January 28, 2015

CymaBay Therapeutics Announces Preclinical Data Demonstrating the Potential of MBX-8025 to Treat Homozygous Familial Hypercholesterolemia

MBX-8025 Produced Decreases of up to 45% in LDL-C Levels in a Genetic Rabbit Model of Homozygous Familial Hypercholesterolemia

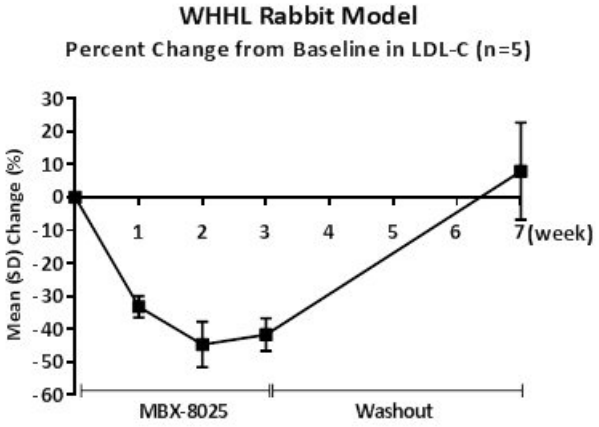
NEWARK, CA -- (Marketwired) -- 01/28/15 -- CymaBay Therapeutics(NASDAQ: CBAY) today announced results from a preclinical study indicating the potential for MBX-8025 to decrease low-density lipoprotein cholesterol (LDL-C) in patients with homozygous familial hypercholesterolemia (HoFH). MBX-8025 is a potent and selective peroxisome proliferator-activated receptor delta (PPARδ) agonist that, in previous clinical studies, has been shown to reduce LDL-C in patients with mixed dyslipidemia. CymaBay believes that MBX-8025 has the potential to markedly improve the lipid profile of patients with various forms of dyslipidemia, including 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. This loss of LDL-R activity results in marked elevations in the plasma levels of 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. Patients with HoFH generally respond poorly to conventional cholesterol lowering drugs because their activities depend directly or indirectly on LDL-R activity. Data from the preclinical study described below support the hypothesis that the LDL-C lowering activity of MBX-8025 is not dependent on having a fully functional LDL-R. Based on these data, CymaBay is in the process of initiating a pilot clinical study evaluating the activity of MBX-8025 in patients with HoFH.

Preclinical Study of MBX-8025 in the Watanabe Rabbit Model of HoFH

The Watanabe-heritable hyperlipidemic (WHHL) rabbit is a preclinical model of HoFH that is characterized by low (< 5%) hepatic LDL-R activity, highly elevated LDL-C and the accompanying development of atherosclerosis. In this study, five WHHL rabbits with highly elevated baseline plasma LDL-C levels (360-592 mg/dL) were dosed by subcutaneous administration of MBX-8025 (30 mg/kg) once daily for three weeks, followed by a four-week washout period. LDL-C concentrations were measured once weekly during treatment (weeks 1-3) and after washout of MBX-8025 (week 7).

Treatment with MBX-8025 resulted in changes from baseline in mean LDL-C of -33, -45 and -42% at weeks 1, 2 and 3, respectively (see figure). All animals experienced absolute decreases in LDL-C (114-302 mg/dL; p < .01 for all changes vs. baseline). Furthermore, this LDL-C lowering effect of MBX-8025 was completely reversed after a washout period of 4 weeks.



"MBX-8025 demonstrated significant and meaningful decreases in LDL-C in this study with WHHL rabbits, a preclinical model of human HoFH," said Charles McWherter, Ph.D., Chief Scientific Officer of CymaBay. "These results strengthen the rationale for using MBX-8025 for the treatment of patients with HoFH because of the observed LDL-C lowering effect in the setting of low LDL-R activity."

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 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-C particles, decreases in triglycerides and increases in high density lipoprotein, as well as decreases in hsCRP, a biomarker of cardiovascular inflammation. CymaBay is in the process of initiating a pilot clinical study evaluating the activity of MBX-8025 in patients with homozygous familial hypercholesterolemia.

About CymaBay

CymaBay Therapeutics, Inc. (NASDAQ: CBAY) is a clinical-stage biopharmaceutical company developing therapies to treat metabolic diseases with high unmet medical need, including serious rare and orphan disorders. Arhalofenate, the company's lead product candidate, has shown two therapeutic actions in a single drug in three prior Phase 2 gout studies. In gout patients, arhalofenate is intended to reduce painful flares in joints while at the same time promoting excretion of serum uric acid (sUA) by the kidney, thereby addressing both the signs and symptoms of gout and the hyperuricemia that is the root cause of the disease. In addition to the studies described above, CymaBay has an ongoing 12-week Phase 2b clinical trial in patients with gout designed to detect statistically significant reductions in gout flares. CymaBay's second product candidate, MBX-8025 is a potent, selective, orally active PPARδ agonist.

Cautionary Statements

The statements in this press release, including but not limited to the statements regarding the potential of MBX-8025 in the treatment of patients with HoFH, are forward looking statements that are subject to risks and uncertainties, including the future development of MBX-8025 and the representative nature of the preclinical study, and the reported results, as indicative of the results of future clinical trials of MBX-8025 in HoFH. MBX-8025 has not been approved by the FDA, and developing a drug candidate, obtaining regulatory approval or commercializing a drug candidate based on MBX-8025 may never be achieved. Additional risks relating to CymaBay and MBX-8025 are contained in CymaBay's Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on November 14, 2014. 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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Source: CymaBay Therapeutics