Conatus Pharmaceuticals' Pan-caspase Inhibitor Emricasan Improves Survival and Portal Hypertension in a Mouse Model of Cirrhosis

July 2, 2018

SAN DIEGO, July 02, 2018 (GLOBE NEWSWIRE) -- Conatus Pharmaceuticals Inc. (Nasdaq:CNAT) today announced the publication[1] of results from preclinical studies of its pan-caspase inhibitor emricasan, demonstrating improvements in portal hypertension (elevated blood pressure in the vein flowing into the liver) and survival in two bile duct ligation mouse models of induced secondary biliary cirrhosis.

In the first of the two current mouse studies, designed to evaluate treatment effect, emricasan decreased fibrosis, reduced portal hypertension and improved survival in mice with cirrhosis induced by bile duct ligation. The reductions in portal hypertension exceeded amounts that could be explained by the decreased fibrosis alone, indicating potential treatment effects both inside and outside the liver.

In the second study, designed to investigate mechanism of action, emricasan reduced liver damage, liver cell death and fibrosis in mice, and these changes were associated with a decrease in circulating microparticles. These microparticles, which are released from damaged cells, have been linked in previous studies to a cascade of detrimental effects in the liver, including inflammation, collagen production, restriction of blood flow through the liver, and restriction of blood flow in and out of liver cells responsible for toxin processing and removal and essential protein production. Previous studies also have shown that circulating microparticles above a threshold level can trigger increased blood flow toward the liver to compensate for the restricted blood flow through the liver, which exacerbates portal hypertension. In the current study, microparticles from placebo mice, but not from emricasan-treated mice, activated endothelial cells *ex vivo*. Endothelial cells lining the blood vessels inside the liver are the gateway between the blood stream and the toxin processing and protein synthesizing cells in the liver, and their activation directly restricts that exchange and thereby reduces liver function. Through these multiple mechanisms, emricasan's suppression of microparticles could be a contributing factor both inside and outside the liver in reducing portal hypertension.

The studies, published in the peer-reviewed *Journal of Molecular Medicine*, were conducted in collaboration with Ariel E. Feldstein, M.D., of the Department of Pediatrics and the School of Medicine at the University of California – San Diego. Al Spada, Ph.D., Executive Vice President of Research and Development, Chief Scientific Officer and co-founder of Conatus, and a co-author on the publication, said, "The current studies confirm and help explain the favorable effects of emricasan seen in other preclinical models and in observed clinically significant reductions in portal pressure in our pilot portal hypertension clinical trial. We understand that caspase inhibition drives multiple mechanisms of action both inside and outside the liver which together can provide both symptomatic and structural improvements. We believe these data support continued clinical evaluation of emricasan in patients with chronic liver disease."

Emricasan Clinical Development

In collaboration with Novartis, Conatus is conducting three randomized, double-blind, placebo-controlled Phase 2b clinical trials, the EmricasaN, a Caspase inhibitOR, for Evaluation (ENCORE) trials, designed to evaluate emricasan in patients with fibrosis or cirrhosis caused by nonalcoholic steatohepatitis (NASH):

- ENCORE-PH (for Portal Hypertension), initiated in the fourth quarter of 2016, in approximately 240 NASH patients with compensated or early decompensated liver cirrhosis and severe portal hypertension, with top-line results expected in the fourth quarter of 2018;
- ENCORE-NF (for NASH Fibrosis), initiated in the first quarter of 2016, in approximately 330 NASH patients with 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 NASH patients with decompensated cirrhosis, with top-line results expected in the second half of 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. 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: the preclinical data encouraging further evaluation of emricasan in chronic liver disease; the timeline for results from the ENCORE 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 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.

[1]Eguchi, A., Koyama, Y., Wree, A. et al. Emricasan, a pan-caspase inhibitor, improves survival and portal hypertension in a murine model of common bile-duct ligation. J Mol Med (2018) 96:575-583. https://doi.org/10.1007/s00109-018-1642-9.

CONTACT: Alan Engbring
Conatus Pharmaceuticals Inc.
(858) 376-2637
aengbring@conatuspharma.com


Primary Logo

Source: Conatus Pharmaceuticals Inc.