Conatus Announces Results from ENCORE-PH Phase 2b Clinical Trial in NASH Cirrhosis

December 5, 2018

- Clinically Meaningful Improvements in Portal Hypertension in High Risk Compensated Cirrhosis Patients -

- Conference Call and Webcast Presentation at 8:30 a.m. ET Today -

SAN DIEGO, Dec. 05, 2018 (GLOBE NEWSWIRE) -- Conatus Pharmaceuticals Inc. (Nasdaq:CNAT) today announced top-line results from the company's Phase 2b ENCORE-PH clinical trial showing clinically meaningful treatment effects in compensated NASH cirrhosis patients at high risk of decompensation. The trial's primary endpoint was change in mean hepatic venous pressure gradient (HVPG) from baseline to Week 24 in any of three emricasan dosing groups compared with placebo. In the overall trial population, changes in HVPG from baseline to Week 24 showed trends consistently favoring emricasan compared with placebo but did not meet the primary endpoint.

The total patient population was composed of two prespecified subgroups – patients with compensated NASH cirrhosis (201 of 263 patients, or 76%) and patients with early decompensated NASH cirrhosis (62 of 263 patients, or 24%). Steven J. Mento, Ph.D., President, Chief Executive Officer and co-founder of Conatus, said, "Based on previous discussions with regulators, we expect that separate registration trials would be needed in compensated and decompensated NASH cirrhosis. This trial purposely enrolled mostly compensated patients, and we are encouraged by the treatment effect shown in this population in these top-line results."

In patients with compensated NASH cirrhosis, post hoc analyses demonstrated consistent improvements in mean HVPG at week 24 over baseline. In these same patients, clinically meaningful differences compared with placebo in mean HVPG at Week 24 were observed in a consistent pattern over multiple baseline HVPG cohorts from ≥13 mmHg through ≥17 mmHg. The magnitude of the improvement in mean HVPG generally increased as the baseline HVPG levels increased. Both the 25mg and 50mg active dose groups achieved a >10% improvement in mean HVPG compared with placebo in all HVPG cohorts from ≥13 mmHg through ≥17 mmHg, while placebo-treated patients showed increases in mean HVPG. The greatest improvement was observed in patients with a baseline HVPG of 16 mmHg or higher.

"Patients with compensated cirrhosis and severe portal hypertension, that is, with HVPG of 12 mmHg or higher, are at risk for decompensation, that is, they are at risk for developing complications such as variceal hemorrhage, hepatic encephalopathy and ascites that significantly decrease their quality of life and survival," said Guadalupe Garcia-Tsao, M.D., Professor of Medicine in the Section of Digestive Diseases at Yale School of Medicine, Director of the Clinical and Translational Core at Yale Liver Center, Chief of the Section of Digestive Diseases at the Veterans Administration-Connecticut Health Care System, and the central reader for the HVPG tracings in the ENCORE-PH clinical trial. "We have recently shown that the risk of decompensation and death rises with progressive increases in HVPG. Conversely, reductions in HVPG as small as 1 mmHg can reduce the risk of decompensation or death. Post-hoc analyses from the ENCORE-PH trial showing that, compared to placebo, emricasan is associated with clinically meaningful incremental reductions in HVPG with worsening baseline HVPG levels, strongly suggest that emricasan has the potential of providing patient benefit."

The high-risk subgroup of compensated patients with HVPG ≥16 mmHg at baseline showed a clinically meaningful ≥2-point improvement in mean HVPG compared with placebo in all three emricasan dosing groups. A favorable trend compared with placebo in responses predictive of clinical benefit (≥20% reduction in HVPG from baseline) was also observed in the total ≥12 mmHg compensated patient population with the greatest responses observed in the ≥16 mmHg cohort. The baseline HVPG ≥16 mmHg cohort resembles the patient population studied in the prior Portal Hypertension pilot study and again shows, now in a placebo-controlled trial, a clinically meaningful improvement in mean HVPG. In addition, HVPG of ≥16 mmHg predicts a higher risk of both clinical events and death[1].

"This trial evaluated the ability of emricasan to reduce HVPG in patients with cirrhosis due to NASH. Although the primary endpoint was not met, the data indicates an amelioration of portal pressures by emricasan," said Arun Sanyal, M.B.B.S, M.D., Professor of Medicine, Physiology and Molecular Pathology at Virginia Commonwealth University School of Medicine, chair of the NIH NASH Clinical Research Network, and chair of the Liver Forum. "Not surprisingly, those with the highest HVPG had the greatest benefit and the trends in all groups on sensitivity analyses favored active therapy. Together, these suggest that the findings are real and support additional investigation of this compound for those with compensated cirrhosis due to NASH and high HVPG, i.e., the population at greatest risk of clinical decompensation for whom there are no alternate approved therapies."

Consistent with safety results from 17 previously completed clinical trials, emricasan was generally well-tolerated in the ENCORE-PH clinical trial, and the overall safety profile was similar in the emricasan and placebo groups. Patients enrolled in the ENCORE-PH clinical trial are continuing treatment or placebo in a six-month extension period to evaluate longer term safety, liver function and clinical outcomes, and results on the extension are expected in mid-2019.

"We believe data from the ENCORE-PH clinical trial as well as data from our two ongoing ENCORE trials that will be available in 2019 will warrant future discussions with regulatory authorities regarding potential pivotal trials in patients with NASH and advanced liver disease," said David T. Hagerty, M.D., Executive Vice President of Clinical Development at Conatus. "We are grateful to the NASH cirrhosis patients who participated unselfishly in the ENCORE-PH clinical trial, and to the principal investigators who treated them in compliance with a rigorous protocol. We also thank the clinical site support staffs and the site monitoring, data collection and analysis teams who maintained schedule integrity from launch through results."

Conference Call/Webcast/Presentation
Conatus will host a conference call and webcast at 8:30 a.m. Eastern Time today, December 5, to discuss the ENCORE-PH 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 9356879. 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 www.conatuspharma.com.

About Emricasan
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. To date, emricasan has been studied in approximately 700 patients in 17 completed clinical trials across a broad range of liver diseases. In multiple Phase 2 clinical trials, emricasan has demonstrated clinically meaningful reductions in severe portal hypertension, improvements in measures of liver function, and evidence of an anti-fibrotic treatment effect, as well as rapid and sustained reductions in elevated levels of key biomarkers of inflammation and cell death, which play a role in the severity and progression of liver disease.

About ENCORE-PH
The randomized, double-blind ENCORE-PH Phase 2b clinical trial, initiated in the fourth quarter of 2016, enrolled 263 NASH patients with compensated or early decompensated liver cirrhosis and severe portal hypertension confirmed by HVPG of ≥12 mmHg at baseline. Patients were randomized 1:1:1:1 to receive 5 mg of emricasan, 25 mg of emricasan, 50 mg of emricasan, or placebo twice daily for 24 weeks. The trial was conducted at 75 U.S. and EU sites.

About Emricasan Clinical Development
ENCORE-PH is one of three randomized, double-blind, placebo-controlled Phase 2b clinical trials being conducted by Conatus in collaboration with Novartis, the EmricasaN, a Caspase inhibitOR, for Evaluation (ENCORE) trials, designed to evaluate emricasan in patients with fibrosis or cirrhosis caused by NASH. Extension of the ENCORE-PH trial as well as two additional ENCORE clinical trials are ongoing:

- ENCORE-PH (for Portal Hypertension) six-month extension, with 48-week liver function and clinical outcome results expected in mid-2019;
- 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 mid-2019.

About Conatus Pharmaceuticals
Conatus is a biotechnology company focused on the development 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. 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: separate registration trials being needed in compensated and decompensated NASH cirrhosis; emricasan's potential to provide clinical benefit; the timeline to announce results from the extension phase of the ENCORE-PH trial in mid-2019; the data from the ENCORE-PH, ENCORE-NF and ENCORE-LF trials warranting future discussions with regulatory authorities regarding pivotal trials; the timelines to announce results from the ongoing ENCORE clinical trials; 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.

[1] Berzigotti A et al. Prognostic value of a single HVPG measurement and Doppler-ultrasound evaluation in patients with cirrhosis and portal hypertension. J Gastroenterol 2011. DOI: 10.1007/s00535-010-0360-z.
Turco L et al. Cardiopulmonary hemodynamics and C-reactive protein as prognostic indicators in compensated and decompensated cirrhosis. J Hepatol 2018. DOI: 10.1016/j.jhep.2017.12.027.

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