June 11, 2019

CymaBay Therapeutics Reports Topline 12-Week Data from an Ongoing Phase 2b Study of Seladelpar in Patients with Nonalcoholic Steatohepatitis

- *Reductions in liver fat were minimal and not significant compared to placebo*
- *Reductions in markers of liver injury were robust and clinically meaningful*
- *Seladelpar appears to be safe and well-tolerated across all doses*
- *Blinded study will continue to 52-week liver biopsy*
- *Conference call today at 8 a.m. ET*

NEWARK, Calif., June 11, 2019 (GLOBE NEWSWIRE) -- CymaBay Therapeutics, Inc. (NASDAQ: CBAY) today announced 12-week topline results from an ongoing 52-week Phase 2b dose-ranging, paired liver biopsy study of seladelpar for the treatment of nonalcoholic steatohepatitis (NASH). Seladelpar is a potent and selective peroxisome proliferator-activated receptor delta (PPARδ) agonist currently in development for NASH and primary biliary cholangitis (PBC).

The double-blind, placebo-controlled study randomized 181 subjects with biopsy-confirmed NASH and a liver fat content (LFC) greater than 10% to receive either placebo or seladelpar 10 mg, 20 mg, or 50 mg once-daily. The enrolled subjects had established NASH with a mean NAFLD Activity Score of 5.2 at baseline, with 83% of subjects having stage 2 or stage 3 fibrosis. Other key baseline characteristics include a mean LFC by magnetic resonance imaging-proton density fat fraction (MRI-PDFF) of 21% as well as elevated mean ALT and AST levels of 62 U/L and 46 U/L, respectively. Approximately half of the subjects enrolled had a diagnosis of type 2 diabetes. The primary endpoint was the relative change in LFC from baseline to 12 weeks. The study remains blinded and will continue to 52 weeks with assessments including a liver biopsy, non-invasive imaging evaluations, and biomarker assessments of inflammation and fibrosis.

Reductions in LFC as measured by MRI-PDFF at week 12 are highlighted in the table below. Treatment with seladelpar resulted in minimal reductions in liver fat that were not significant when compared to placebo.

	Placebo (n=26)	Seladelpar 10 mg (n=50)	Seladelpar 20 mg (n=47)	Seladelpar 50 mg (n=48)
Relative Change in LFC from Baseline (LS Mean, SE)	-20.8% (5.6)	-9.8% (4.2) p=0.087	-14.2% (4.3) p=0.32	-13.0% (4.3) p=0.23
Proportion of Subjects with ≥ 30% Relative Reduction in LFC	30.8%	24.0% p=0.66	25.5% p=0.47	18.8% p=0.23
Absolute Change in LFC from Baseline (LS Mean, SE)	-4.7% (1.1)	-2.6% (0.9) p=0.10	-3.3% (0.9) p=0.28	-2.7% (0.9) p=0.14
Proportion of Subjects with ≥ 5% Absolute Reduction in LFC	34.6%	30.0% p=0.41	38.3% p=0.48	25.0% p=0.049

mITT = modified intent-to-treat population; LFC = Liver Fat Content LS Mean = Least-Square mean; p-values relative to placebo

Treatment with seladelpar resulted in robust and clinically meaningful reductions in markers associated with liver injury as highlighted in the table below. Alanine aminotransferase (ALT) declined up to 37.5% or 32 U/L in 12 weeks. These reductions in ALT are significantly greater than the 17 U/L threshold that has been correlated with histologic improvement in NASH. Gamma glutamyl transferase (GGT) also decreased significantly, suggesting a reduction in hepatocellular oxidative stress. Significant reductions in alkaline phosphatase (AP) at 12 weeks were observed, supportive of a decrease in hepatocellular bile acids. The marked changes in these liver enzymes collectively suggest the potential to impact ballooning and lobular inflammation, the two key components of NASH resolution.

Relative Change from Baseline to Week 12 (LS Mean, SE)	Placebo (n=27)	Seladelpar 10 mg (n=53)	Seladelpar 20 mg (n=51)	Seladelpar 50 mg (n=50)
ALT	-8.9% (5.1) p=0.08	-22.9% (3.8) p<0.0001	-32.0% (4.0) p<0.0001	-37.5% (4.0) p<0.0001
AST	-12.9% (5.8) p=0.03	-11.6% (4.4) p=0.009	-15.2% (4.5) p=0.001	-17.3% (4.5) p=0.0002
GGT	-4.5% (4.3) p=0.3	-28.2% (3.2) p<0.0001	-37.6% (3.3) p<0.0001	-43.1% (3.4) p<0.0001
AP	4.4% (2.9) p=0.12	-19.1% (2.1) p<0.0001	-25.1% (2.2) p<0.0001	-33.4% (2.2) p<0.0001

ALT, AST, GGT, AP from safety population; p-values relative baseline

Dr. Stephen Harrison, MD, Medical Director of Pinnacle Clinical Research, founder of Summit Clinical Research and principal coordinating investigator of the seladelpar Phase 2b NASH Study, commented, “NASH is a complex, multifactorial disease that can lead to liver injury and fibrosis. These data demonstrated a notable decrease in biochemical markers of liver injury despite lack of overall improvement in liver fat. The dose response relationship in serum ALT reduction is very encouraging and supports the potential histopathologic benefit of seladelpar in patients with NASH. We are looking forward to the 52-week histology results.”

Professor Mary Rinella, MD, Department of Gastroenterology and Hepatology, Northwestern University, stated, “It is encouraging to see the impressive decrease in ALT and GGT consistent with a reduction in hepatic inflammation and possibly oxidative stress. The

magnitude of reduction in ALT exceeds thresholds shown in recent publications to correlate with histologic improvements in the context of NASH."

Treatment with seladelpar also resulted in reductions in low-density lipoprotein cholesterol (LDL-C) and triglycerides. At 12 weeks, the median percent changes in LDL-C were 7.8, -7.5, -8.4, and -14.4 in the placebo, seladelpar 10, 20, and 50 mg groups, respectively. The median percent change in triglycerides were 14.4, -9.1, -4.0, and -10.0 in the placebo, seladelpar 10, 20, and 50 mg groups, respectively. There were no significant changes in high-density lipoprotein cholesterol. High sensitivity C-reactive protein (hs-CRP), a key marker of inflammation and cardiovascular risk, decreased by a greater magnitude in seladelpar-treated subjects, with median percent changes were -3.1, -16.7, -20.7, and -22.6 in the placebo, seladelpar 10, 20, and 50 mg groups, respectively.

Seladelpar demonstrated a favorable safety and tolerability profile at all doses evaluated in this study. The most common (>5%) treatment emergent adverse events included nausea, constipation, dizziness, headache, gastroesophageal reflux disease and upper abdominal pain. The majority of treatment emergent adverse events were mild to moderate in severity and deemed unrelated to study drug. There were two serious adverse events that occurred after randomization through week 12, neither of which were deemed to be related to study drug.

Dr. Pol Boudes, MD, Chief Medical Officer of CymaBay Therapeutics, added, "While the reductions in liver fat were minimal, we remain encouraged by the significant improvements in biochemical markers of liver injury that we observed at week 12. The 52-week liver biopsy data will allow us to understand whether the improvement in liver injury markers will translate into histological improvement. The observed improvement in markers of liver injury are consistent with the observed effects of seladelpar in PBC and further support the potential for seladelpar to improve liver health."

Conference Call

CymaBay will host a conference call today at 8 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# 13691603. A slide presentation to be used in connection with the call entitled "Seladelpar 12-Week Data – Phase 2b Study in NASH" will be posted on CymaBay's website at http://ir.cymabay.com/presentations. 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.

About the Phase 2b NASH Study

The randomized, placebo-controlled study (NCT03551522) enrolled 181 subjects who had a diagnosis of NASH with fibrosis established by liver biopsy. Prior to a baseline biopsy, subjects were required to have a liver fat content greater than 10% using the magnetic resonance imaging-proton density fat fraction (MRI-PDFF) method. Subjects were randomized to receive either seladelpar 10 mg, 20 mg, or 50 mg or placebo once daily. In addition, subjects were stratified at randomization by the stage of liver fibrosis and the presence or absence of type 2 diabetes. The primary efficacy outcome is the change from baseline in liver fat content at 12 weeks as measured by MRI-PDFF. Among the secondary measures of efficacy, most notable is the evaluation of histological improvement in NASH and fibrosis as assessed by comparing liver biopsy samples taken at baseline and 52 weeks. Additional important planned assessments include MRI-PDFF measurements at 26

and 52 weeks of treatment, as well as the use of the latest available additional technologies for biochemical markers and non-invasive imaging, which reflect inflammation, fibrosis and liver health. Additional information can be found at https://clinicaltrials.gov/ct2/show/NCT03551522?cond=seladelpar&rank=2.

About NASH

Nonalcoholic steatohepatitis (NASH) 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 NASH. Patients with NASH are at increased risk of cirrhosis and hepatocellular carcinoma, and NASH is projected in the coming years to be the leading reason for liver transplant. Further, most patients with NASH 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 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 study of seladelpar for 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, the continuation of trials, CymaBay's expectations and plans regarding 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; unexpected clinical results; any delays or inability to obtain or maintain regulatory approval of CymaBay's product candidates; and the ability of CymaBay to obtain sufficient financing to complete development, regulatory approval and commercialization of its product candidates. 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.

Contact:
Hans Vitzthum
LifeSci Advisors, LLC
212-915-2568
Hans@LifeSciAdvisors.com

Source: CymaBay Therapeutics, Inc.