Xeris Pharmaceuticals Announces Positive Topline Results from the Phase 2 Comparative Study of a Novel Pramlintide-insulin Co-formulation (XP-3924) in Adults with Type 1 Diabetes Mellitus

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XP-3924 resulted in a 62% reduction of hyperglycemia after a glucose challenge

XP-3924 showed improved glucose control when compared to Humulin® R alone

XP-3924 showed promising glucose control when compared to both Humulin® R and co-administered injections of Humulin® R and Symlin®

XP-3924 was observed to be safe and well tolerated in this study

CHICAGO--(BUSINESS WIRE)--Jun. 18, 2020-- Xeris Pharmaceuticals, Inc. (Nasdaq: XERS), a specialty pharmaceutical company leveraging its novel technology platforms to develop and commercialize ready-to-use injectable and infusible drug formulations, today announced positive topline results from a proof-of-concept Phase 2 study of a novel Xerisol™ pramlintide-insulin co-formulation (XP-3924) in adults with type 1 diabetes mellitus

XP-3924 is designed to improve the synergistic combination of two complementary therapies: pramlintide (an amylin-analog) and insulin. The separate administration of these existing therapies in combination reduces both post-prandial glucose excursions and glucose variability, as well as improves overall glycemic control. A pramlintide-insulin co-formulation may help reduce the daily burden associated with pramlintide co-administration (e.g., reduce the multiple additional injections needed per day). This reduction in the multiple injection burden using XP-3924 may also improve longer term pramlintide treatment adherence and persistency.

The completed Phase 2 study was a randomized, open-label, active comparator-controlled, three-period cross-over study, which enrolled 18 adult participants with type 1 diabetes. This study aimed to investigate the pharmacokinetics, pharmacodynamics, and the safety and tolerability of a single dose of XP-3924 (administered based upon the subjects' insulin:carbohydrate ratio), when compared to co-administration of regular insulin (Humulin® R) and pramlintide (Symlin®), and to an injection of regular insulin alone (Humulin® R). Subjects were randomly allocated to a sequence of three treatments: XP-3924 (with 50% insulin reduction), regular insulin, or regular insulin (with 50% insulin reduction) plus pramlintide co-administered as separate injections. The study drugs were administered subcutaneously (SC) before the intake of a standardized 75-gram oral glucose challenge. The subjects' blood glucose levels were monitored for 6 hours after drug dosing. For more information, visit www.clinicaltrials.gov; Identifier: NCT04074317.

Treatment with XP-3924 resulted in a 62.3% reduction of hyperglycemia (blood glucose >180 mg/dL) after the glucose challenge when compared to Humulin® R ($p<0.001$). Additionally, XP-3924 exhibited comparable postprandial glycemic control to that of the co-administered injections of Humulin® R and Symlin®. The mean absolute change in blood glucose was less in XP-3924 when compared to both Humulin® R and co-administered injections of Humulin® R and Symlin® after the oral glucose challenge. The glucose variability after treatment with XP-3924 was less than both Humulin® R and co-administered injections of Humulin® R and Symlin®, as defined by the comparison of the coefficient of variation of all plasma glucose readings across the 6-hour duration of study treatments.

The incidence and severity of treatment emergent adverse events was comparable across all treatment arms, as were the overall number of hypoglycemic events during dosing visits. There were minimal gastrointestinal side-effects reported in any treatment arm. There was a comparable incidence of injection site reactions and no edema was noted, across all treatment arms. XP-3924 was safe and well tolerated, and no serious adverse events occurred in this study.

"Amylin is a natural hormone that works in tandem with insulin and plays an important physiologic role in maintaining normal metabolic homeostasis by preventing glucose appearance after meals, thus preventing the post prandial rise that is so common in T1D. Developing a co-formulation of pramlintide and regular insulin could play an important role in the clinical care of people who need meal time insulin," said Dr. Steven V. Edelman, Clinical Professor of Medicine, Division of Endocrinology and Metabolism, UC San Diego School of Medicine.

"The results of this Phase 2 study are exciting as they suggest that the co-formulation of insulin with pramlintide may reduce postprandial hyperglycemia while reducing iatrogenic hyperinsulinemia. The co-formulation may be a way to realize the benefits of pramlintide therapy while reducing some of the barriers to previous clinical implementation including an additional injection before each meal," said Dr. Jeremy Pettus, Assistant Professor of Medicine, Division of Endocrinology and Metabolism, UC San Diego School of Medicine.

"Results from our proof-of-concept study demonstrate that XP-3924, our XeriSol pramlintide-insulin co-formulation, reduced postprandial glycemic excursions and has the potential to significantly improve the management of glycemic conditions of people with diabetes," said Paul R. Edick, Xeris' Chairman and CEO. "Pramlintide has many patient benefits yet is underutilized because of its additional daily injection burden. We believe our XP-3924 co-formulation can reduce this burden and may improve long-term pramlintide treatment adherence and persistency. Additionally, the prolonged pramlintide levels observed in XP-3924 may enhance the additional patient-focused benefits observed with delayed gastric emptying and satiety. Longer term evaluation of XP-3924 for overall glycemic control is warranted." Mr. Edick continued, "We anticipate an end-of-phase 2 meeting with the FDA later this year to discuss a path forward."

About Pramlintide

Pramlintide is an analog of amylin, a natural hormone that inhibits glucagon secretion, delays gastric emptying, and is known to help increase satiety. Pramlintide is indicated for patients with type 1 or type 2 diabetes who use mealtime insulin and have failed to achieve desired glycemic control despite optimal insulin therapy. It works by slowing the movement of food through the stomach. This prevents blood sugar from rising too high after a meal and

may decrease appetite and cause weight loss. Pramlintide use with insulin has been associated with an increased risk of severe hypoglycemia, particularly in patients with type 1 diabetes.

About Xeris Pharmaceuticals, Inc.

Xeris (Nasdaq: XERS) is a specialty pharmaceutical company delivering innovative solutions to simplify the experience of administering important therapies that people rely on every day around the world. With a novel technology platform that enables ready-to-use, room-temperature stable formulations of injectable and infusible therapies, the company is advancing a portfolio of solutions in various therapeutic categories, including its first commercial product, Gvoke™. Its proprietary XeriSol™ and XeriJect™ formulation technologies have the potential to offer distinct advantages ove conventional product formulations, including eliminating the need for reconstitution, enabling long-term, room-temperature stability, significantly reducing injection volume, and eliminating the requirement for intravenous (IV) infusion. With Xeris' technology, new product formulations are designed to be easier to use by patients, caregivers, and health practitioners and help reduce costs for payers and the healthcare system.

Xeris is headquartered in Chicago, IL. For more information, visit www.xerispharma.com, or follow us on Twitter, LinkedIn or Instagram.

Forward-Looking Statements

Any statements in this press release about future expectations, plans and prospects for Xeris Pharmaceuticals, Inc., including statements regarding an end-of-phase meeting with the FDA to discuss a clinical path forward for XP-3924, the market and therapeutic potential of its product candidates, expectations regarding clinical data, the timing or likelihood of regulatory approval and commercialization of its product candidates, the timing or likelihood of expansion into additional markets, the potential utility of its formulation platforms and other statements containing the words "will," "would," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including, without limitation, the regulatory approval of its product candidates, its ability to market and sell its products, if approved, its reliance on a single source supplier for Gvoke HypoPen™ and other factors discussed in the "Risk Factors" section of the most recently filed Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission, as well as discussions of potential risks, uncertainties, and other important factors in Xeris' subsequent filings with the Securities and Exchange Commission. Any forward-looking statements contained in this press release speak only as of the date hereof, and Xeris expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise. The Company intends to use the investor relations portion of its website as a means of disclosing material non-public information and for complying with disclosure obligations under Regulation FD.

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Xeris Investor Contact
Allison Wey
Senior Vice President, Investor Relations and Corporate Communications
awey@xerispharma.com
312-736-1237

Source: Xeris Pharmaceuticals, Inc.