Evaluate Vantage

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Can Conatus reinvigorate the NASH bubble?

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With a several promising datasets in multiple aspects of liver disease, Conatus Pharmaceuticals is dangling partnering bait in front of bigger pharma groups looking to enter this flourishing space.

Results from a phase II study in liver cirrhosis joined favourable-looking ones in portal hypertension and non-alcoholic steatohepatitis (NASH) released in the past 10 months, although none has been sufficiently positive to boost shares back to levels seen a year ago. With no more than $30m in cash at the end of 2015 and the likely need to enrol thousands of patients in confirmatory trials, the California-based group needs to hope that it has provided sufficient enticement for a big pharma player looking for a late-stage asset.

Laying down a biomarker

In liver cirrhosis Conatus's sole project emricasan managed to show significant improvements in most biomarker endpoints including caspase 3/7 and cleaved cytokeratin-18 after three months of treatment versus placebo. It did not do so on liver function parameters like Child-Pugh score or the model for end-stage liver disease (MELD), the surrogate endpoints being considered by the US FDA.

But, as emricasan was showing positive trends on the surrogate endpoints at the three-month measurement in the 86-patient trial, Conatus's chief executive, Steven Mento, said the company hoped for significant improvement after six months of treatment. Patients in the trial became cirrhotic as a result of numerous conditions, including NASH, heavy alcohol consumption and hepatitis C.

As with the portal hypertension trial, more severely ill patients – those with MELD scores of greater than 15, making them transplant-eligible – did show a statistically significant benefit on the surrogate endpoints, although the numbers were small (*Conatus makes a splash in NASH, September 24, 2015*).

That subgroup numbered only nine patients in the emricasan arm and 10 in the placebo cohort – four of the nine on active treatment arm and one placebo recipient saw their MELD scores drop to 14 or less after three months of treatment.

The excitement over NASH specifically, and degenerative liver disease more generally, was built around the surprise results for Intercept Pharmaceuticals' obeticholic acid two years ago, an event that prompted Conatus's own 12-month share-price bubble (*Boom! Trial halt turns Intercept into an improbable midcap company, January 10, 2014*).

The lesson from that initial tumult is that the FDA is looking for longer-term data in this disease area, which is where the Conatus story becomes a little more blurry.

Willing to wait?

Conatus already tapped investors in 2015 to the tune of $21.4m in April and shares halved by year-end. Today its stock opened up 34% at $3.84, perhaps providing an opportunity to raise money again, but it is doubtful that this would be enough to complete phase III trials – for example, Intercept raised $367m last April to support its phase III programme of more than 2,000 patients.

The question is which company might want to partner emricasan? Gilead Sciences, which saw its NASH candidate simtuzumab fail in a separate idiopathic pulmonary fibrosis test yesterday, has shown an interest in this space – although it has two other NASH candidates in addition to simtuzumab.

Shire and AstraZeneca have also been active in this arena. And of course there might be companies that remain convinced that NASH and degenerative liver disease represent a coming "tsunami", as Intercept's chief executive has described it, and have been waiting for a phase III-ready asset.

The smart money might be on bigger players delaying until the six-month data are available to see if the trends on the surrogate endpoints turn significant. The chase for scarce assets, however, could force the hands of those needing to fill their late-stage pipelines.

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