CymaBay Presents Results on the Potential of Seladelpar in Treatment of Patients with Primary Biliary Cholangitis at ACG 2023

Cholestatic pruritus expert leads plenary discussion of correlated decreases in serum IL-31 levels and pruritus among patients with PBC treated with seladelpar

A second presentation of baseline trial data suggests that any elevation in key liver biomarkers may put PBC patients at risk for disease progression and poor outcomes

VANCOUVER, British Columbia, Oct. 23, 2023 (GLOBE NEWSWIRE) -- CymaBay Therapeutics, Inc. (NASDAQ: CBAY), a biopharmaceutical company focused on innovative therapies for patients with liver and other chronic diseases, announced today the presentation of findings from its post-hoc analysis of the Phase 3 ENHANCE study of seladelpar for the treatment of primary biliary cholangitis (PBC), showing baseline intensity of patient-reported pruritus was associated with higher levels of serum IL-31. The presentation, named the recipient of this year’s International Award by the American College of Gastroenterology, will be presented by Professor Andreas E. Kremer, MD, Ph.D., MHBA, a leading authority in cholestatic pruritus from the University of Zurich. Featured results included novel aspects of the anti-pruritic and anti-cholestatic mechanisms of seladelpar, CymaBay’s first-in-class oral, selective PPARδ agonist, or “delpar,” being investigated for the treatment of patients with PBC.

The data were previously presented at the European Association for the Study of the Liver (EASL)’s The International Liver Congress™ 2023 in Vienna, Austria.

“Despite pruritus being an excruciating symptom experienced by many patients with PBC, to date, there has been limited understanding of the underlying pathology of itch and how to effectively treat this issue,” said Dr. Kremer. “These results offer a glimmer of hope in that they link IL-31 levels in patients with PBC to itch. What we are seeing in our research is that treatment with seladelpar is correlated with a significant decrease in both IL-31 levels and levels of patient-reported itch. This is a unique opportunity for researchers to further explore the relationship between the IL-31 pathway and itch, which may help us improve how we address an important, and often distressing, unmet need for patients.”

The company also presented a post-hoc analysis of four seladelpar clinical trials from 2015 to 2022, which found that PBC patients previously treated with ursodeoxycholic acid (UDCA, the first-line therapy for PBC) with elevated alkaline phosphatase (ALP) who did not meet current clinical guidelines for second-line treatment, nevertheless had a significant risk of disease progression.

“Across our clinical trials, we see that patients with any level of ALP elevation have multiple factors that pose a risk for disease progression, even though many of them do not meet the
current requirements for second-line treatment under current treatment guidelines,” said Charles McWherter, Ph.D., Chief Scientific Officer and President of Research and Development at CymaBay. “We already know there is an unmet need for treatment options for patients with this rare, devastating liver disease. These data suggest there may be an even greater number of patients who could benefit from earlier treatment to slow disease progression than are currently accounted for in medical practice.”

Presentation Details:

Seladelpar treatment resulted in correlated decreases in serum IL-31 and pruritus in patients with PBC: post-hoc results from the Phase 3 randomized, placebo-controlled ENHANCE study
October 23rd 2:35pm – 2:45pm PT
Presentation 17, Plenary Session 1B - Liver
Presenter: Andreas Kremer

A post-hoc analysis of the Phase 3 ENHANCE trial showed a correlation between serum IL-31 levels and self-reported pruritus improvements in patients with PBC after three months of treatment with seladelpar. This included seladelpar 5 mg (3.8 to 1.7 pg/mL, p < 0.001), 10 mg (4.2 to 1.7 pg/mL, p < 0.001) compared to placebo (4.3 to 3.9 pg/mL, not significant). The IL-31 pathway is a validated therapeutic target for pruritus in other diseases, such as atopic dermatitis.

Patients with clinically meaningful improvement in pruritus (≥ 2 decreases in numerical rating scale, or NRS, score) showed greater dose-dependent reductions in IL-31 from baseline than those without pruritus improvement.

Significant correlations were also observed between changes in IL-31 versus reported pruritus NRS scores (r = 0.54, p < 0.0001), alkaline phosphatase (ALP) levels (r = 0.40, p <0.01), and total bile acids (r = 0.63, p < 0.0001) in the seladelpar 10mg group. These results suggest a relationship between IL-31 levels and severity of itch, a symptom associated with PBC that remains an outstanding unmet need for patients.

The ACG International Award for this abstract will be presented to Dr. Kremer during the ACG Awards Reception, taking place from 6:30 to 7:30 p.m. on Monday, October 23, 2023 in Room 302 at the Vancouver Convention Center.

Baseline characteristics and risk profiles of 1111 patients with PBC in need of second-line therapy
October 24th 10:30am – 4:00pm PT
Poster #P3788
Presenter: Gideon Hirschfield

A post-hoc analysis of four seladelpar clinical trials from 2015 to 2022 looked at 1111 patients in 27 countries with PBC after treatment with UDCA for greater than or equal to 12 months, or who had intolerance to UDCA. The analysis compared the baseline characteristics and risk profiles of PBC patients with elevated ALP levels (greater than or equal to 1.67x upper limit of normal, or ULN) to patients who did not meet this standard ALP threshold for inclusion yet still had a slightly elevated ALP level (above ULN, but below 1.67x ULN). Additional elevated risk was identified based on Enhanced Liver Fibrosis (ELF) scores
and liver stiffness using Fibroscan®. Elevated risk due to ELF was identified in 43.2% of patients who currently meet guidelines for second-line treatment vs. 27.2% within patient groups not recommended for second-line treatment.

The data showed that patients previously treated with UDCA with persistent elevation of ALP, but who were not currently recommended by guidelines for second-line treatment, had a significant risk for disease progression, highlighting the need for second-line therapy for a broader patient group.

About PBC
PBC is a rare, chronic inflammatory liver disease primarily affecting women (1 in 1,000 women over the age of 40 or about 130,000 total people in the US). PBC is characterized by impaired bile flow (known as cholestasis) and the accumulation of toxic bile acids in the liver, leading to inflammation and destruction of the bile ducts within the liver and causing increased levels of ALP and total bilirubin. The most common early symptoms of PBC are pruritus (itching) and fatigue, which can be debilitating for some patients. Progression of PBC is associated with an increased risk of liver-related mortality.

About Seladelpar
Seladelpar, an investigational treatment for people with PBC, is a first-in-class oral, selective peroxisome proliferator-activated receptor (PPAR) delta agonist, or delpar, shown to regulate critical metabolic and liver disease pathways in indications with high unmet medical need. Preclinical and clinical data support its ability to regulate genes involved in bile acid synthesis, inflammation, fibrosis and lipid metabolism, storage, and transport.

About CymaBay
CymaBay Therapeutics, Inc. is a clinical-stage biopharmaceutical company focused on improving the lives of people with liver and other chronic diseases that have high unmet medical need through a pipeline of innovative therapies. Our deep understanding of the underlying mechanisms of liver inflammation and fibrosis, and the unique targets that play a role in their progression, have helped us receive breakthrough therapy designation (U.S. Food and Drug Administration), Priority Medicines status (European Medicines Agency) and orphan drug status (U.S. and Europe) for seladelpar, a first-in-class investigational treatment for people with PBC. Our evidence-based decision-making and commitment to the highest quality standards reflect our relentless dedication to the people, families, and communities we serve. To learn more, visit www.cymabay.com and follow us on X (formerly Twitter) and LinkedIn.

Cautionary Statements
Any statements made in this press release regarding the potential for seladelpar to treat PBC and potentially improve clinical symptoms of the disease, the potential benefits to patients and the future filing plans of CymaBay 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; and effects observed in trials to date that may not be repeated in the future. 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, its Quarterly Reports on Form 10-Q 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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