New data show breakthrough microRNA-targeted therapy holds promise as new treatment for hepatitis C

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A study published online in this week's *Science* shows that SPC3649, a breakthrough microRNA-targeted therapy developed by Santaris Pharma A/S, 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. Approximately 3-4 million Americans are chronically infected with an estimated 40,000 new infections per year . In Europe, there are about 4 million carriers.

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 . 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 .

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 Řrum, 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."

Source: Santaris Pharma A/S