# Santaris Nears End of Phase II Trial of miRNA HCV Rx, Seeks Partnership Since GSK Opted Out

By **Doug Macron**

**Santaris Pharma is nearing completion** of a phase II trial of its microRNA-targeting hepatitis C treatment miravirsen and expects to report initial data from the study at the end of the year, a company official told *Gene Silencing News* this week.

At the same time, Santaris is in discussions with bigger drug firms about a development and commercialization arrangement for the agent after GlaxoSmithKline passed on a licensing option last year, although the official offered no timeline for when a deal might be struck.

Formerly known as SPC3649, miravirsen is a locked nucleic acid targeting miR-122, a liver-expressed miRNA shown to play a role in HCV replication, cholesterol regulation, and lipid metabolism. It became the first miRNA-targeting agent to enter human testing in 2008 (*GSN* **5/29/2008**).

To date, miravirsen has been evaluated in two phase I safety studies, the first examining a single dose of the drug and the other testing multiple doses. In the first trial, Santaris said the drug was safe and well-tolerated, and treatment resulted in reductions in serum cholesterol — a biomarker for miR-122 inhibition.

Data from the second phase I trial have not been publicly disclosed, but last year Santaris CSO Henrik Orum told Gene Silencing News that the company was "happy with the results" (*GSN* **4/29/2010**). This week, he confirmed that both studies showed that miravirsen led to "dose-dependent, long-lasting reductions" in cholesterol "reminiscent of the reductions we had seen in all of the preclinical models, both in time of onset and scale."

In light of those data, the company advanced miravirsen into phase II testing late last year (*GSN* **9/23/2010**). According to Orum, it is a double-blind study evaluating three dose levels of the drug — 3 mg/kg, 5 mg/kg, and 7 mg/kg — administered via subcutaneous injection to treatment-naive patients with chronic hepatitis C infection.

Patients in the lowest-dose cohort are evaluated after three weeks, and patients in the other two cohorts are evaluated after six weeks, at which point a physician may also

begin treating them with standard interferon therapy, he noted.

Orum said that Santaris has dosed and completed evaluations for the first and second cohorts, and has finished dosing the in third. Unblinding of the data has begun, and the company expects to present them at the upcoming American Association for the Study of Liver Diseases in November.

Meantime, Santaris remains on the lookout for a partner to help with the further development and eventual commercialization of miravirsen.

"The HCV field is very fast moving, and ... we believe that for competitive reasons, this drug is best served by finding a big partner," Orum said this week. He noted that Santaris is already in contact with potential partners, adding that there is "quite of a lot of interest" in miravirsen.

One company whose early interest floundered, however, was GlaxoSmithKline.

In late 2007, the British drugs giant forged a still-ongoing alliance with Santaris to develop LNA-based antivirals (*GSN* **12/20/2007**). Though the arrangement was not focused on miRNA-targeting drugs, it did give GlaxoSmithKline an option to license miravirsen.

However, GlaxoSmithKline ultimately let that option expire and instead decided to collaborate with Regulus Therapeutics on that company's miR-122-targeting HCV therapy (*GSN* **2/25/2010**).

Although officials from neither Santaris nor GlaxoSmithKline have commented directly on the situation, industry watchers have pointed to intellectual property concerns as possibly driving the decision to go with Regulus.

Specifically, Regulus holds an exclusive license to US patent families related to miR-122, and is developing its own HCV drug that targets the small, non-coding RNA through an arrangement with Stanford University and the Max Planck Institute. The company has stated that this IP is essential for developing HCV drugs against the miRNA.

Orum declined to comment on whether Santaris would continue developing miravirsen if it is unable to find an industry ally, only stating that "we're very excited by this drug, and we will take all the activities that are necessary for seeing it develop at the appropriate speed."

He did state, though, that Santaris views the drug as ultimately being developed as a part of a therapeutic cocktail for HCV, and that the next clinical trial will combine it with a "direct-acting" antiviral.

"We think [our drug], with the profile we've seen to date, has the characteristics to make it a centerpiece of the cure that hopefully, eventually gets developed," he said, adding that "I don't think anybody in the field expects a single drug to cure HCV."

Though miravirsen is Santaris' most advanced drug candidate, it is the sole miRNA-targeting agent within the company's formal pipeline; the five other compounds currently in human testing are all directed against other types of targets.

Still, the company views miRNAs as promising drug targets, Orum said, and it has "a number of programs" focused on the class of non-coding RNAs in preclinical development, including one focused on miR-33.

Earlier this year, Santaris announced that it had licensed IP from Massachusetts General Hospital related to the use of the miRNA as a target for cardiovascular disorders including hypercholesterolemia (*GSN* **3/3/2011**).

Orum said that work continues on miR-33 and that the company would "probably" present data from that effort in the first quarter of next year.

Ultimately, however, the approach Santaris takes with its other miRNA drugs will depend on how miravirsen performs in the clinic, he noted.

"We think that microRNAs are a very interesting group of targets, but obviously the outcome of [the phase II study] is going to be a guideline for how this field opens up," he said.