RESS RELEASE
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Elcelyx Therapeutics Reports Positive Data for NewMet in Type 2 Diabetes at 2013 American Diabetes Association Scientific Sessions

Study Reveals Groundbreaking Understanding of Metformin Mechanism of Action

SAN DIEGO, June 22, 2013 /PRNewswire/ -- Elcelyx Therapeutics announced today that clinical study results confirm that the primary site of action of Type 2 diabetes medicine metformin is in the lower bowel rather than in the circulation. The study revealed that contrary to popular belief, greater exposure in the plasma of metformin does not improve efficacy of the most prescribed diabetes medicine in the world. Elcelyx's Phase 2a study demonstrated this by comparing the glucose-lowering effects of NewMet(TM), the company's proprietary delayed-release formulation of metformin, to generic metformin in patients with Type 2 diabetes.

NewMet is formulated to target the entire dose to the lower bowel and limit absorption into the blood. In the crossover study, 5-day treatment with NewMet had similar fasting and post-meal glucose reductions from baseline as 5-day treatment with generic metformin despite greater than 45% reductions in metformin plasma concentrations. In addition, NewMet had less gastrointestinal (GI) side effects than generic metformin. Results of the clinical trial will be presented at ADA on Sunday by Dr. Ralph DeFronzo, Professor of Medicine and Chief of the Diabetes Division at the University of Texas Health Science Center and the Audie L. Murphy Memorial Veterans Administration Hospital in San Antonio, Texas.

The significantly lower metformin plasma concentration observed with NewMet suggests that it might be safely used by patients with moderate and severe renal impairment, a population of patients that is unable to use currently available metformin formulations due to the risk of lactic acidosis caused by too much metformin in the blood. Mark Fineman, Ph.D., Senior Vice President of Research & Development at Elcelyx will present a second poster, accepted as a late-breaker that describes a model designed to predict concentrations of metformin in the blood that would occur if patients with Type 2 diabetes and mild, moderate or severe renal impairment were to take NewMet. The results of the model suggest that patients with renal impairment taking effective doses of NewMet would not have an increased risk of lactic acidosis caused by accumulation of metformin in the blood. Elcelyx will be initiating a pharmacokinetic study this summer in Type 2 diabetes patients with mild, moderate and severe renal impairment to confirm the predictions of the model.

"Metformin is the preferred initial pharmacological agent for Type 2 diabetes, but in the U.S., 40% of patients with diabetes are not taking it primarily due to issues of GI tolerability or due to the contraindication of their renal impairment. Moreover, of the 60% who are taking metformin, only about 40% are able to titrate to fully effective doses due to tolerability issues," said John Buse, M.D., Professor of Medicine and Director, Diabetes Care Center, Chief, Division of Endocrinology, Executive Associate Dean for Clinical Research at University of North Carolina School of Medicine, Chapel Hill, North Carolina. "The NewMet results to date hold the promise of addressing all these patient segments. This is very encouraging news for physicians who would like to be in compliance with ADA treatment guidelines and have their patients benefit from metformin therapy." Dr. Buse was an advisor on the Phase 2a NewMet clinical study.

To confirm results observed to date, a multicenter, double-blind dose-finding Phase 2b trial evaluating NewMet once-daily doses of 1,000, 800 and 600 milligrams compared to placebo is

underway. There are also two comparator arms with generic extended-release metformin dosed once-daily at 1,000 and 2,000 milligrams. The primary endpoint of the study is fasting plasma glucose at four weeks of treatment. Secondary endpoints through 12 weeks include changes in fasting plasma glucose, hemoglobin A1c, body weight and measures of safety and tolerability. The study is fully enrolled with 240 patients with Type 2 diabetes.

Phase 2a Study Details

The randomized, double-blind, three-way crossover study compared the pharmacokinetics and pharmacodynamics of NewMet to generic metformin in patients with Type 2 diabetes. Twenty-four patients were randomized to receive twice-daily oral dosing of metformin HCl immediate release (1,000 mg), low dose NewMet (500 mg), and high dose NewMet (1,000 mg) for five days each separated by a one week washout. All treatments demonstrated similar reductions from baseline values in fasting plasma glucose (16-22 mg/dL, $p<0.01$ for all) and postprandial glucose (8%-12%, $p<0.001$ for all) despite a 45%-57% reduction in circulating metformin in the high and low dose NewMet arms, respectively. Gut hormones (GLP-1 and PYY) were increased similarly by more than 50% across all treatments. No safety concerns were noted for either NewMet or metformin.

Elcelyx Therapeutics' Posters at ADA: Links to Abstracts

Dissociation between metformin plasma exposure and its glucose-lowering effect: A novel gut-mediated mechanism of action

-- Date and Time: Sunday, June 23, 2013, 12:00 p.m. to 2:00 p.m. CT

-- Poster #, Category: 1087-P, 01-D Clinical Therapeutics/New Technology -- Oral Agents

Delayed-release metformin may be suitable for use in diabetes patients with renal impairment that are contraindicated for currently available metformin formulations

-- Date and Time: Sunday, June 23, 2013, 12:00 p.m. to 2:00 p.m. CT

-- Poster #, Category: 75-LB, 01-D Clinical Therapeutics/New Technology -- Oral Agents

About Elcelyx Therapeutics

Elcelyx Therapeutics develops pharmaceutical and consumer healthcare products based on its proprietary Gut Sensory Modulation (GSM) platform. Pharmaceutical product candidate NewMet(TM) is being developed for use by Type 2 diabetes patients who have difficulty tolerating generic metformin or are contraindicated for its use. In the consumer health area, Elcelyx is developing Lovidia(TM) as a dietary supplement for weight management. These product candidates are backed by rigorous science and clinical data and present near-term, blockbuster commercial opportunities. Elcelyx is based in San Diego, CA. For more information, visit www.Elcelyx.com.

SOURCE Elcelyx Therapeutics

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