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CymaBay Therapeutics Announces Positive Results from its Pilot Phase 2 Clinical Study of MBX-8025 in Patients with Homozygous Familial Hypercholesterolemia

NEWARK, Calif., March 17, 2016 (GLOBE NEWSWIRE) -- CymaBay Therapeutics, Inc. (NASDAQ:CBAY) today announced top line results from its pilot Phase 2 clinical study of MBX-8025 in patients with homozygous familial hypercholesterolemia (HoFH). The study demonstrated that the range of responses to MBX-8025 was broad, but that MBX-8025 provided a clinically meaningful reduction in low-density lipoprotein cholesterol (LDL-C) for a subset of patients. This is the first study to demonstrate the potential utility of a PPARδ agonist in HoFH.

“This pilot study provides the first evidence that MBX-8025 has potential utility for the treatment of HoFH, an ultra-orphan disease in which patients remain in need of additional LDL-C lowering,” said Harold Van Wart, Chief Executive Officer of CymaBay.

Study objectives and design

This was an open label, dose escalation study of 12 weeks duration conducted at five centers in Europe and Canada. Thirteen patients were enrolled, all of whom had genetically confirmed HoFH, including two subjects who had functionally negative mutations in their LDL receptor (LDL-R) genes. All of the subjects were taking ezetimibe and were on maximum statin therapy. None of the study participants received lomitapide, mipomersen or a PCSK9 inhibitor. Eight patients were undergoing concomitant apheresis on a weekly or biweekly schedule. Despite being on maximal conventional therapy, the average baseline LDL-C was 368 mg/dL. Subjects received once daily treatment with 50 mg of MBX-8025 for 4 weeks, after which the dose was escalated to 100 and 200 mg in successive 4-week periods. The goals of the study were to evaluate the effect on LDL-C as well as a spectrum of other lipid-related parameters, including PCSK9 levels, and to collect safety information.

Results

Two per-protocol analyses were performed on 12 subjects. The data for one subject was excluded because of multiple missed apheresis visits throughout the study which caused marked fluctuations in LDL-C levels. A responder analysis was carried out which reflects the largest decrease in LDL-C observed during treatment for each subject. Three subjects (25%) exhibited a greater than or equal to 30% decrease. Five subjects (42%) had a greater than or equal to 20% decrease, including one patient that was receptor negative, and 7 (58%) had a greater than or equal to 15% decrease. Five subjects (42%) had a less than 15% decrease. The average maximum decrease in the study was 19%. Because of the high baseline LDL-C levels in these individuals, these percentage decreases correspond to significant absolute decreases in LDL-C (mean decrease of 109 mg/dL for the subjects with a greater than or equal to 15% decrease). Although reductions in LDL-C tended to be greater at the higher doses, no clear dose response was observed.

In a second analysis, the mean change in LDL-C for each subject was calculated by averaging values across all doses and dosing periods while on treatment. The overall mean change for all 12 subjects was a decrease of 10%. Eight of these subjects had a mean decrease in LDL-C of 16%, including 3 with a greater than 20% decrease. This included one patient that was receptor negative. This was offset by 4 patients who showed a mean increase of 4%.

Mean PCSK9 was elevated at baseline (544 +/- 133 ng/mL), as anticipated for patients with HoFH, and increased significantly during treatment by a mean of 43%. During the study, decreases in the mean levels of alkaline phosphatase (30%), gamma glutamyl transferase (27%) and total bilirubin (22%), which are markers of cholestasis, were also observed. There were three SAEs, none drug related, and three treatment discontinuations for AEs possibly related to MBX-8025.

“Despite the availability of new therapies, including PCSK9 inhibitors, most patients with HoFH remain far from their LDL-C targets and there is still a need for new therapeutic approaches,” said Dr. Evan Stein, Director Emeritus of

the Medpace Metabolic and Atherosclerosis Research Center. “The finding that MBX-8025 lowers LDL-C, despite the unexpected increase in PCSK9, suggests that studies on top of PCSK9 inhibitors may be warranted to further assess the potential of MBX-8025 treatment in patients with HoFH.”

“We are encouraged by the meaningful response in LDL-C reductions observed in a number of patients in the study and plan to evaluate the feasibility of conducting a pilot study of MBX-8025 in combination with a PCSK9 inhibitor,” said Harold Van Wart.

Conference Call

CymaBay will host a conference call today, March 17, 2016, at 4:30 p.m. ET / 1:30 p.m. PT to discuss the results of this pilot Phase 2 study. The call can be accessed by dialing 877-407-0784 (domestic) and 201-689-8560 (international) five minutes prior to the start of the call. A slide presentation to be used in connection with the call entitled “MBX-8025 Pilot Study in HoFH Top Line Data” has been posted on CymaBay’s website and can be accessed at http://ir.cymabay.com/presentations. A live audio webcast of the call can be accessed under the Investors section of CymaBay’s website at http://ir.cymabay.com/events and will be available for 14 days following the call.

About MBX-8025

MBX-8025 is a potent and selective agonist of PPARδ, a nuclear receptor important for lipid transport, storage and metabolism in liver and muscle. MBX-8025 has shown favorable effects on lipid and other metabolic parameters in a Phase 2 study in patients with mixed dyslipidemia. Treatment effects observed include lowering of LDL-C with selective depletion of pro-atherogenic dense LDL particles, decreases in triglycerides and increases in HDL, as well as decreases in hsCRP, a biomarker of cardiovascular and systemic inflammation. MBX-8025 also decreased levels of alkaline phosphatase and gamma glutamyl transferase, which are markers of cholestasis. The U.S. Food and Drug Administration (FDA) has granted the Company orphan drug designation for MBX-8025 as a treatment for HoFH and Fredrickson types I and V hyperlipoproteinemia. CymaBay has also initiated a Phase 2 study of MBX-8025 in patients with primary biliary cholangitis.

About HoFH

HoFH is a rare, life-threatening, autosomal genetic disease characterized by loss-of-function mutations in both alleles of the LDL receptor (LDL-R) gene. The accompanying loss of LDL-R activity results in marked elevations in the plasma levels of LDL cholesterol (LDL-C), causing premature cardiovascular disease that often presents during the first decades of life and which can result in myocardial infarction, ischemic stroke and premature death.

About CymaBay

CymaBay Therapeutics, Inc. (CBAY) is a clinical-stage biopharmaceutical company developing therapies to treat metabolic diseases with high unmet medical need, including serious rare and orphan disorders. MBX-8025 is a potent, selective, orally active PPARδ agonist. A Phase 2 study of MBX-8025 in patients with mixed dyslipidemia established that it has an anti-atherogenic lipid profile. CymaBay has completed a pilot Phase 2 study of MBX-8025 in patients with homozygous familial hypercholesterolemia and has an ongoing Phase 2 study in patients with primary biliary cholangitis. Arhalofenate, CymaBay’s other product candidate, is a potential Urate-Lowering Anti-Flare Therapy that has completed five Phase 2 studies in gout patients. Arhalofenate has been found to reduce painful flares in joints while at the same time promoting excretion of uric acid by the kidney. This dual action addresses both the signs and symptoms of gout while managing the underlying pathophysiology of hyperuricemia.

Cautionary Statements

The statements in this press release, including those statements regarding the structure and conduct of clinical trials, future performance of CymaBay's product candidates, the potential of MBX-8025 to treat homozygous familial hypercholesterolemia or primary biliary cholangitis, the therapeutic and commercial potential of MBX-8025, and any of the targeted indications for the potential future development or commercialization of MBX-8025 are forward looking statements that are subject to risks and uncertainties. Actual results and the timing of events regarding the further development of MBX-8025 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 of MBX-8025; effects observed in trials to date which 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 Quarterly Report 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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