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CymaBay Therapeutics Announces Oral Late-Breaking Presentation of Positive Results from the ENHANCE Global Phase 3 Study Evaluating Seladelpar for Primary Biliary Cholangitis at The Liver Meeting® 2020

- *Seladelpar demonstrated anti-cholestatic, anti-inflammatory, and anti-pruritic activity through 3 and 6 months*
- *Results highlight the potential for seladelpar to offer patients an efficacious and safe second line treatment option*
- *Global 52-week Phase 3 registration study (**RESPONSE**) to begin enrolling patients in Q1 of 2021*

NEWARK, Calif., Nov. 16, 2020 (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 an oral late-breaking presentation of the positive results from the **ENHANCE** phase 3 study evaluating seladelpar for primary biliary cholangitis (PBC). These data were presented online today during the late-breaking session at The Liver Meeting® of the American Association for the Study of Liver Diseases (AASLD).

In an oral presentation titled, ‘**ENHANCE**: Safety and efficacy of Seladelpar in Patients with Primary Biliary Cholangitis (PBC) – A Phase 3, International, Randomized, Placebo-Controlled Study,’ Professor Gideon Hirschfield, FRCP PhD, Lily and Terry Horner Chair in Autoimmune Liver Disease at the University of Toronto, presented results from **ENHANCE**, a phase 3 study of seladelpar in patients with PBC. Eligible PBC patients with either an inadequate response, defined as alkaline phosphatase (ALP) greater than or equal to 1.67 times the upper limit of normal (ULN), or intolerance to ursodeoxycholic acid (UDCA) were randomized to daily seladelpar 5 or 10 mg or placebo (pbo). The primary endpoint was a composite response of ALP <1.67x ULN, ALP decrease ≥15% and total bilirubin (TB) ≤ULN at Month 12. Secondary endpoints were ALP normalization at Month 12 and change in pruritus numerical rating scale (NRS) at Month 6. 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. After only 3 months, 78.2% of patients on seladelpar 10 mg versus 12.5% on placebo achieved the primary composite outcome (p<0.0001). In addition, 27.3% of patients on seladelpar 10 mg versus zero on placebo experienced normalization of ALP by 3 months (p<0.0001).

Treatment with seladelpar 10 mg also resulted in a statistically significant improvement in pruritus ($p < 0.05$) for patients with moderate-to-severe itch at baseline versus placebo. Additional data highlighted the sustained anti-cholestatic, anti-inflammatory, and anti-pruritic effects of seladelpar through six months. Overall, seladelpar appeared to be safe and well-tolerated in this study. The only AE in $>10\%$ of patients was pruritus in 12.6%, 3.4%, and 11.2% in the pbo, 5 and 10 mg groups, respectively. There were no treatment-related serious adverse events and 2 treatment-emergent AEs led to study discontinuation.

“These findings suggest that seladelpar treatment is well positioned to be a preferred second line treatment for patients with PBC,” said Professor Hirschfield. “Data from this study show that seladelpar appears efficacious, safe, and well-tolerated. Given the high unmet need that exists in the PBC population, I believe investigators and patients will continue to support CymaBay’s efforts to make this breakthrough therapy available to patients.”

A second clinical presentation titled, “A 52-Week Multi-Center Double-Blind Randomized Phase 2 Study of Seladelpar, a potent and selective peroxisome proliferator-activated receptor delta (PPAR- δ) agonist, in Patients with Nonalcoholic Steatohepatitis (NASH),” was presented by Dr. Stephen A. Harrison, MD, Medical Director of Pinnacle Clinical Research. This electronic poster presentation was selected by AASLD for special recognition as a “Poster of Distinction” and highlighted the effects of seladelpar on liver fat, liver enzymes, and key histologic endpoints recognized by regulators for registration, including NASH resolution and reduction in fibrosis.

Sujal Shah, CEO of CymaBay Therapeutics, commented, “The results from the **ENHANCE** study provide encouraging evidence of the anti-cholestatic, anti-inflammatory and anti-pruritic effects of seladelpar in patients with PBC. We look forward to further collaboration with the medical community as we anticipate the initiation of our **RESPONSE** global Phase 3 registration study. In addition to our core focus in PBC, we continue to explore how this novel PPAR δ agonist can advance care and target other indications with high unmet needs.”

CymaBay’s presentations from The Liver Meeting® 2020 can be found at: <https://ir.cymabay.com/presentations>.

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 PPAR δ agonist currently in development for the treatment of patients with primary biliary cholangitis (PBC). CymaBay is currently planning a global, Phase 3 registration study of seladelpar for PBC. This study is a 52-week, placebo-controlled, randomized, phase 3 study to evaluate the safety and efficacy of seladelpar (**RESPONSE**) in patients with PBC.

About RESPONSE

RESPONSE (NCT04620733) is a 52-week, placebo-controlled, randomized, global phase 3 study to evaluate the safety and efficacy of seladelpar in patients with primary biliary cholangitis (PBC). It is expected to be conducted in more than 20 countries over five continents (North America, South America, Europe, Australia and Asia). Approximately 180 PBC patients will be randomized to seladelpar 10 mg/day, or placebo. Patients must have an inadequate response to UDCA (defined as a serum alkaline phosphatase level $\geq 1.67 \times$ 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 UDCA treatment during the study. The primary outcome measure will be the responder rate at 52 weeks. A responder is defined as a patient who achieves an alkaline phosphatase level $< 1.67 \times$ 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 for patients with moderate to severe pruritus at baseline assessed by a numerical rating scale recorded with an electronic diary. Additional information can be found at <https://www.clinicaltrials.gov/>. After completing the study, patients will be able to continue treatment in **ASSURE**, an open-label, long-term study. Patients on placebo will be able to start seladelpar treatment in the **ASSURE** study.

About Seladelpar

Seladelpar is a potent, selective, orally active PPAR δ agonist that has been in development for the treatment of the liver diseases primary biliary cholangitis (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 for early stage PBC and PRiority MEdicine status from the EMA.

Cautionary Statements

The statements in this press release regarding the potential for seladelpar to treat PBC or NASH, the potential benefits to patients, CymaBay's expectations and plans regarding 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 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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