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CymaBay Therapeutics Presents Positive Phase 2 Data for Seladelpar in Patients with Primary Biliary Cholangitis at the International Liver Congress™ 2019

NEWARK, Calif., April 12, 2019 (GLOBE NEWSWIRE) -- CymaBay Therapeutics, Inc. (NASDAQ: CBAY), a biopharmaceutical company focused on developing and providing access to innovative therapies for patients with liver and other chronic diseases, today announced positive results from its Phase 2 study of seladelpar in a subset of cirrhotic patients with primary biliary cholangitis (PBC). These data are being presented today at The International Liver Congress™ 2019 of the European Association for the Study of Liver (EASL) in Vienna, Austria, along with three other seladelpar clinical and preclinical presentations. Seladelpar is a potent and selective peroxisome proliferator-activated receptor delta (PPARδ) agonist currently in development for PBC and nonalcoholic steatohepatitis (NASH).

In an oral presentation titled “Seladelpar for the treatment of primary biliary cholangitis: Experience with 25 cirrhotic patients,” Marilyn J Mayo MD, Associate Professor at the University of Texas, Southwestern Medical Center in Dallas, will be reporting the results of a subset of patients with compensated cirrhosis (Child-Pugh A) from an ongoing Phase 2 study designed to assess the safety and efficacy of seladelpar at a daily dose of 5 mg or 10 mg in PBC patients who had an inadequate response (alkaline phosphatase [AP] ≥ 1.67 x upper limit of normal [ULN]) or an intolerance to ursodiol and a total bilirubin ≤ 2 mg/dL. Cirrhosis was diagnosed using liver biopsy, liver elastography, or liver imaging. Patients initiated on 5 mg could be dose-escalated to 10 mg after 12 weeks of treatment if it was tolerated and AP threshold criterion was not met (5/10 mg group). The primary outcome was percent change from baseline in AP. Secondary outcome measures included ALT, total bilirubin, and pruritus using the visual analogue scale (VAS). At 52 weeks in patients with cirrhosis, mean relative decreases in AP were -36% and -43% in the 5/10 mg and 10 mg group, respectively. Treatment with seladelpar also demonstrated robust anti-inflammatory activity with a decrease in ALT comparable to what was observed in non-cirrhotic patients. Total bilirubin remained stable throughout 52 weeks. Seladelpar was well tolerated and appeared safe. Three patients with cirrhosis experienced an SAE, all unrelated to seladelpar. Total bilirubin, platelets, albumin, and INR remained stable. No liver decompensation events were observed. There was no transaminase safety signal, and importantly, seladelpar treatment was not associated with drug-induced pruritus or hepatotoxicity.

“These findings suggest that seladelpar treatment in PBC patients with Child-Pugh A cirrhosis maintained a potent anti-cholestatic effect over 52 weeks,” said Dr. Mayo. “In addition, seladelpar treatment appeared to be safe, was well-tolerated, and was not associated with pruritus or hepatotoxicity which is encouraging given the high unmet need that exists in this population. Confirmation of these findings in the ongoing ENHANCE Phase 3 registration study would be an important advancement in the treatment of PBC.”

A second clinical presentation demonstrates that single dose oral administration of seladelpar was well tolerated and appeared safe in subjects with varying degrees of hepatic impairment (Child-Pugh A-C) and thus provided important information on seladelpar pharmacokinetic exposure and implications for dosing in this challenging population. Additionally, a presentation using the validated GLOBE score to model PBC clinical progression suggests that seladelpar treatment has the potential to be associated with long-term improvement in disease progression.

Finally, a preclinical presentation highlights that seladelpar demonstrated substantial anti-fibrotic and anti-steatotic activity in an obese mouse model of NASH.

Dr. Pol Boudes, Chief Medical Officer of CymaBay, commented, “We are encouraged by the Phase 2 PBC study results of seladelpar in a subset of patients with compensated cirrhosis. We look forward to our continued collaboration with the medical community through our ENHANCE global Phase 3 registration study as well as other ongoing clinical studies to explore how this novel PPARd delta agonist can advance the care and quality of life for patients with PBC and NASH.”

CymaBay’s presentations from The International Liver Congress™ 2019 can be found at: https://ir.cymabay.com/presentations.

About PBC
Primary biliary cholangitis (PBC) is a serious and potentially life-threatening autoimmune disease of the liver characterized by impaired bile flow (cholestasis) and accumulation of toxic bile acids. There is an accompanying inflammation and destruction of the intrahepatic bile ducts, which can progress to fibrosis, cirrhosis and liver failure. Other clinical symptoms of PBC include fatigue and pruritus, which can be quite disabling in some patients. PBC is primarily a disease of women: 1 in 1000 women over the age of 40 lives with PBC.

About NASH
Nonalcoholic steatohepatitis involves the development of a fatty liver that, in patients at risk, triggers inflammation and hepatocellular injury with or without liver fibrosis. The prevalence of nonalcoholic fatty liver disease is increasing, with estimates ranging from 20% to 40% of adults in countries adopting a western diet. Ten to 20% of patients with fatty liver disease progress to nonalcoholic steatohepatitis. Patients with nonalcoholic steatohepatitis are at increased risk of cirrhosis and hepatocellular carcinoma, and nonalcoholic steatohepatitis is projected in the coming years to be the leading reason for liver transplant. Further, most patients with nonalcoholic steatohepatitis have coexisting obesity, insulin resistance with or without type 2 diabetes, hypertension, and dyslipidemia manifested by high serum cholesterol and triglycerides levels.

About Seladelpar
Seladelpar is a potent, selective, orally active PPARδ agonist that is in development for the treatment of the liver diseases PBC and NASH. For PBC, seladelpar has received an orphan designation from the US Food and Drug Administration (FDA) and the European Medicine Agency (EMA). Seladelpar also received Breakthrough Therapy Designation from the FDA and PRIority MEdicine status from the EMA for PBC.

About ENHANCE
ENHANCE (NCT03602560) is a 52-week, placebo-controlled, randomized, Phase 3 study to

evaluate the safety and efficacy of seladelpar. It will be conducted in more than 20 countries over five continents (North America, South America, Europe, Australasia and Asia). Approximately 240 PBC patients will be randomized to seladelpar 10 mg/day, seladelpar 5/10 mg/day (starting treatment at 5 mg with the possibility to escalate dose to 10 mg after 6 months), or placebo. Patients must experience an inadequate response to UDCA (defined as a serum alkaline phosphatase level ≥ 1.67 x the upper limit of normal after at least 12 months of treatment) or an intolerance to UDCA to be eligible for the study. Patients who are inadequate responders to UDCA will continue their treatment during the study, and UDCA will be provided free of charge. The primary outcome measure is the responder rate after 52 weeks. A responder is defined as a patient who achieves an alkaline phosphatase level < 1.67 x the upper limit of normal with at least a 15% decrease from baseline and has a normal level of total bilirubin. Additional key outcomes of efficacy will compare the rate of normalization of alkaline phosphatase at 52 weeks and the level of pruritus at 6-months assessed by a numerical rating scale recorded with an electronic diary. Additional information can be found at https://www.clinicaltrials.gov/ct2/show/NCT03602560?term=seladelpar&rank=2. After completing the study, patients will be offered to continue treatment in an open label extension study. Patients on placebo will be offered to start seladelpar in the extension study.

About CymaBay

CymaBay Therapeutics, Inc. is a clinical-stage biopharmaceutical company focused on developing therapies for liver and other chronic diseases with high unmet medical need. CymaBay's lead development candidate, seladelpar, is a potent, selective and orally active PPARδ agonist currently in development for the treatment of patients with primary biliary cholangitis (PBC), an autoimmune liver disease, and with nonalcoholic steatohepatitis (NASH). Two Phase 2 studies of seladelpar established proof-of-concept in PBC. CymaBay is currently enrolling patients in a global, Phase 3 registration study of seladelpar for PBC. This study is a 52-week, plac**E**bo-co**N**trolled, randomized, p**HA**se 3 study to evaluate the safety a**N**d effi**C**acy of s**E**ladelpar (ENHANCE) in patients with PBC. CymaBay is also conducting a Phase 2b proof-of-concept study of seladelpar in patients with NASH.

Cautionary Statements

The statements in this press release regarding the potential for seladelpar to treat PBC and NASH, the potential benefits to patients, CymaBay's expectations and plans regarding future clinical trials and CymaBay's ability to fund current and planned clinical trials are forward looking statements that are subject to risks and uncertainties. Actual results and the timing of events regarding the further development of seladelpar could differ materially from those anticipated in such forward-looking statements as a result of risks and uncertainties, which include, without limitation, risks related to: the success, cost and timing of any of CymaBay's product development activities, including clinical trials; effects observed in trials to date that may not be repeated in the future; any delays or inability to obtain or maintain regulatory approval of CymaBay's product candidates in the United States or worldwide; and the ability of CymaBay to obtain sufficient financing to complete development, regulatory approval and commercialization of its product candidates in the United States and worldwide. Additional risks relating to CymaBay are contained in CymaBay's filings with the Securities and Exchange Commission, including without limitation its most recent Annual Report on Form 10-K and other documents subsequently filed with or furnished to the Securities and Exchange Commission. CymaBay disclaims any obligation to update these forward-looking statements except as required by law.

For additional information about CymaBay visit www.cymabay.com.

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