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CymaBay Therapeutics Announces Successful Completion of End-of-Phase 2 Discussions With FDA for Arhalofenate

Agreement on Phase 3 Program to Capture Novel Dual Actions of Arhalofenate

NEWARK, Calif., Jan. 20, 2016 (GLOBE NEWSWIRE) -- CymaBay Therapeutics, Inc. (NASDAQ:CBAY), a clinical-stage biopharmaceutical company developing therapies to treat metabolic diseases with high unmet medical need, today announced that it has successfully concluded its end-of-phase 2 meeting discussions with the U.S. Food and Drug Administration (FDA) on the Phase 3 development program for arhalofenate. Correspondence with the FDA subsequent to the formal end-of-Phase 2 meeting has resolved the remaining details of the Phase 3 design. Arhalofenate is a novel dual-acting product candidate for the treatment of gout that both lowers serum uric acid (sUA) and reduces gout flares. It is the first compound in a new class of investigational gout therapy that CymaBay refers to as Urate Lowering Anti-Flare Therapy (ULAFT). CymaBay is developing arhalofenate as a combination product with febuxostat.

CymaBay reached agreement with the FDA on all of the key elements of a Phase 3 program that would support registration. The program would include two Phase 3 studies of arhalofenate in combination with febuxostat in patients with chronic gout and a third study in tophaceous gout, a more advanced form of the disease in which patients have deforming nodular deposits of urate crystals in soft tissues and joints referred to as tophi.

Agreement was reached on coprimary efficacy endpoints for the two separate clinical actions of arhalofenate. The sUA lowering would be assessed as responder rates for patients achieving the targets of <6 and <5 mg/dL for chronic and tophaceous gout, respectively. The data could support an indication for the management of hyperuricemia associated with gout in combination with febuxostat in these two patient populations. Flare data will be collected with an electronic diary and assessed using the same flare definition successfully used in the Phase 2 program. These data could support an indication for flare prophylaxis. In addition, agreement was reached on the methodology to be used for assessing the resolution of tophi in patients with tophaceous gout.

In total, the agreed upon Phase 3 program would enroll approximately 1300 patients intended to receive treatment for at least 12 months. Each Phase 3 study would consist of three parallel arms to assess the sUA and flare endpoints after 6 months of treatment. Patients in arm 1 would receive the combination of arhalofenate and febuxostat, those in arm 2 febuxostat alone together with flare prophylaxis (NSAID or colchicine) and those in arm 3 febuxostat alone. The dose of arhalofenate would be 800 mg in all three studies. For the two trials in chronic gout, the febuxostat dose would be 40 mg, while in the tophaceous gout study, it would be 80 mg. No arhalofenate monotherapy arms are required in the Phase 3 program. The coprimary sUA endpoint would be assessed by comparing the responder rates for arm 1 vs. the combined arms 2 and 3 in each of the three studies. The coprimary flare rate endpoint would be assessed by comparing arm 1 vs. 3, while a secondary flare rate endpoint would be a comparison of arm 1 vs. 2, in each of the three studies. It was agreed that a safety database of approximately 650 patients treated with the arhalofenate-febuxostat combination for 12 months would be sufficient, together with efficacy data, to assess the risk benefit profile.

“If successful in Phase 3, the arhalofenate-febuxostat combination would be the first dual acting treatment for gout providing needed sUA lowering as well as the clinically important benefit of reduction in painful flares,” commented Michael A. Becker, MD, Professor Emeritus of Medicine, The University of Chicago Pritzker School of Medicine. “If realized, this would be an important distinction from other gout treatment options.”

“We are very pleased with the positive outcome and constructive advice received from the FDA during our end-of-Phase 2 discussions,” commented Harold Van Wart, Chief Executive Officer of CymaBay. “We now have clear direction as to how to conduct a Phase 3 program that could capture the dual benefits of arhalofenate in two separate patient populations with gout. This clarity relating to the Phase 3 program will also help us move forward with our partnering discussions with the goal of starting Phase 3 in 2016.”

About Arhalofenate

Arhalofenate is an oral, once-daily dual-acting drug candidate for the treatment of gout that both lowers serum uric acid (sUA) and suppresses flares. It is the first compound in a new class of investigational gout therapy that CymaBay refers to as Urate Lowering Anti-Flare Therapy (ULAFT).

Arhalofenate lowers sUA by blocking the reabsorption of uric acid in the proximal tubules of the kidney by inhibiting a renal uric acid transporter called URAT1. This leads to increased excretion of uric acid into the urine with concomitant lowering of sUA. Arhalofenate produces its uricosuric effect gradually and appears to have a favorable overall and renal safety profile in studies completed to date in over 1,100 patients. The sUA lowering of arhalofenate is complementary and additive to that produced by the xanthine oxidase inhibitor febuxostat, which works by blocking the production of uric acid. The anti-flare activity of arhalofenate is attributable to the suppression of the urate crystal-induced production of IL-1β in gouty joints.

Current treatment guidelines for gout recommend the use of urate lowering therapies (ULTs) to reverse hyperuricemia in order to remove deposits of pro-inflammatory urate crystals. The minimal goal of this treatment is to reduce sUA levels to below 6 mg/dL. The goal for patients with a more advanced form of the disease called tophaceous gout is <5 mg/dL. Many patients treated with currently marketed xanthine oxidase inhibitors (allopurinol or febuxostat) alone do not reach these goals. In previous studies, arhalofenate in combination with febuxostat has been shown to significantly increase the number of patients achieving their sUA goals.

Paradoxically, the initiation of ULT triggers an increased risk of gout flares. The anti-inflammatory activity of arhalofenate has been shown in clinical studies to suppress flares, making it uniquely suited for the potential treatment of gout.

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, has shown two therapeutic actions in a single drug in multiple Phase 2 gout studies. In gout patients, arhalofenate is intended to prevent painful flares in joints while at the same time promoting excretion of uric acid by the kidney, thereby addressing both the signs and symptoms of gout and the hyperuricemia that is the root cause of the disease. 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 two ongoing clinical studies for MBX-8025 including a pilot Phase 2 study in patients with homozygous familial hypercholesterolemia and a Phase 2 study in patients with primary biliary cholangitis.

Cautionary Statements

The statements in this press release, including those statements regarding any future clinical trials and the planned Phase 3 program for arhalofenate, future performance of CymaBay's product candidates, the potential of arhalofenate to treat gout, the therapeutic and commercial potential of arhalofenate and MBX-8025, and the anticipated timing and therapeutic and commercial potential of the product candidates of CymaBay Therapeutics, Inc. are forward looking statements that are subject to risks and uncertainties. Actual results and the timing of events regarding the further development of arhalofenate and 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 any future clinical trials of arhalofenate and MBX-8025; any delays or inability to obtain or maintain regulatory approval of CymaBay's product candidates in the United States or worldwide; the ability of CymaBay to attract funding partners or collaborators with development, regulatory and commercialization expertise; 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; and the market potential for CymaBay's product candidates. Additional risks relating to CymaBay are contained in CymaBay's Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on November 12, 2015. 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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