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Conatus Pharmaceuticals Announces Publication Demonstrating that Emricasan Ameliorates Portal Hypertension, Improves Liver Structure and Function in a Preclinical Model of Advanced Cirrhosis

SAN DIEGO, April 30, 2019 (GLOBE NEWSWIRE) -- Conatus Pharmaceuticals Inc. (Nasdaq:CNAT) today announced a new publication[1] in *Hepatology Communications* detailing results following seven-day treatment with emricasan, the company's first-in-class pan-caspase inhibitor, in rats with advanced cirrhosis including increased portal pressure induced by chronic carbon tetrachloride administration. Portal pressure was significantly reduced in emricasan-treated rats relative to vehicle-treated control animals. Reduced portal pressure was associated with significantly better liver function, reduced liver inflammation, and reduced fibrosis. Improvements in expression of markers of liver function, including increased expression of vasodilators and reduced expression of vasoconstrictors, were observed in liver cells isolated from emricasan-treated cirrhotic rats. *In vitro* experiments treating human cirrhotic liver cells with emricasan improved the synthetic capacity of hepatocytes from cirrhotic livers and increased expression of specific markers of liver function.

The publication's authors concluded that, "This study demonstrates that emricasan improves liver sinusoidal microvascular dysfunction in cirrhosis, which leads to marked amelioration in fibrosis, portal hypertension and liver function, and therefore encourages its clinical evaluation in the treatment of advanced chronic liver disease."

"The current study provides mechanistic support for the results from clinical studies evaluating emricasan's ability to reduce portal hypertension in patients with advanced cirrhosis," said Al Spada, Ph.D., Executive Vice President of Research and Development, Chief Scientific Officer and co-founder of Conatus, and an author on the publication. "We believe the insights provided by the cumulative body of preclinical data, coupled with the corresponding results from human clinical testing, support continued evaluation in NASH cirrhosis patients."

Emricasan Clinical Development
The company is currently conducting two double-blind, placebo-controlled Phase 2b clinical trials in collaboration with Novartis – the EmricasaN, a Caspase inhibitOR, for Evaluation (ENCORE) trials, designed to evaluate emricasan in patients with liver cirrhosis caused by nonalcoholic steatohepatitis (NASH).

- The ENCORE-LF (for Liver Function) clinical trial, initiated in the second quarter of 2017, has enrolled approximately 210 patients with stable decompensated NASH

cirrhosis. The primary endpoint is event-free survival, which is a composite of all-cause mortality, new decompensation events, or ≥4 points progression in Model for End-stage Liver Disease (MELD) score. Enrollment was completed in the first quarter of 2019. Top-line results triggered by reaching a prespecified number of events are expected in mid-2019.

- The ENCORE-PH (for Portal Hypertension) clinical trial, initiated in the fourth quarter of 2016, enrolled 263 patients with compensated or early decompensated NASH cirrhosis and severe portal hypertension. 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. Top-line results were reported in December 2018 showing HVPG trends consistently favoring emricasan compared with placebo in the overall population but not meeting the primary endpoint. The greatest improvement was observed in patients with a baseline HVPG of 16 mmHg or higher. Patients had the option to continue on their assigned doses of treatment or placebo in a double-blind 24-week extension period. Results following the extension period are expected in mid-2019 and will include longer term safety, liver function and clinical outcomes, but there will be no additional HVPG measurements.

About Conatus Pharmaceuticals
Conatus is a biotechnology company focused on the development and commercialization of novel medicines to treat chronic diseases with significant unmet need. In collaboration with Novartis, Conatus is developing its lead in-licensed compound, emricasan, for the treatment of patients with NASH-driven chronic liver diseases. Conatus is independently developing its lead internally developed compound, CTS-2090, for the treatment of patients with chronic diseases involving inflammasome pathways. 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 the timeline for results from the ENCORE trials. 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: results of future clinical trials of emricasan; the uncertainty of the U.S. Food and Drug Administration's and other regulatory agencies' approval processes and other regulatory requirements; and those risks described in the company's prior press releases and in the periodic reports it files with the Securities and Exchange Commission. The events and circumstances reflected in the company's 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, the company 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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[1] Gracia-Sancho J *et al*. Emricasan Ameliorates Portal Hypertension and Liver Fibrosis in Cirrhotic Rats Through a Hepatocyte-Mediated Paracrine Mechanism. *Hepatol Comm.* 2019. DOI 10.1002/hep4.1360.

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