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Metabolex Announces Positive Results From its Clinical Study of Arhalofenate in Combination With Febuxostat

HAYWARD, Calif., Dec. 8, 2011 /PRNewswire/ -- Metabolex today announced positive results from its clinical study of arhalofenate in combination with febuxostat (Uloric™, Takeda Pharmaceutical Company Limited). A key goal in the treatment of gout is to address the patient's underlying hyperuricemia by treatment with drugs that lower serum uric acid (sUA). In the US, the goal of treatment is to reduce sUA levels to below 6 mg/dL. However, patients with severe tophaceous gout would benefit from reducing their sUA values below 5 or even 4 mg/dL because this would result in more rapid dissolution of their UA crystal deposits. Most patients treated with currently marketed xanthine oxidase inhibitors (allopurinol or febuxostat) alone do not reach these goals. Arhalofenate, Metabolex's lead product candidate for the treatment of hyperuricemia and gout, is a uricosuric agent that could provide additional sUA lowering when used in combination with xanthine oxidase inhibitors and be a treatment option for patients with tophaceous gout.

Clinical Study of Combination of Arhalofenate and Febuxostat

This study was an open label clinical pharmacology study on a single cohort of 11 gout patients with sUA levels of at least 8 mg/dL (mean of 9.1 mg/dL). The primary goal of the study was to assess the response rate (percentage of patients reaching goal) for the sUA targets of 5 and 4 mg/dL when treated in combination with the highest dose (80 mg) of febuxostat approved in the US and two doses (400 and 600 mg) of arhalofenate. The patients were either treatment naive or had discontinued uric acid lowering therapies for a period prior to entering the study. All patients received colchicine throughout the study for flare prophylaxis. After a two week run-in period for sUA stabilization, all 11 patients received febuxostat (80 mg) for one week. Subsequently, patients were administered 400 mg of arhalofenate for two weeks followed by up-titration of arhalofenate to 600 mg for an additional two weeks. All patients were followed for an additional two weeks.

Treatment with febuxostat alone resulted in response rates of 55 and 9%, for the sUA targets of less than or equal to 5 and 4 mg/dL, respectively. After two weeks of treatment with 400 mg of arhalofenate, these response rates were increased to 100 and 36%, respectively. After treatment with 600 mg of arhalofenate, the response rates were 100 and 82%, respectively. Relative to treatment with febuxostat alone, the combination with arhalofenate (600 mg) increased the response rate to the 4 mg/dL target by 73% ($p = 0.013$). Thus, arhalofenate markedly increases the response rates over those observed with febuxostat alone.

The combination of arhalofenate and febuxosat was well tolerated. There were no serious or severe adverse events and no discontinuations due to adverse events. There were no significant changes from baseline in laboratory parameters, including creatinine levels or liver function parameters.

"These results confirm the potential of arhalofenate to be used in combination with febuxostat to provide additional clinically and statistically meaningful lowering of serum uric acid for patients with tophaceous gout," said Raymond W. Urbanski, M.D. Ph.D., Chief Medical Officer of Metabolex. "This combination of oral agents has the potential to lower serum uric acid levels into the range needed to promote dissolution of debilitating uric acid crystals, thereby providing a potential treatment alternative for this patient population."

About Arhalofenate

Arhalofenate has previously completed eight Phase 1 and four Phase 2 studies in patients with type 2 diabetes which demonstrate that it has excellent safety and tolerability in more than 550 patients for up to 6 months of treatment. The drug has completed all preclinical safety studies including the carcinogenicity studies and is therefore highly de-risked with regard to both preclinical and clinical safety.

The clinical data from the diabetes trials showed that arhalofenate exhibited robust, dose-dependent reductions in sUA. These reductions were fully retained in patients with mild to moderate renal insufficiency, while showing excellent renal safety. In addition to lowering glucose, arhalofenate lowered triglycerides and markers of inflammation. Thus, arhalofenate is a potential best-in-class uric acid lowering agent that not only corrects the hyperuricemia associated with gout, but also addresses metabolic comorbidities such as insulin resistance and hypertriglyceridemia that are prevalent in this patient population.

Metabolex has two other on-going 28-day Phase 2b studies for arhalofenate in gout patients. The first study is a randomized double-blind placebo-controlled study that will evaluate the safety and sUA lowering activity of 400 and 600 mg of arhalofenate used as monotherapy. Enrollment into this study of 67 patients with hyperuricemia and a diagnosis of gout has been completed. The second is a randomized double-blind placebo-controlled study in which the safety and sUA lowering activity of arhalofenate (400 and 600 mg) is being assessed in combination with the xanthine oxidase inhibitor allopurinol in ~90 patients who are refractory to allopurinol (do not reach their sUA goal of below 6 mg/dL). The study will examine the percentage of these refractory patients that reach goal when treated with arhalofenate.

About Hyperuricemia and Gout

Gout is a chronic, progressive rheumatic disease, caused by an inflammatory response to uric acid crystals deposited in joints and soft tissues as a result of excess uric acid in the blood (hyperuricemia). Elevated sUA levels cause urate crystals to form in joints triggering acute arthritic flares, chronic destructive arthropathy and formation of tophi. According to the NHANES (2007-2008) study, the incidence of hyperuricemia in the US is over 45 million and over 8 million have progressed to a gout diagnosis.

About Metabolex

Metabolex is a privately-held biopharmaceutical company focused on the discovery and development of proprietary new medicines for the treatment of metabolic diseases. The company has three clinical-stage compounds: arhalofenate, which has completed five Phase 2 trials and is currently in two additional Phase 2b trials for gout; MBX-2982, which has recently completed a Phase 2a trial in patients with type 2 diabetes; and MBX-8025, which

has completed a Phase 2 trial in patients with dyslipidemia.

For additional information about Metabolex and its development pipeline, visit www.metabolex.com.

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