**Santaris Pharma A/S Completes Enrollment in Phase 2 Clinical Trial of Miravirsen In Null Responders to Pegylated Interferon and Ribavirin for the Treatment of the Hepatitis C Virus**

-- Enrollment also begins in study investigating miravirsen in combination with telaprevir and ribavirin in null responders to pegylated interferon and ribavirin --

**Hørsholm, Denmark/San Diego, California, August 27, 2013** — Santaris Pharma A/S, a clinical-stage biopharmaceutical company focused on the discovery and development of RNA-targeted therapies, today announced the completion of enrollment of its Phase 2 miravirsen 12-week monotherapy study of miravirsen, a host-targeted, pan-HCV genotype antiviral agent, in subjects who were "null responders" to pegylated interferon alpha and ribavirin (peg-IFNα/RBV). The company also announced the enrollment of the first patient into another Phase 2 study of miravirsen in combination with telaprevir and ribavirin, also in null responders to peg-IFNα/RBV.

"The current standard of treatment for HCV is a combination of a direct acting-antiviral agent protease inhibitor with pegylated-interferon plus ribavirin. However, there remains a pressing need for therapeutic regimens that can attain high sustained virologic responses without peg-IFNα/RBV, which is poorly tolerated, and without drug-drug interactions. Miravirsen's unique mode-of-action has shown potential in providing antiviral activity in patients who have failed previous treatment regimens for the hepatitis C virus," said Maribel Rodriguez-Torres, M.D., president of Fundacion de Investigacion and the study's Principal Investigator. "We are excited to have completed enrollment and look forward to following the enrolled patients and reporting the data from this study. So far, the emerging viral load data suggest that miravirsen might be a unique treatment option, in combination with other antivirals, for the treatment of this type of difficult to treat patients."

The Phase 2, open-label study assesses the safety, antiviral activity and pharmacokinetics of miravirsen monotherapy over a total of 12 weeks of treatment. Patients enrolled in the study were chronically infected with HCV genotype 1 and had previously failed treatment with peg-IFNα/RBV therapy. Miravirsen was given as a total of five doses over five weeks, followed by a further four doses once every other week over seven weeks.

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 levels of HCV RNA are profoundly reduced.

Santaris Pharma A/S has also enrolled its first patient into another Phase 2 clinical trial that will assess the safety, tolerability and antiviral activity of miravirsen given for 12 weeks in combination with telaprevir (TVR) and ribavirin (RBV) in patients with HCV infection who are non-responders to peg-IFNα/RBV.

"We are pleased to report on the progress in the miravirsen clinical program," said Michael R. Hodges, MD, Vice President and Chief Medical Officer at Santaris Pharma A/S. "We hope that data from these two 12-week studies in the hard to treat patients will confirm the earlier promising efficacy and safety data from the four-week monotherapy study in treatment naïve patients that was recently published in the New England Journal of Medicine. We continue to believe that miravirsen given in combination with direct acting-antiviral agent(s) has the potential to cure chronic HCV infection in hard-to-treat patients."

The first series of non-clinical and clinical studies demonstrated the following key attributes for miravirsen:

- Miravirsen has a novel mechanism of action, inhibits a well conserved hepatic host target thus has an high barrier to resistance with predicted activity against all HCV genotypes, is not metabolized by cytochrome P450 enzymes therefore drug interactions are unlikely
- In *in vitro* studies, miravirsen was active against all six HCV genotypes, additive activity to direct acting antiviral agents (DAAs), active against DAA resistant virus and a showed a high barrier to resistance
- In clinical trials with four weeks of monotherapy, miravirsen was well tolerated, showed dose dependent antiviral activity that can be maintained weeks after the end of therapy
- In two separate drug-drug interaction clinical trials, miravirsen showed no interactions with peg-IFNα/RBV or with telaprevir

## 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]. Even though in Europe and the United States genotype 1 is the most prevalent, there are 50-70 million people worldwide that are infected with a non-genotype 1 virus. In these patients, the combination of pegylated-interferon α and ribavirin remains the currently approved standard of care treatment[iii]. 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[iv].

## 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 is also sometimes referred to as BNA (Bicyclic or Bridged Nucleic Acid). LNA-based drugs are a promising new class of therapeutics that enable scientists to develop drugs that 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 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 address a range of therapeutic areas including cancer, cardiovascular disease, infectious and inflammatory diseases, and rare genetic disorders. The company has strategic partnerships with RaNA Therapeutics, Bristol-Myers Squibb, miRagen Therapeutics, Shire, 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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