

## **Santaris Pharma A/S Phase 2a data of miravirsen shows dose-dependent, prolonged viral reduction of 2-3 logs HCV RNA after four-week treatment in Hepatitis C patients**

- New Phase 2a clinical data to be presented in late-breaking oral presentation at AASLD –
- *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 Hepatitis C Virus (HCV) RNA (log<sub>10</sub> IU/mL) that was maintained for more than four weeks beyond the end of therapy*
- *Four out of nine patients treated at the highest dose with miravirsen became HCV RNA undetectable during the study, providing clinical evidence that miravirsen's unique mechanism-of-action offers high barrier to viral resistance and the potential for treatment cures with monotherapy*
- *Miravirsen, the first microRNA-targeted drug to enter clinical trials, works by inhibiting miR-122, a microRNA required for HCV accumulation, was well tolerated in patients with chronic HCV infection*
- *Miravirsen's long-lasting suppression of HCV RNA, high barrier to viral resistance, low propensity for drug interactions and favorable tolerability profile holds promise as pivotal new treatment option given as monotherapy or in combination with direct acting antiviral agents as an interferon-free treatment to eradicate chronic HCV infection in multiple genotypes*

**Hoersholm, Denmark/San Diego, California, November 5, 2011** – Santaris Pharma A/S, a clinical-stage biopharmaceutical company focused on the discovery and development of RNA-targeted therapies, presents new data from the Phase 2a trial showing that miravirsen given as a four-week monotherapy treatment provided robust dose-dependent anti-viral activity with a mean reduction of 2 to 3 logs from baseline in HCV RNA (log<sub>10</sub> IU/mL) that was maintained for more than four weeks beyond the end of therapy. These new clinical data as well as the data in the abstract are being presented in a late-breaking oral presentation on November 7 at 4p.m., at The Liver Meeting® 2011, the 62nd annual meeting of the AASLD, in San Francisco, California<sup>1</sup>.

New clinical data from the Phase 2a study demonstrate that four out of nine patients treated at the highest dose (7 mg/kg) with miravirsen became HCV RNA undetectable with just four weeks of dosing. These data provide clinical evidence that miravirsen's unique mechanism-of-action offers high barrier to viral resistance and the potential for cure with monotherapy. Miravirsen was also well tolerated in patients with HCV, signaling a possible advantage over standard of care treatment.

“The miravirsen Phase 2a data is very promising considering that with only four weeks of treatment, miravirsen provided robust antiviral activity and throughout the study there was no sign of viral resistance,” said Harry Janssen, M.D. Ph.D., Head of Liver Unit at the Erasmus MC University Hospital Rotterdam, The Netherlands and Lead Clinical Investigator of the study, who is presenting the data at AASLD. “These data, taken together with the observation that four patients became HCV RNA undetectable at the highest dose, show that longer duration of miravirsen monotherapy has the potential to produce sustained virological responses.”

Data from the Phase 2a study show that the mean change from baseline in HCV RNA (log<sub>10</sub> IU/mL) at 10 weeks after initiation of therapy was -0.57, -2.16, -2.73 in the 3, 5 and 7 mg/kg miravirsen dose groups respectively vs. -0.01 in the placebo group (Table 1).

“Due to its unique mechanism of action in targeting miR-122, miravirsen has the potential to change the way Hepatitis C is treated,” said Stefan Zeuzem, M.D., Professor of Medicine and Chief of the Department of Medicine at the JW Goethe University Hospital, Frankfurt, Germany and Lead Clinical Investigator of the trial. “Miravirsen has the potential to be used as the central backbone treatment in combination with direct acting anti-viral agents as part of an interferon-free, infrequent dosing regimen.”

Table 1: Mean HCV RNA (Log10 IU/mL) Change from Baseline in all 3 Cohorts

Dose Group	Mean HCV RNA decline IU/mL (SEM) at week 10	p-value (t) MIR vs. placebo
Pooled placebo	-0.01 (0.19)	---
Miravirsen 3 mg/kg	-0.57 (0.13)	0.034
Miravirsen 5 mg/kg	-2.16 (0.58)	0.007
Miravirsen 7 mg/kg	-2.73 (0.55)	<0.001

“We are excited to show that miravirsen, the first microRNA-targeted drug to be given to patients, provides long-lasting suppression of HCV RNA, has a high barrier to viral resistance and a favorable tolerability profile.” said Michael R. Hodges, MD, Vice President and Chief Medical Officer at Santaris Pharma A/S. “Miravirsen has a low propensity for drug interactions, and is ideally placed to be used in combination with direct acting anti-viral agents to limit the selection of resistant variants, prevent viral break through, and improve overall cure rates in patients with all types of HCV genotypes.”

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 with chronic HCV genotype 1 infection 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.

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

### 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 about 3% of the world’s population has 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<sup>2</sup>. Approximately 3-4 million Americans are chronically infected with an estimated 40,000 new infections per year<sup>3</sup>. In Europe, there are about 4 million carriers<sup>4</sup>. Treatment with pegylated interferon in combination with ribavirin is effective in only about 50% of those treated<sup>2</sup>. 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<sup>4</sup>.

### 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 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, have manufactured 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](http://www.santaris.com) for more information.

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- <sup>1</sup> A Randomized, Double-blind, Placebo Controlled Safety and Anti-viral Proof of Concept Study of Miravirsin, an Oligonucleotide Targeting miR-122, In Treatment Naïve Patients with Genotype 1 Chronic HCV Infection, Abstract AASLD
  - <sup>2</sup> World Health Organization - <http://www.who.int/csr/disease/hepatitis/Hepc.pdf>
  - <sup>3</sup> American Association for the Study of Liver Diseases - <http://www.aasld.org/patients/Pages/LiverFastFactsHepC.aspx>
  - <sup>4</sup> 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>.