Conatus Pharmaceuticals Announces Top-line Results from Phase 2b POLT-HCV-SVR Clinical Trial

April 4, 2018

Biopsy-based Proof of Concept in Liver Fibrosis and Cirrhosis Supports Further Evaluation

Conference Call and Webcast Presentation at 4:30 p.m. ET Today

SAN DIEGO, April 04, 2018 (GLOBE NEWSWIRE) -- Conatus Pharmaceuticals Inc. (Nasdaq:CNAT), a biotechnology company focused on the development of novel medicines to treat liver disease, today announced top-line results from the company's exploratory Phase 2b POLT-HCV-SVR proof-of-concept clinical trial in liver transplant patients with fibrosis or cirrhosis. Although the trial did not meet its primary endpoint in the heterogeneous overall trial population, the emricasan treatment effect in the subgroup of patients where the histology endpoint is most relevant, patients with advanced fibrosis and early cirrhosis, supports further evaluation. POLT-HCV-SVR has a separate patient population versus the other three Phase 2b clinical trials in the company's collaboration with Novartis, which are in non-viral indications in patient populations with nonalcoholic steatohepatitis (NASH) fibrosis or cirrhosis.

Patients were stable transplant recipients who were an average of seven years post-transplant on chronic immunosuppression. Hepatitis C virus (HCV), the initial cause of the inflammatory insult to the transplanted liver, was eliminated by antiviral therapies prior to the study.

This is the first demonstration of the anti-fibrotic efficacy with emricasan using a histology endpoint in patients with fibrosis. Consistent with the previous 16 clinical trials, emricasan was generally well-tolerated in the POLT-HCV-SVR clinical trial, and the overall safety profile was similar in the emricasan and placebo groups.

A descriptive summary of the observed response rates (patients with both a baseline and two-year biopsy) after two years of dosing for different stages of fibrosis is provided below. All p values noted are ad hoc, as prospective statistical powering was not feasible in this previously unstudied patient population.

Analyses of Overall Population and Prespecified Subgroups

Ishak Fibrosis Score at Baseline	Emricasan Response Rate % (n/N)	Placebo Response Rate % (n/N)	Difference	Ad hoc p value
Overall Population	77.4 (24/31)	75.0 (15/20)	2.4	0.842
F2*	83.3 (5/6)	100 (5/5)	-16.7	1.000
F2, F3, F4	92.0 (23/25)	66.7 (10/15)	25.3	0.081
F3, F4	94.7 (18/19)	50.0 (5/10)	44.7	0.011
F3, F4, F5*	95.0 (19/20)	58.3 (7/12)	36.7	0.019
F2, F3, F4, F5	92.3 (24/26)	70.6 (12/17)	21.7	0.093
F6*	0 (0/5)	100 (3/3)	-100	0.018

*Prespecified subgroup population

Emricasan provided evidence of an anti-fibrotic treatment effect in the prespecified subgroup of patients with advanced fibrosis or early cirrhosis (F3-F5 at baseline), with 95.0% of patients (19/20) in the emricasan arm achieving responses in Ishak Fibrosis Score after two years of treatment, compared with 58.3% (7/12) in the placebo arm, a 36.7 percentage point difference in response rate ($p<0.02$). Inflammatory activity markers (ALT, cCK18, flCK18, Knodell activity index components) were either normal or only slightly elevated at baseline in both the emricasan and placebo groups.

Steven J. Mento, Ph.D., President, Chief Executive Officer and co-founder of Conatus, said, "These are the first biopsy-based efficacy results for emricasan. We are particularly encouraged by the 95% response rate in a subgroup of advanced fibrosis and early cirrhosis patients with a favorable two-year safety profile. In addition, in patients with the potential to continue worsening, those less than F6 at baseline, only 2 of 26 (7.7%) on emricasan compared with 5 of 17 (29.4%) on placebo showed an increase in fibrosis score at year 2 – a treatment difference of 21.7 percentage points. We also plan to evaluate responses in additional subgroups in a variety of secondary and exploratory endpoints to learn as much as possible from this data-rich trial."

"We are most grateful to the patients who participated in the trial, which required three biopsy procedures over a two-year period," said David T. Hagerty, M.D., Executive Vice President of Clinical Development at Conatus, "and to the clinical investigators and support staff who treated and monitored these patients, as well as the site monitoring, data collection and analysis teams who kept this long and complex trial on schedule."

The POLT-HCV-SVR trial, initiated in the second quarter of 2014, enrolled post-orthotopic liver transplant (POLT) recipients whose transplanted livers were damaged by recurrent HCV infection. They subsequently achieved a sustained viral response (SVR) following HCV antiviral therapy, but their transplanted livers had residual fibrosis or cirrhosis (baseline Ishak Fibrosis Score of F2 to F6). Patients were randomized 2:1 to receive 25 mg of emricasan, the company's first-in-class, orally active pan-caspase inhibitor, or placebo, twice daily for two years. Biopsies were taken at baseline, after one year of treatment, and after two years of treatment.

The primary endpoint was defined as the difference in percentage of responders between the treatment and placebo arms at the two-year biopsy compared with the baseline biopsy. A response was defined as improvement or stability in Ishak Fibrosis Score for patients with baseline scores of F2 to F5 or improvement in Ishak Fibrosis Score for patients with baseline scores of F6. The prespecified goal was a difference of 15 percentage points or more in response rates between the treatment and placebo arms.

Emricasan Clinical Development

POLT-HCV-SVR studied a separate patient population versus the other three Phase 2b clinical trials in the company's collaboration with Novartis, with the remaining three in non-viral indications – the EmricasaN, a Caspase inhibitOR, for Evaluation (ENCORE) trials, designed to evaluate emricasan in patients with fibrosis or cirrhosis caused by NASH:

- ENCORE-PH (for Portal Hypertension), initiated in the fourth quarter of 2016, in approximately 240 patients with NASH cirrhosis and severe portal hypertension, with top-line results expected in the second half of 2018;

- ENCORE-NF (for NASH Fibrosis), initiated in the first quarter of 2016, in approximately 330 patients with NASH fibrosis, with top-line results expected in the first half of 2019; and

- ENCORE-LF (for Liver Function), initiated in the second quarter of 2017, in approximately 210 patients with decompensated NASH cirrhosis, with top-line results expected in the second half of 2019.

Conference Call/Webcast/Presentation
Conatus will host a conference call and webcast at 4:30 p.m. Eastern Time today, April 4, to discuss the initial top-line results. To access the conference call, please dial 877-312-5857 (domestic) or 970-315-0455 (international) at least five minutes prior to the start time and refer to conference ID 4888617. An associated presentation and live and archived audio webcast of the call will be available in the Investors section of the company's website at http://ir.conatuspharma.com/events.cfm.

About Conatus Pharmaceuticals
Conatus is a biotechnology company focused on the development and commercialization of novel medicines to treat liver disease. In collaboration with Novartis, Conatus is developing its lead compound, emricasan, for the treatment of patients with chronic liver disease. Emricasan is a first-in-class, orally active pan-caspase inhibitor designed to reduce the activity of enzymes that mediate inflammation and apoptosis. Conatus believes that by reducing the activity of these enzymes, caspase inhibitors have the potential to interrupt the progression of a variety of diseases. For additional information, please visit www.conatuspharma.com.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical facts contained in this press release are forward-looking statements, including statements regarding: further evaluation of emricasan based on the POLT-HCV-SVR trial results; emricasan's potential treatment effect and anti-fibrotic efficacy; plans for evaluation of additional subgroups in a variety of secondary and exploratory endpoints; the timelines to announce results from the ENCORE clinical trials in 2018 and 2019; and caspase inhibitors' potential to interrupt the progression of a variety of diseases. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or other similar expressions. These forward-looking statements speak only as of the date of this press release and are subject to a number of risks, uncertainties and assumptions, including: reported top-line results are based on preliminary analysis of key data and as a result, such top-line results may change following a more comprehensive review and may not accurately reflect the complete results of the clinical trial; Conatus' ability to successfully enroll patients in and complete its ongoing clinical trials; Novartis continuing development and commercialization of emricasan; Conatus' reliance on third parties to conduct its clinical trials, including the enrollment of patients, and manufacture its clinical drug supplies of emricasan; potential adverse side effects or other safety risks associated with emricasan that could delay or preclude its approval; results of future clinical trials of emricasan; and those risks described in Conatus' prior press releases and in the periodic reports it files with the Securities and Exchange Commission. The events and circumstances reflected in Conatus' forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, Conatus does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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