Conatus Pharmaceuticals Inc.
Form 8-K
January 08, 2015

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the
Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 8, 2015

CONATUS PHARMACEUTICALS INC.
(Exact Name of Registrant as Specified in its Charter)

Delaware	001-36003	20-3183915
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

16745 West Bernardo Drive, Suite 200 San Diego, CA	92127
(Address of Principal Executive Offices)	(Zip Code)

Registrant's telephone number, including area code: (858) 376-2600

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 8.01 Other Events.

On January 8, 2015, Conatus Pharmaceuticals Inc. (the "Company") announced aggregate top-line results from three pharmacokinetic and pharmacodynamic clinical trials in organ-impaired patients, which include a Phase 2 clinical trial in patients with acute-on-chronic liver failure ("ACLF"), a Phase 1 clinical trial in patients with mild, moderate and severe hepatic impairment and a Phase 1 clinical trial in patients with severe renal impairment. All three trials provided important information on the effects of renal and hepatic impairment on the pharmacokinetics and pharmacodynamics of emricasan, and provided support for emricasan's continued development in patients with liver cirrhosis. While more severe forms of cirrhosis may be associated with concomitant renal impairment, emricasan pharmacokinetics were only modestly affected by severe renal impairment. A separate trial assessed the effect of stable mild, moderate or severe hepatic impairment upon the pharmacokinetics of emricasan. Emricasan pharmacokinetics were not affected by stable mild hepatic impairment while systemic drug exposures were progressively increased in patients with both moderate and severe hepatic impairment. In the ACLF trial, which assessed patients with acutely decompensated severe hepatic impairment, emricasan exposure after the first dose was more than twice the exposure in patients with stable severe hepatic impairment.

Emricasan was well-tolerated at all doses tested, regardless of the affected organ (liver or kidney) or degree of organ impairment. There were no drug-related serious adverse events or dose-limiting toxicities. Adverse events observed were reflective of the patient populations being studied. After reviewing safety data, an independent Data Monitoring Committee recommended continuation of the ACLF trial to completion, but also recognized the logistical challenges of conducting a controlled trial in this patient population and agreed with the Company's decision to an early termination of the clinical trial. An important observation in patients with hepatic impairment, and especially ACLF patients, was that caspase-mediated activity (involved in both apoptosis and inflammation) was highly elevated at baseline and could be rapidly decreased by emricasan.

Top-Line Trial Results

The ACLF trial was designed to assess the pharmacokinetics of emricasan, as well as biomarker and clinical responses, following twice daily ("BID") oral dosing of emricasan or placebo for 28 days. Twenty of 21 patients enrolled in the ACLF clinical trial had alcohol-associated liver disease consistent with alcoholic liver disease being a major contributor to the ACLF patient population. Data evaluation was focused on the first 7 days of treatment as by Day 14, only 12 patients remained on study due to discontinuations and patients lost to follow-up in this difficult-to-manage population.

As expected, alanine aminotransferase ("ALT") levels were not increased in the ACLF patient population. By contrast, levels of key mechanism-specific biomarkers of caspase activity and inflammation – caspase-cleaved cytokeratin 18 ("cCK18"), Caspase 3/7, and Interleukin-18 ("IL-18") – and a biomarker of more generalized cell death – full-length cytokeratin 18 ("flCK18") – were all elevated at baseline, demonstrating their important role in the ACLF disease process. These biomarkers also showed increasing elevations at baseline as a function of worsening hepatic impairment.

Dose-related responses to emricasan in elevated biomarkers were apparent with no response noted in the placebo cohort, limited or no response in the 5 mg BID cohort, an initial rapid but transitory response in the 25 mg BID cohort, and a rapid and sustained response in almost all of the 50 mg BID cohort. Emricasan 25 mg and 50 mg BID oral dosing reduced cCK18, flCK18 and Caspase 3/7 levels within 24 hours post administration (Study Day 2) by at least 30%. More modest ~20% reductions in elevated IL-18 levels were also observed in the 25 mg and 50 mg BID cohorts by day 7. Only the emricasan 50 mg dose resulted in sustained reductions in cCK18 over the entire dosing period in the majority of patients. The median reduction in the 50 mg BID cohort on Day 2 was 54% compared with a median reduction of 7%, 13% and 44% in the placebo, 5 mg and 25 mg cohorts respectively. The observed reduction in cCK18 was maintained in the 50 mg BID cohort (median reduction of 56% and 50% on Day 4 and Day 7,

respectively) but not maintained in the other cohorts. For example, the median reduction in the 25 mg BID cohort was 30% on Day 4 and 6% on Day 7, suggesting that higher doses of emricasan may need to be explored in the ACLF patient population. Reductions of these elevated biomarkers demonstrated emricasan's rapid, on-target effect, and further verified tolerability.

The hepatic impairment trial also showed similar reductions in caspase-mediated biomarkers following treatment with emricasan. Patients in the mild, moderate and severe hepatic impairment groups, who had progressive elevations in these caspase-mediated biomarkers at baseline, responded rapidly to a single 50 mg dose of emricasan. In the severe renal impairment trial, impaired patients had modest or no elevations in caspase-mediated biomarkers at baseline compared with healthy control subjects, and neither cohort had notable changes following the single 50 mg dose of emricasan. The degree of hepatic impairment in the acutely decompensated ACLF trial population was, as anticipated, much more severe than the stable severe patient cohort in the hepatic impairment trial. Baseline levels of cCK18 were markedly higher in the ACLF patients, and reductions in cCK18 after treatment with emricasan were less rapid and less robust, again suggesting that higher doses may be beneficial in ACLF patients.

In addition to biomarker responses, patients in the ACLF trial were also assessed for clinical responses to emricasan. Two of four patients (50%) in the placebo cohort had positive clinical responses, compared with 3 of 5 patients (60%) in the 50 mg BID cohort. A patient was defined as a clinical responder if the patient survived to Day 28 or last known follow-up and met at least one of the following laboratory response parameters, evaluated at Day 28 or last known follow-up: (i) improvement of 2 points from baseline in the chronic liver failure-sequential organ failure assessment ("CLIF-SOFA") score; (ii) improvement of 5 points from baseline in Model For End-Stage Liver Disease ("MELD") score; or (iii) improvement in total bilirubin levels by approximately 50%. Reported deaths in this trial were related to progression of underlying disease or exacerbation of associated complications of cirrhosis, and not to study drug. Small patient numbers and the large number of patients who discontinued or were lost to follow-up reflects a complex, high-risk patient population and poor patient compliance, making interpretation of clinical response data difficult. Elevated levels of cCK18 decreased in all patients as they recovered, confirming that caspase activation plays a role in ACLF. Patients who did respond clinically tended to have at least a 30% reduction in cCK18 levels consistent with the proposed mechanism of action.

The Company remains on track to provide: 1) top-line results from its ongoing nonalcoholic fatty liver disease/nonalcoholic steatohepatitis trial in the first quarter of 2015; 2) initial interim results from its ongoing post liver transplant hepatitis C virus clearance with unresolved fibrosis trial in the first half of 2015; 3) top-line results from its ongoing portal hypertension trial in the third quarter of 2015; and 4) top-line interim results from its ongoing liver cirrhosis trial in the second half of 2015.

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This Current Report on Form 8-K 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 Current Report on Form 8-K are forward-looking statements, including statements regarding continued development of emricasan for patients with liver cirrhosis and exploration of higher doses of emricasan in the ACLF patient population, and the timing and release of results from the Company's ongoing clinical trials. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend, "project," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or other expressions. These forward-looking statements speak only as of the date of this Current Report on Form 8-K and are subject to a number of risks, uncertainties and assumptions, including: the applicability of certain biomarkers as potential drivers of liver disease progression; the effect on liver disease of decreasing certain biomarkers; the Company's ability to successfully enroll patients in and complete its ongoing and planned clinical trials; the potential for competing products to limit the clinical trial enrollment in the Company's clinical trials; the Company's ability to successfully enroll patients in and complete its Phase 2 clinical trials; the allowance by regulatory authorities to explore higher doses of emricasan in renal and hepatic impaired patients and patients with liver cirrhosis; the Company's 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; the Company's ability to obtain additional financing in order to complete the development and commercialization of emricasan; and those risks

described in the Company's 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.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: January 8, 2015

CONATUS PHARMACEUTICALS INC.

By: /s/ Charles J. Cashion
Name: Charles J. Cashion
Title: Senior Vice President, Finance, Chief Financial Officer & Secretary