CymaBay Announces Positive Topline Results from ENHANCE for Seladelpar in Patients with Primary Biliary Cholangitis

- The study demonstrated seladelpar to be efficacious, safe and well-tolerated
- 78.2% of patients on seladelpar 10 mg versus 12.5% on placebo achieved the primary composite outcome after only 3 months (p<0.0001)
- 27.3% of patients on seladelpar 10 mg versus zero on placebo normalized ALP by 3 months (p<0.0001)
- Statistically significant improvement in pruritus (p<0.05) for patients with moderate-to-severe itch demonstrated for seladelpar 10 mg versus placebo
- Strongly supports re-initiation of Phase 3 study to confirm the potential of seladelpar to be a best-in-class treatment for PBC
- Conference call today at 8:00 a.m. ET

NEWARK, Calif., Aug. 03, 2020 (GLOBE NEWSWIRE) -- CymaBay Therapeutics, Inc. (NASDAQ: CBAY) today announced positive topline results from ENHANCE, a placebo-controlled, randomized, Phase 3 study evaluating the safety and efficacy of seladelpar for the treatment of primary biliary cholangitis (PBC). Seladelpar is a potent and selective peroxisome proliferator-activated receptor delta (PPARδ) agonist that has demonstrated anti-cholestatic and anti-inflammatory effects in clinical studies for PBC.

Sujal Shah, CEO and President of CymaBay Therapeutics, said, “We are thrilled with the results which highlight the safety and efficacy of seladelpar in patients with PBC. Although ENHANCE was terminated prior to completion of the 52-week treatment period, topline data for patients through 12 and 26 weeks of treatment demonstrate robust anti-cholestatic, anti-inflammatory and anti-pruritic activity of seladelpar. These results confirm what was observed in our Phase 2 open-label study and serve to reinforce our confidence in developing seladelpar as a new therapy addressing the key unmet needs for patients as we re-initiate a Phase 3 registration study in PBC. We would like to thank all of the patients and investigators who participated in ENHANCE and who continue to support our efforts.”

ENHANCE was a double-blind, placebo-controlled, global study that randomized 265 PBC patients to placebo, seladelpar 5 mg, or seladelpar 10 mg once daily. Eligible patients had an inadequate response to UDCA (serum alkaline phosphatase level (ALP) ≥ 1.67 x the upper limit of normal (ULN) after at least 12 months) or an intolerance to UDCA. The primary outcome measure was the responder rate defined as a patient who achieved an ALP level < 1.67 x the ULN with at least a 15% decrease from baseline and a normal level of total bilirubin after 52 weeks. Due to the early termination of the study and the small number of patients who had reached the 52 week timepoint, the primary outcome measure was amended prior to database lock to a 3 month timepoint which was reached by 167 of 265
patients. Additional key analyses compared the rate of normalization of ALP and the burden of pruritus assessed by a numerical rating scale (NRS); these were also adjusted to a 3 month timepoint. At baseline, mean ALP levels were 293, 290, and 291 IU/L in the placebo, 5 mg, and 10 mg groups, respectively. Approximately 30% of patients enrolled had moderate-to-severe pruritus based on a NRS (0-10) score ≥4 for itch at baseline. The baseline characteristics were balanced between the 3 groups and representative of a high-risk PBC patient population.

Seladelpar achieved the primary composite outcome with high statistical significance in 78.2% of patients in the 10 mg group (n=55) and 57.1% in the 5 mg group (n=56) compared to 12.5% on placebo (n=56) after 3 months (p<0.0001). Rapid, dose-dependent reductions in ALP were observed as early as one month in seladelpar treated patients with mean decreases of 38%, 30%, and 2% in the 10 mg (n=78), 5 mg (n=78) and placebo groups (n=78), respectively. The anti-cholestatic effect of seladelpar was further substantiated with normalization of ALP levels at 3 months in 27.3% of patients in the 10 mg group vs 0% in the placebo group (p<0.0001). A similar pattern was achieved in these endpoints at 6 months but with smaller numbers of patients reaching this point in the study.

Seladelpar also demonstrated a strong, dose-dependent reduction in pruritus after just 3 months of treatment in those patients with an NRS ≥4 when compared to placebo. A mean reduction of 3.2 points in pruritus NRS from baseline was observed in the 10 mg group compared to a mean 1.6 point reduction in the placebo group (p<0.05).

Professor Marlyn Mayo, M.D., UT Southwestern Medical Center, commented, “Pruritus is a troubling symptom of PBC experienced by as many as 70% of the overall patient population. For patients with moderate-to-severe pruritus, the negative consequences to quality of life can be significant. Seladelpar’s effects on reducing pruritus in this controlled data set provided a significant number of patients a clinically meaningful benefit that has not been demonstrated in a well-controlled, global study with any other treatment alternative studied in PBC patients to date. With no approved therapies for cholestatic pruritus, seladelpar has the potential to be a groundbreaking treatment alternative for patients with PBC."

Treatment with seladelpar also demonstrated robust anti-inflammatory activity at 3 months with mean ALT decreases of 17% in the 10 mg group vs 3% in the placebo group (p<0.05). The effect of seladelpar treatment on gamma-glutamyl transferase (GGT) was also highly significant with a decrease of 36% in the 10 mg group compared to 7% in the placebo group (p<0.0001).

Total bilirubin remained stable across all 3 groups. Seladelpar demonstrated a favorable safety and tolerability profile. The adverse events were similar across the seladelpar and placebo groups. There were no grade 3 or higher ALT elevations observed.

Professor Gideon Hirschfield, M.D., University of Toronto, said, “The results presented are exciting and are a cause for optimism for patients living with PBC. Data from this study show that seladelpar appears safe and well tolerated and the efficacy demonstrated points to the potential for seladelpar to be a best-in-class treatment alternative for patients with PBC. There is now a significant level of experience in the medical community with seladelpar. I believe investigators and patients will continue to support CymaBay’s future efforts to make this a breakthrough therapy ultimately available to patients with PBC living everywhere."
Conference Call
CymaBay will host a conference call today at 8:00 a.m. ET to discuss the topline results from this study. To access the live conference call, please dial 877-407-0784 from the U.S. and Canada, or 201-689-8560 internationally, Conference ID# 13708029. To access the live and archived webcast of the conference call, go to the Investors section of the CymaBay website at http://ir.cymabay.com/events. A slide presentation will be visible on the webcast during the call and will also be available in the Investors section of the CymaBay website.

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 Seladelpar
Seladelpar is a potent, selective, orally active PPARδ agonist that has been in development for the treatment of the liver diseases PBC and nonalcoholic steatohepatitis (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 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.

Cautionary Statements
Any statements made in this press release and accompanying conference call regarding the potential for seladelpar to treat PBC and potentially improve clinical symptoms of the disease, the potential benefits to patients, CymaBay's expectations and plans regarding its intended future interactions with the FDA, its current and 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 seladelpar histological findings that have not yet been submitted to the FDA, and there is no guarantee as to how or when the FDA will respond; 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 or to potentially restart clinical trials. 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](http://www.cymabay.com).

**Public Relations Contact:**

Glenn Silver  
Lazar-FINN Partners  
(973) 818-8198  
[Glenn.silver@finnpartners.com](mailto:Glenn.silver@finnpartners.com)

**Investor Relations Contact:**

Hans Vitzthum  
LifeSci Advisors, LLC  
(617) 430-7578  
[Hans@LifeSciAdvisors.com](mailto:Hans@LifeSciAdvisors.com)

Source: CymaBay Therapeutics, Inc.