



New data show breakthrough microRNA-targeted therapy developed using Santaris Pharma A/S proprietary LNA technology holds promise as new treatment for Hepatitis C

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- SPC3649 successfully inhibits miR-122, a microRNA important for Hepatitis C viral replication, thereby significantly reducing Hepatitis C virus in the bloodstream in chimpanzees chronically infected with the Hepatitis C virus
- SPC3649 demonstrates efficacy with no evidence of viral resistance and no serious adverse events in the treated animals – signaling a potential benefit for patients who are not responsive to or cannot tolerate current standard of care therapies
- SPC3649 is the first microRNA-targeted drug to enter human clinical trials; Phase 1 clinical trials ongoing
- Santaris Pharma A/S proprietary Locked Nucleic Acid (LNA) Drug Platform fundamental in developing effective RNA-targeted therapies with high affinity, target specificity and remarkable potency for a range of diseases

Hoersholm, Denmark/San Diego, California, December 3, 2009 — A study published online in this week's Science shows that SPC3649, a breakthrough microRNA-targeted therapy developed by Santaris Pharma A/S using its proprietary Locked Nucleic Acid (LNA) technology, holds promise as a novel treatment for patients infected with the Hepatitis C virus (HCV).

The World Health Organization estimates about 3% of the world's population has been infected with HCV and that some 170 million are chronic carriers at risk of developing liver cirrhosis and/or liver cancer[1]. Approximately 3-4 million Americans are chronically infected with an estimated 40,000 new infections per year[2]. In Europe, there are about 4 million carriers[3].

Santaris Pharma A/S, the first company to have advanced both mRNA and microRNA targeted drugs into clinical trials, is an international biopharmaceutical company focused on the discovery and development of RNA-targeted therapies for a range of diseases including metabolic disorders, infectious and inflammatory diseases, cancer and rare genetic disorders.

In this preclinical study, SPC3649 successfully inhibited miR-122, a liver-expressed microRNA important for Hepatitis C viral replication. By inhibiting miR-122, SPC3649 dramatically reduced Hepatitis C virus in the liver and in the bloodstream in chimpanzees chronically infected with the Hepatitis C virus[4]. Four HCV chronically infected chimpanzees were treated weekly with 5 or 1 mg/kg of SPC3649 for 12 weeks followed by a treatment free period of 17 weeks. The two animals that received the 5 mg/kg dose had a significant decline in viral levels in the blood and liver of approximately 2.5 orders of magnitude or approximately 350 fold[5].

"In collaborating with Santaris Pharma, we proved that the drug worked exceptionally well in treating HCV infections in chimpanzees," said Robert Lanford, Ph.D., a scientist at the Southwest Foundation for Biomedical Research and one of the lead authors on the study. "The current standard anti-HCV treatment, which combines pegylated interferon-alpha with ribavirin, is effective in only about 50% of patients and is often associated with severe side effects. Because of the unique mechanism of action of SPC3649 and its tolerability profile, this new therapy could have the potential to replace interferon to treat disease progression or be combined with current treatments."

SPC3649 provided continued efficacy in the animals up to several months after the treatment period with no adverse events and no evidence of viral rebound or resistance, an important factor that distinguishes SPC3649 from direct antiviral HCV therapeutics.

Current antiviral therapies that target the virus directly are challenged as the HCV continually mutates to develop resistance to treatment. Because SPC3649 inhibits miR-122, an important microRNA involved in HCV

replication, the HCV is blocked from replicating without the apparent selection of resistant mutants. SPC3649 has other important properties that make it attractive as a therapeutic agent for HCV. The preclinical data show changes in the expression of key genes that may help patients who do not respond to interferon treatment to become responsive.

SPC3649 is the first microRNA-targeted drug to enter human clinical trials and is currently undergoing Phase 1 clinical studies in healthy volunteers. These preclinical data provide even greater impetus to further examine the potential of SPC3649 for treating patients infected with HCV.

“Advancing the first microRNA-targeted therapy, SPC3649, into human clinical trials was certainly a breakthrough in science and we are very encouraged by these preclinical findings demonstrating that SPC3649 has the potential to be an effective treatment for patients infected with the Hepatitis C virus,” said Henrik Ørum, PhD, Vice President and Chief Scientific Officer of Santaris Pharma A/S. “In drug discovery and development programs internally and with our partners, we continue to demonstrate that our proprietary LNA Drug Platform is fundamental in developing effective RNA-targeted therapies with high affinity, target specificity and remarkable potency for a range of diseases.”

Santaris Pharma A/S has a robust product pipeline based on its proprietary LNA technology including mRNA and microRNA drug discovery and development partnerships and collaborations with Shire (rare genetic disorders), Wyeth, now part of Pfizer, (delivery of lead candidates against up to ten targets), GlaxoSmithKline (four viral disease drug candidates) and Enzon Pharmaceuticals (eight cancer targets successfully delivered).

About Locked Nucleic Acid (LNA) Drug Platform

The Locked Nucleic Acid (LNA) Drug Platform developed by Santaris Pharma A/S creates synthetically modified chemical versions of the normal nucleic acid building blocks of ribonucleic acids (RNA). These modified chemical versions called LNAs improve the drug-like qualities of resulting therapeutics (oligonucleotides) by improving affinity to their target RNA, boosting resistance to metabolism and improving tissue uptake. Upon systemic administration of these “naked” molecules, LNA-based therapeutics are delivered to many different tissues where they show potencies many-fold better than other oligonucleotide therapeutics.

About Santaris Pharma A/S

Santaris Pharma A/S is a clinical-stage biopharmaceutical company focused on the discovery and development of RNA-targeted therapies. The Company’s proprietary Locked Nucleic Acid (LNA) drug platform, in combination with its highly specialized and targeted drug development capabilities, offers potential partners pre-screened drug candidates for commercial consideration across a multitude of disease states. The Company’s own research and development activities focus on infectious diseases and metabolic disorders while partnerships with major pharmaceutical companies include a range of therapeutic areas including cancer, rare genetic disorders and inflammatory diseases. Santaris Pharma A/S, founded in 2003, is privately-held and headquartered in Denmark with operations in the US. The Company has strategic partnerships with Enzon Pharmaceuticals, GlaxoSmithKline, Wyeth Pharmaceuticals (now part of Pfizer) and Shire plc. Please visit www.santaris.com for more information.

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[1] World Health Organization - <http://www.who.int/csr/disease/hepatitis/Hepc.pdf>

[2] American Association for the Study of Liver Diseases - <http://www.aasld.org/patients/Pages/LiverFastFactsHepC.aspx>

[3] World Health Organization - <http://www.who.int/csr/disease/hepatitis/Hepc.pdf>

[4] The chimpanzee is the only animal other than humans that is susceptible to HCV

[5] Lanford et al, Therapeutic silencing of microRNA-122 in primates with chronic hepatitis C virus infection, Science online

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