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Tobira Therapeutics Announces Late-Breaking Oral Presentation of CENTAUR Phase 2b Trial Results at the American Academy for the Study of Liver Diseases Annual Meeting

Cenicriviroc Significantly Improved Fibrosis without Worsening of NASH at One Year

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)-- Tobira Therapeutics, Inc. (NASDAQ: TBRA), a clinical-stage biopharmaceutical company focused on developing and commercializing therapies for non-alcoholic steatohepatitis (NASH) and other liver diseases, today announced the acceptance of the company's late breaking abstract as an oral presentation at the American Academy for the Study of Liver Diseases (AASLD) Annual Meeting (the Liver Meeting®), being held in Boston, MA from November 11-15, 2016.

The abstract entitled "Cenicriviroc versus placebo for the treatment of non-alcoholic steatohepatitis with liver fibrosis: Results from the Year 1 primary analysis of the Phase 2b CENTAUR study," will be presented by Arun Sanyal, M.D., Charles Caravati Distinguished Professor and Chair, Division of Gastroenterology, Hepatology and Nutrition at Virginia Commonwealth University on Monday, November 14, 2016.

"I am excited to be presenting data from the CENTAUR study, showing that in the treated population CVC was well tolerated and resulted in twice as many patients achieving at least a one-stage improvement in fibrosis with no worsening of steatohepatitis compared to placebo, after only one year of treatment," said Dr. Sanyal. "With 9 to 15 million people impacted in the U.S., and no currently approved treatment, NASH is an emerging health crisis, and is predicted to become the leading cause of liver transplant in the U.S. by 2020. These data are a critical step forward in potentially bringing a much needed treatment option to patients."

Cenicriviroc (CVC), an oral chemokine receptor CCR2/5 antagonist, has potent anti-inflammatory and antifibrotic activity in animal models of acute and chronic liver diseases. Its efficacy and safety as a treatment for NASH and liver fibrosis are being evaluated in adults at increased risk of progression to cirrhosis.

CENTAUR DATA

In the intent-to-treat (ITT) population, CVC was well tolerated and resulted in twice as many subjects achieving one stage or greater improvement in fibrosis and no worsening of steatohepatitis compared to placebo, after only one year of treatment (p=0.023). Importantly, greater treatment benefits were observed in subjects with higher NASH disease activity and fibrosis stage and thus at risk of progression. Improvement in fibrosis by two stages was observed in 11 subjects (8 CVC; 3 placebo). Seven subjects progressed to cirrhosis (2 CVC; 5 placebo). A similar proportion of patients treated with CVC compared to placebo achieved the non-alcoholic fatty liver disease activity score (NAS) and resolution of steatohepatitis endpoints. Interleukin-6 (IL-6), high-sensitivity C-reactive protein (hs-CRP), and fibrinogen levels, all markers associated with systemic inflammation, were significantly decreased with CVC compared to placebo.

The most common drug-related, treatment-emergent adverse events of Grade 2 or higher severity occurring in 2 percent or more of subjects were: fatigue (2.8%) and diarrhea (2.1%) for CVC and headache (3.5%) for placebo. There were no notable differences in laboratory abnormalities or premature discontinuations between CVC and placebo.

CENTAUR primary and key secondary efficacy endpoints (ITT; missing Year 1 biopsy = non response; logistic regression analysis)	CVC 150 mg (N=145)	Placebo (N=144)	Odds Ratio (95% CI)	p value (logistic regression)
Primary endpoint: ≥2-Point improvement in NAS (with ≥1-point reduction in lobular inflammation or hepatocellular ballooning) and no worsening of fibrosis, n (%)	23 (16%)	27 (19%)	0.8 (0.44, 1.52)	0.519
Key secondary endpoint (1): Complete resolution of Steatohepatitis and no worsening of fibrosis, n (%)	11 (8%)	8 (6%)	1.4 (0.54, 3.63)	0.494
Key secondary endpoint (2): Improvement in fibrosis by ≥1 stage (NASH CRN system) and no worsening of steatohepatitis, n (%)	29 (20%)	15 (10%)	2.2 (1.11, 4.35)	0.023
Subgroup analyses for fibrosis improvement (key secondary endpoint 2) by baseline				

NAS ≥5	21/89 (24%)	9/94 (10%)	2.9 (1.26, 6.78)	0.013
Hepatocellular ballooning grade ≥2	18/64 (28%)	6/69 (9%)	4.1 (1.51, 11.16)	0.006
Fibrosis stage 1	6/44 (14%)	2/42 (5%)	3.2 (0.60, 16.6)	0.175
Fibrosis stages 2 and 3	23/82 (28%)	13/84 (16%)	2.2 (1.00, 4.69)	0.049

CENTAUR Trial Design

CENTAUR is a Phase 2b, randomized, double-blind, placebo-controlled, ongoing 2-year multinational study of 289 subjects with a primary analysis at Year 1. Subjects with histologically defined NASH (NAS ≥4), liver fibrosis (stages 1-3 NASH CRN), and diabetes or metabolic syndrome (MetS) were randomized to receive 150 mg of CVC 150 once daily or placebo. NAS, resolution of steatohepatitis, and fibrosis stage were assessed on Year 1 liver biopsies. Markers of systemic inflammation, treatment-emergent adverse events (TEAEs), and laboratory abnormalities were also evaluated.

The trial participants were 53 percent female with a mean BMI of 34 kg/m^2 (standard deviation: 6.5). The study population had advanced disease: 52 percent of patients were diagnosed with diabetes, 72 percent were diagnosed with the metabolic syndrome, 74 percent had a NAS of 5 or greater, and 67 percent had liver fibrosis of Stage 2-3.

About Cenicriviroc (CVC)

CVC is an oral, once-daily, potent immunomodulator that blocks two chemokine receptors, CCR2 and CCR5, which are intricately involved in the inflammatory and fibrogenic pathways in NASH that cause liver damage and often lead to cirrhosis, liver cancer, or liver failure. Because of this unique mechanism of action, targeting two of the main engines driving NASH, CVC has the potential to play a differentiated role in the management of NASH and may form the cornerstone of NASH combination treatment strategies, both as a single agent and in combination with other agents targeting metabolic pathways. CVC has been granted Fast Track status in patients with NASH and liver fibrosis, the patient population at highest risk of progression to cirrhosis.

The safety and efficacy of CVC for NASH with liver fibrosis is being investigated in the CENTAUR study (NCT02217475). CENTAUR is a Phase 2b multinational, randomized, double-blind study comparing CVC to placebo in 289 adults with NASH and liver fibrosis. In July 2016, Tobira announced that CENTAUR met the key secondary endpoint of improvement in liver fibrosis by at least one stage with no worsening of steatohepatitis after one year of treatment, which was recommended by regulators as an endpoint for Phase 3 studies to support a marketing application. The CENTAUR study continues for a second year analysis of endpoints, which is expected in the third quarter of 2017. The company plans to initiate a Phase 3 program in 2017.

In addition to CENTAUR, CVC is also being evaluated in the PERSEUS study (identifier NCT02653625), a Phase 2 proof-of-concept study of CVC in patients with primary sclerosing cholangitis, a rare inflammatory liver disease.

About Non-Alcoholic Steatohepatitis (NASH)

NASH is a severe type of non-alcoholic fatty liver disease (NAFLD), which is characterized by the accumulation of fat in the liver with no other apparent causes. NASH occurs when the accumulation of liver fat is accompanied by inflammation and cellular damage. The inflammation can lead to fibrosis (scarring) of the liver and eventually progress to cirrhosis, portal hypertension, liver cancer, and eventual liver failure.

NASH is an emerging health crisis impacting 3 percent to 5 percent of the U.S. population and 2 percent to 4 percent globally, and is the fastest growing cause of liver cancer and liver transplant in the U.S. The increasing prevalence of NASH is attributed to the growing obesity epidemic and the disease is often diagnosed in patients who have diabetes, high cholesterol or high triglycerides. There is currently no approved treatment for NASH.

About Tobira Therapeutics

Tobira is a clinical-stage biopharmaceutical company focused on the development and commercialization of therapies for non-alcoholic steatohepatitis (NASH) and other liver diseases. The company's lead product candidate, cenicriviroc (CVC), is a first-in-class immunomodulator and dual inhibitor of CCR2 and CCR5 in late-stage development for the treatment of NASH, a serious liver disease that can progress to cirrhosis, liver cancer and liver failure. CVC is also being investigated to address primary sclerosing cholangitis (PSC), a disease which causes inflammation and scarring of the bile ducts,

eventually leading to serious liver damage. Tobira's pipeline also includes evogliptin, a selective DPP-4 inhibitor, which it is developing for NASH in combination with CVC. Learn more about Tobira at www.tobiratx.com.

Tobira® is a registered trademark owned by Tobira Therapeutics, Inc.

Forward Looking Statements

This release contains forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements reflect management's current knowledge, assumptions, judgment and expectations regarding future performance or events. Although management believes that the expectations reflected in such statements are reasonable, they give no assurance that such expectations will prove to be correct and you should be aware that actual results could differ materially from those contained in the forward-looking statements. Forward-looking statements are subject to a number of risks and uncertainties including, but not limited to, the company's clinical development of cenicriviroc (CVC) and evogliptin (EVO); the potential timing and outcomes of clinical studies of Tobira's product candidates undertaken now or in the future; the ability of the company to timely source adequate supply of its development products from third party manufacturers on whom the company depends; the company's limited cash reserves and its ability to obtain additional capital on acceptable terms, or at all; the company's ability to successfully progress, partner or complete further development of its programs; the uncertainties inherent in clinical testing; the timing, cost and uncertainty of obtaining regulatory approvals; the company's ability to protect its intellectual property; competition; changes in the regulatory landscape or the imposition of regulations that affect the company's products; and other factors listed under "Risk Factors" in the company's other filings with the Securities and Exchange Commission.

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