Xeris Pharmaceuticals Announces New Results From Ready-To-Use Liquid Glucagon Clinical Development Program

- Data Presented at 77th Scientific Session of the American Diabetes Association (ADA) -

CHICAGO, IL and AUSTIN, TX; June 16, 2017 (GLOBE NEWSWIRE) – Xeris Pharmaceuticals, Inc. ("Xeris") today announced that results from three clinical studies of the company's investigational ready-to-use liquid glucagon formulation were presented at the 77th Scientific Session of the American Diabetes Association (ADA) in San Diego from June 9-13, 2017. In a pilot study, patients with Type 1 diabetes (T1D) experienced normalization of plasma glucose levels and demonstrated complete resolution of symptoms of severe, experimentally induced hypoglycemia following a rescue dose of the company's glucagon formulation. In two proof-of-concept studies, mini-doses of the same glucagon formulation were found to be as effective as carbohydrates at treating or preventing mild-moderate and exercise-induced hypoglycemia. "Individuals with diabetes who require insulin and their caregivers face a number of challenges, including the management of hypoglycemia," said Paul Edick, Chief Executive Officer of Xeris. "We are encouraged by the data presented at ADA and are committed to the further clinical development and commercialization of Xeris' novel ready-to-use liquid glucagon formulation to address their needs."

A Pilot Study in Adults with T1DM to Examine the Efficacy of Stable Non-Aqueous Glucagon for Treatment of Severe Hypoglycemia (Abstract 140-LB)

This study was conducted in adults with type 1 diabetes to explore whether a subcutaneous injection of liquid-stable glucagon (0.5 or 1 mg) could rescue subjects from insulin-induced severe hypoglycemia. After an overnight fast, subjects were administered intravenous (IV) insulin under controlled conditions to induce plasma glucose < 50 mg/dL for 5 minutes. This procedure resulted in symptoms typical of hypoglycemia in most subjects. Following the 1 mg glucagon dose, 7/7 subjects achieved primary response with plasma glucose > 70 mg/dL in an average time of 11.9 minutes (range: 8.1-15.9 minutes). Following the 0.5 mg dose, 6/6 subjects achieved plasma glucose > 70 mg/dL in an average time of 14.4 minutes (range: 9.5-19.7 minutes). Symptomatic relief began within 5 minutes of dosing with glucagon, and all subjects experienced complete resolution of hypoglycemia symptoms in a median time of 20 minutes (range 10-30). No significant safety concerns were noted.

This pilot study informed the design of the ongoing Phase 3 clinical development program which may lead to a first-in-class, ready-to-use glucagon auto-injector for treatment of severe hypoglycemia. Further information on the ongoing clinical studies can be found at ClinicalTrials.gov (adult study: NCT02656069; pediatric study: NCT03091673).

Efficacy and Safety of Mini-dose Glucagon for Treatment of Non-Severe Hypoglycemia in Adults with Type 1 Diabetes (Abstract 1068-P)

Twenty adults with type 1 diabetes using an insulin pump and continuous glucose monitor (CGM) and experiencing frequent mild hypoglycemia participated in a crossover trial (two 3-week periods) comparing non-aqueous mini-dose glucagon (MDG) (150 µg) versus oral glucose tablets (TABS) (16 g) to treat hypoglycemia (blood glucose [BG] 40-69 mg/dL). Successful treatment was defined as BG ≥50 mg/dL at 15 minutes and ≥70 mg/dL at 30 minutes after intervention.

Sixteen participants (mean age 39 years, 75% female, mean diabetes duration 23 years, mean HbA1c 7.2%) had 118 analyzable events with initial BG 50-69 mg/dL. Successful treatment criteria were met for 58 (94%) of 62 events during the MDG period and 53 (95%) of 56 events during the TABS period (adjusted p=0.99). CGM-measured time with blood glucose in the range of 70-180 mg/dL data did not differ between treatment groups during the 2 hours post-events, but TABS resulted in higher maximum glucose (116 vs 102 mg/dL; p=0.01) over the first hour. Some participants reported injection site discomfort (MDG) as well as nausea (MDG and TABS).

This was the first controlled outpatient study to demonstrate that small doses of glucagon can address mild-to-moderate hypoglycemia and may offer a useful alternative to oral carbohydrates. This research was supported by the Leona M. and Harry B. Helmsley Charitable Trust.

Mini-dose Glucagon as a Novel Approach to Prevent Exercise-Induced Hypoglycemia in Type 1 Diabetes (Abstract 67-LB)

Patients with type 1 diabetes (T1D) who perform aerobic exercise often experience a decrease in blood glucose concentration that can result in hypoglycemia. Current approaches to prevent exercise-induced hypoglycemia include reduction in insulin delivery or ingestion of carbohydrates, but either strategy can result in hypo- or hyperglycemia. This study sought to determine whether mini-dose glucagon (MDG) given subcutaneously before exercise could prevent subsequent glucose lowering, and to compare the glycemic response to current approaches.

The study was a randomized, 4-period crossover trial involving 15 adults with T1D who exercised at ~55% VO_{2max} for 45 min with either (1) no intervention (control), (2) 50% basal insulin reduction, (3) 40 g oral glucose tabs, or (4) 150 µg glucagon, administered 5 min. before exercise. During exercise, mean plasma glucose increased slightly with MDG compared to a decrease with control and insulin reduction, and with a greater increase with glucose tabs. Insulin levels were not different, while glucagon increased with MDG. Six subjects experienced hypoglycemia (< 70 mg/dl) during control, 5 during insulin reduction and none with glucose tabs or MDG; 5 subjects experienced hyperglycemia (≥250 mg/dl) with glucose tabs and 1 with MDG. No significant safety concerns were noted.

The study suggests MDG may be an effective alternative to insulin reduction for preventing exercise-induced hypoglycemia, and may potentially result in less post-intervention hyperglycemia than ingestion of carbohydrate. This research was supported by the Leona M. and Harry B. Helmsley Charitable Trust.

More information regarding these abstracts can be found at https://professional.diabetes.org/content-page/abstracts

About Glucagon

Glucagon is a metabolic hormone secreted by the pancreas that raises blood glucose levels by causing the liver to rapidly convert glycogen (the stored form of glucose) into glucose, which is then released into the bloodstream. Glucagon and insulin are two critical hormones in a glycemic control system that keeps blood glucose at the right level in healthy individuals. In people with diabetes who are dependent on insulin, this control system is disrupted and insulin must be injected prior to meals to avoid high levels of blood glucose (hyperglycemia). The opposite effect of low blood glucose (hypoglycemia) is also prevalent in this population due to dysregulated glucagon secretion. Severe hypoglycemia is a serious condition and can lead to seizures, coma, potential brain injury and, if untreated, death. Xeris' proprietary formulation technology has the potential to provide the first soluble, room

temperature stable, ready-to-use glucagon for use by people with diabetes and other indications to prevent or manage both moderate and severe hypoglycemia, and achieve optimal glucose control.

About Xeris Pharmaceuticals, Inc.
Xeris is a Chicago, IL and Austin, TX-based, specialty biopharmaceutical company developing improved and differentiated injectable therapeutics for multiple indications including diabetes. The company's proprietary XeriSol™ and XeriJect™ formulation technologies allow for the subcutaneous and intradermal delivery of highly concentrated, non-aqueous, ready-to-use formulations of peptides, proteins, antibodies and small molecules using auto-injectors, multi-dose pens and pumps. Xeris' proprietary formulation platforms have the potential to offer distinct advantages over existing products and formulations including: up to 1000-fold lower injection volumes, long term room-temperature stability, elimination of reconstitution and refrigeration. All of these attributes can lead to products that are easier to use by patients, caregivers, health practitioners, and can reduce costs for payers and the healthcare system. For more information please visit the Xeris website at: www.xerispharma.com.

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