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Press Release

Zydus announces clinical trials of Saroglitazar in patients with Severe Hypertriglyceridemia in USA

Ahmedabad, India, 18 November 2015

Zydus today announced that USFDA has endorsed company's plan to initiate a Phase 2 clinical trial of Saroglitazar in patients with severe hypertriglyceridemia (TG > 500 mg/dL). This randomized, double-blind 12 week Phase 2 trial will evaluate 3 doses of Saroglitazar (1 mg, 2 mg and 4 mg) versus placebo. The trial will be conducted across several medical sites in the USA. The primary endpoint of the study is percent change in triglycerides from baseline after 12 weeks of dosing.

More than four million American adults are living with Severe Hypertriglyceridemia (TG>500 mg/dL). High triglyceride levels can lead to increased triglyceride accumulation in the pancreas which puts patients at very high risk of pancreatitis, a serious and potentially life-threatening illness. In addition, excessive accumulation of triglycerides in the liver can cause serious conditions like Non-alcoholic Fatty Liver Disease (NAFLD) and Non-alcoholic steatohepatitis (NASH).

Zydus presented data from clinical and non-clinical studies on Saroglitazar (Lipaglyn™) during the 75th ADA scientific session in June. Lipaglyn™ is a rationally designed novel drug developed after 12 years of intense scientific efforts and extensive preclinical and clinical investigations, including more than 25 months of real-time clinical experience at the time of this reporting in patients in India. Lipaglyn™ has a unique biological profile reflected in predominant PPARα agonism with a moderate PPARγ agonism. It binds differently to the PPAR receptors, leading to differential target gene expression pattern, maintaining the beneficial effects on lipids and glycemic control with lesser adverse effects as observed in clinical trials & real-time clinical practice. Lipaglyn™ has demonstrated potent ability to lower triglyceride levels without affecting body weight in humans.

Speaking on the development, Mr. Pankaj Patel, Chairman and Managing Director of Zydus Cadila said, "This development is a significant milestone for Zydus. Patients with severe hypertriglyceridemia often have to take multiple medications because of associated diabetes or fatty liver disease. Zydus is committed to develop Lipaglyn™ (Saroglitazar) for millions of patients living with Severe Hypertriglyceridemia and Fatty Liver Diseases."

About Lipaglyn™ (Saroglitazar)

Lipaglyn™ (Saroglitazar) is currently approved in India as a prescription medicine for the treatment of Hypertriglyceridemia and Diabetic Dyslipidemia in Patients with Type 2 Diabetes not controlled by statins. The recommended dose of Lipaglyn™ is 4 mg once-a-day. Lipaglyn™ (Saroglitazar) was launched in India during September 2013. Since then more than 150,000 patients have been treated with Lipaglyn™ in India to date. A one year post-marketing patients surveillance study (PMS) was conducted in India to study the safety and efficacy of Lipaglyn™ in real-time clinical practice, and data was presented at scientific and medical conferences in USA (AACE 2015 and ADA 2015 meetings).

Saroglitazar for Hypertriglyceridemia: In randomized, controlled, Phase III clinical studies (PRESS V and PRESS VI) Saroglitazar 4 mg was found to be safe and well tolerated by patients, and demonstrated up to

45% reduction in Triglycerides, along with beneficial effects on both lipid and glycemic parameters. Additional Phase III trials are ongoing in non-alcoholic steatohepatitis (NASH), lipodystrophy and few additional indications. A post-marketing Phase-IV study is currently ongoing in 1010 patients with hypertriglyceridemia in India.

Saroglitazar for Non-alcoholic steatohepatitis (NASH): Zydus has initiated a 52 week Phase III clinical trial of Lipaglyn™ in India to treat patients with biopsy proven NASH. Saroglitazar has demonstrated good efficacy in animal models of NASH, along with associated biomarkers. It has reduced hepatic steatosis, ballooning, inflammation and fibrosis in liver. Recently completed phase 2 studies of Saroglitazar in patients with biopsy proven NASH has shown improvement in liver enzymes along with favorable effects on lipid and glycemic indices.

Publications:

» Chatterjee S, Majumder A, Ray S. Observational study of effects of Saroglitazar on glycaemic and lipid parameters on Indian patients with type 2 diabetes. Scientific Reports 2015; 5: 1-5.

» Sadanand RS, Soumitra K, Mathur RP, et al. Observational study to evaluate the safety and efficacy of Saroglitazar in Indian diabetic dyslipidemia patients. Indian Heart Journal 2015; 67: 23-26.

» Jani RH, Pai V, Jha P, et al. A multicenter prospective randomized double-blind study to evaluate the safety and efficacy of Saroglitazar 2 & 4 mg compared with placebo in type 2 diabetes mellitus patients having hypertriglyceridemia not controlled with atorvastatin therapy (PRESS VI). Diabetes Technology & Therapeutics 2014; 16: 63-71.

» Pai V, Paneerselvam A, Mukhopadhyay S, et al. A multicenter prospective randomized double-blind study to evaluate the safety and efficacy of Saroglitazar 2 & 4 mg compared to pioglitazone 45 mg in diabetic dyslipidemia (PRESS V). Journal of Diabetes Science and Technology 2014; 8: 132-41.

» Jani RH, Kansagra K, Jain MR, et al. Pharmacokinetics, Safety, and Tolerability of Saroglitazar (ZYH1), a Predominantly PPARa Agonist with Moderate PPARc Agonist Activity in Healthy Human Subjects. Clin Drug Investig (2013) 33:809–816.

» Jain MR, Giri SR, Trivedi C, et al. Saroglitazar, a novel PPARα/γ agonist with predominant PPARα activity, shows lipid-lowering and insulin-sensitizing effects in preclinical models. Pharmacology Research & Perspectives 2015; 3(3): 1-14.

Posters and Presentations :

» Lipid Lowering Effects of Saroglitazar in Preclinical Models: Potential Synergistic Interaction with Statins. (Abstract #693-P, 75th Annual Scientific Sessions of the American Diabetes Association (ADA) in Boston, Massachusetts, USA)

» Saroglitazar Shows Beneficial Effects on Insulin Sensitivity, Dyslipidemia, and Blood Pressure in Zucker Fatty Rats. (Abstract #703 -P, 75th Annual Scientific Sessions of the American Diabetes Association (ADA) in Boston, Massachusetts, USA)

» Effect of Saroglitazar, a Dual PPAR-a/γ agonist, on Lipid and Glycemic Parameters in Indian Patients with Diabetic Dyslipidemia—A 27-Week, Retrospective Analysis. (Abstract #704-P, 75th Annual Scientific Sessions of the American Diabetes Association (ADA) in Boston, Massachusetts, USA)

» To Assess the Effect of 4mg Saroglitazar on Patients of Diabetes Dyslipidemia with Nonalcoholic Fatty Liver Disease for 24 Weeks at Diabetes Care Centre. (Abstract #712-P, 75th Annual Scientific Sessions of the American Diabetes Association (ADA) in Boston, Massachusetts, USA)

» Effect of Saroglitazar on Fatty Acid Metabolism in Zucker Fa/Fa Rats (Abstract #1187-P, 75th Annual Scientific Sessions of the American Diabetes Association (ADA) in Boston, Massachusetts, USA)

» Saroglitazar Shows Therapeutic Benefits in Mouse Model of Nonalcoholic Fatty Liver Disease (NAFLD) and Nonalcoholic Steatohepatitis (NASH) (Abstract #1957-P, 75th Annual Scientific Sessions of the American Diabetes Association (ADA) in Boston, Massachusetts, USA)

» Saroglitazar in Diabetic Dyslipidemia: 1 year data (Abstract #126-LB, 75th Annual Scientific Sessions of the American Diabetes Association (ADA) in Boston, Massachusetts, USA)

» 9-month safety and efficacy of Saroglitazar in Diabetic Dyslipidemia (Abstract #1233, American Association of Clinical Endocrinologists 24th Annual Scientific and Clinical Congress in Nashville, TN, USA)

» Lipaglyn™ Presentation (2015 Keystone Symposia Conference on Liver Metabolism and Nonalcoholic Fatty Liver Disease (NAFLD) in British Columbia, Canada)

» Efficacy of Saroglitazar, a Novel PPAR a/y Agonist in a mouse model of non-alcoholic steatohepatitis. (Poster #2011, 2015 Keystone Symposia Conference on Liver Metabolism and Nonalcoholic Fatty Liver Disease (NAFLD) in British Columbia, Canada)

About Zydus

Zydus Cadila is an innovative, global pharmaceutical company that discovers, develops, manufactures and markets a broad range of healthcare therapies, including small molecule drugs, biologic therapeutics and vaccines. The group employs over 16,500 people worldwide including over 1200 scientists engaged in R & D and is dedicated to creating healthier communities globally. For more information, pl. visit www.zyduscadila.com