicities or discontinuations due to adverse events
- Miravirsen was associated with dose-dependent reductions in HCV RNA that were sustained well beyond the end of the four-week dosing period
- Four out of nine patients treated at the highest dose (7 mg/kg) with miravirsen became HCV RNA undetectable with just five weekly doses of miravirsen monotherapy

"We are excited because the data show that miravirsen offers long-lasting suppression of HCV RNA, a high barrier to viral resistance, a favorable tolerability and dosing profile, a low propensity for drug interactions and a very long duration of action. All of these properties suggest that miravirsen's unique mechanism-of-action may offer a potential cure for Hepatitis C patients, either in combination with other antiviral agents or as a monotherapy" said Harry Janssen, M.D., Head of the Liver Clinic at Toronto Western and Toronto General Hospital and lead author of the NEJM publication. "Due to its ability to target the host factor miR-122, miravirsen has the potential to change the way Hepatitis C is treated. This study is also the first to prove that blocking microRNA can be effective in treating Hepatitis C in humans without limiting side effects. This trial is a landmark study for new therapeutic modalities in many other diseases where microRNA's play a role, such as in cardiovascular disease, cancer and metabolic disorders."

Developed using Santaris Pharma A/S proprietary Locked Nucleic Acid (LNA) Drug Platform, miravirsen is an inhibitor of miR-122, a liver specific microRNA that the Hepatitis C virus requires for replication. Miravirsen is designed to recognize and sequester miR-122, making it unavailable to the Hepatitis C virus. As a result, the replication of the virus is effectively inhibited and the level of Hepatitis C virus is profoundly reduced.

"This is a seminal moment for the microRNA community as miravirsen is the first microRNA targeted drug to show efficacy in clinical trials, and we are honoured that such a prestigious journal as the *New England Journal of Medicine* has published this work," said Henrik Stage, Chief Executive Officer at Santaris Pharma A/S. "It's amazing to think that the journey from bench to bedside has occurred over

such a short span of time. Recall that human microRNAs were only discovered in 2001, and miR-122's role in the HCV lifecycle determined in 2005. Based on the published results, microRNA targeted therapy has shown its potential to become a new important class of drugs, and the LNA platform has demonstrated its role as the chemistry of choice for RNA targeted therapies."

The randomized, double-blind, placebo-controlled, ascending multiple-dose Phase 2a study assessed the safety and tolerability of miravirsen in treatment-naïve patients with chronic HCV genotype 1 infection. Patients were enrolled sequentially to one of three cohorts (9 active: 3 placebo per cohort) at doses of 3, 5 and 7 mg/kg. Miravirsen was given as a total of 5 weekly subcutaneous injections over 29 days.

"These study results are the culmination of over 6 years of microRNA research at Santaris Pharma A/S," said Michael R. Hodges, MD, Vice President and Chief Medical Officer at Santaris Pharma A/S. "The results of this study highlight miravirsen's exceptional *high barrier to resistance*, long duration of action and good tolerability. Miravirsen would be especially suitable for treatment of hard-to-treat patients, for example those patients who have already failed treatment with pegylated-interferon and ribavirin combination or protease inhibitor triple therapy." Dr. Hodges continued, "Longer treatment durations of miravirsen are currently being tested in clinical trials in subjects who have failed initial therapy for HCV infection."

About Hepatitis C

Hepatitis C infection is a viral disease caused by the Hepatitis C virus that leads to inflammation of the liver. The World Health Organization estimates that approximately 3 percent of the world's population have been infected with HCV and that some 170 million have chronic hepatitis C and are at risk of developing liver cirrhosis and/or liver cancer[i]. Approximately 3-4 million Americans are chronically infected with an estimated 40,000 new infections per year[ii]. In Europe, there are about 4 million carriers[i]. The current standard of care treatment for genotype 1 is a protease inhibitor given with pegylated-interferon α and ribavirin. This triple combination is effective in about 70-80% of those treated[ii]. Patients that are not effectively treated have an increased risk for the progression of liver disease. By 2029, total annual medical costs in the United States for people with Hepatitis C are expected to more than double, from $30 billion in 2009 to approximately $85 billion[iii].

About microRNAs

MicroRNAs have emerged as an important class of small 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. Recent studies have demonstrated that microRNAs are associated with many disease processes. Because they are single molecular entities that dictate the expression of fundamental regulatory pathways, microRNAs represent potential drug targets for controlling many biologic and disease processes.

About Locked Nucleic Acid (LNA) Drug Platform

The LNA Drug Platform and Drug Discovery Engine developed by Santaris Pharma A/S combines the company's proprietary LNA chemistry with its highly specialized and targeted drug development capabilities to rapidly deliver LNA-based drug candidates against RNA targets, both mRNA and microRNA, for a range of diseases including cardiometabolic disorders, infectious and inflammatory diseases, cancer and rare genetic disorders. LNA-based drugs are a promising new class of therapeutics that are enabling scientists to develop drug candidates to work through previously inaccessible clinical pathways. The LNA Drug Platform overcomes the limitations of earlier antisense and siRNA technologies to deliver potent single-stranded LNA-based drug candidates across a multitude of disease states. The unique

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combination of small size and very high affinity allows this new class of drugs candidates to potently and specifically inhibit RNA targets in many different tissues without the need for complex delivery vehicles. The most important features of LNA-based drugs include excellent specificity providing optimal targeting; increased affinity to targets providing improved potency; and favorable pharmacokinetic and tissue-penetrating properties that allow systemic delivery of these drugs without complex and potentially troublesome delivery vehicles.

About Santaris Pharma A/S

Santaris Pharma A/S is a privately held clinical-stage biopharmaceutical company focused on the discovery and development of RNA-targeted therapies. The Locked Nucleic Acid (LNA) Drug Platform and Drug Discovery Engine developed by Santaris Pharma A/S combine the company's proprietary LNA chemistry with its highly specialized and targeted drug development capabilities to rapidly deliver potent single-stranded LNA-based drug candidates across a multitude of disease states. The company's research and development activities focus on infectious diseases and cardiometabolic disorders, while partnerships with major pharmaceutical companies include a range of therapeutic areas including cancer, cardiovascular disease, infectious and inflammatory diseases, and rare genetic disorders. The company has strategic partnerships with miRagen Therapeutics, Shire plc., Pfizer, GlaxoSmithKline, and Enzon Pharmaceuticals. As part of its broad patent estate, the company holds exclusive worldwide rights to manufacture and sell products that comprise LNA as active ingredient for studies performed with a view to obtaining marketing approval. Santaris Pharma A/S, founded in 2003, is headquartered in Denmark with operations in the United States. Please visit www.santaris.com for more information.

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[ii] Jacobson IM. Telaprevir for previously untreated chronic hepatitis C virus infection. NEJM 2011;364:2405-16
[iii] Institute of Medicine of the National Academies. Hepatitis and liver cancer: a national strategy for prevention and control of hepatitis B and C. Colvin HM and Mitchell AE, ed. Available at: http://www.iom.edu/Reports/2010/Hepatitis-and-Liver-Cancer-A-National-Strategy-for-Prevention-and-Control-of-Hepatitis-B-and-C.aspx.