Liquid Stable Glucagon for Congenital Hyperinsulinism

CHI Family Conference
September 2018

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Background

Xeris Pharmaceuticals

Who is Xeris Pharmaceuticals?

Our Company

- We are a specialty pharmaceutical company leveraging our novel non-aqueous formulation technology platforms, XeriSol and XeriJect, to develop and commercialize ready-to-use injectable and infusible drug formulations.

- We have developed a ready-to-use, room-temperature stable liquid glucagon formulation that, unlike any currently available products, can be administered without any preparation or reconstitution.

- Our lead product candidate, Glucagon Rescue Pen, delivers ready-to-use glucagon via a commercially-available auto-injector for the treatment of severe hypoglycemia, a potentially life-threatening condition, in people with diabetes.

Who is Xeris Pharmaceuticals?

Ready-to-Use Glucagon for Hypoglycemia Associated with Intermittent and Chronic Conditions

- We are studying ready-to-use, liquid-stable glucagon formulation to treat five intermittent and chronic conditions with significant unmet medical need:
  - Post-Bariatric Hypoglycemia, or PBH;
  - Congenital Hyperinsulinism, or CHI;
  - Hypoglycemia-Associated Autonomic Failure, or HAAF;
  - Exercise-Induced Hypoglycemia, or EIH; and
  - Management of diabetes via glucagon in a fully-integrated, bi-hormonal artificial pancreas closed-loop system.

We have received two orphan drug designations

- We have received orphan drug designation from the FDA:
  - Ready-to-use glucagon for both congenital hyperinsulinism (CHI) and post bariatric hypoglycemia (PBH).

Congenital Hyperinsulinism Program

Xeris Pharmaceuticals

Glucagon Infusion in CHI

- Cook Children's Medical Center - glucagon experience
- 7 patients treated with glucagon during stabilization pre-surgery (4 focal, 3 diffuse)
  - Birth weight (Kg) mean 4.3 range 3.1 -5.3
  - Age at start of glucagon(days) mean 21 range 3 - 45
  - Dose of glucagon (mcg/kg/hr) mean 10 range 7.9 – 13
  - Max GIR pre glucagon(mg/kg/min) mean 23 range 14 – 41
  - Min GIR on glucagon(mg/kg/min) mean 7.2 range 1.8 – 8
  - Duration of glucagon(days) mean 9.4 range 4 - 15
- Complications
  - 5 of 8 PICC lines became blocked and needed replacement (1.9F PICC lines)
  - Hypoglycemia occurred in each patient with a blocked line
- 2 patients arrived on glucagon; weaned off for diagnosis (1 focal, 1 diffuse)
- 1 patient with Transient Perinatal Stress HI treated for 74 days due to complex medical problems weaned to 1.4mcg/kg/hr and maintained euglycemia w/ GIR 4.1mg/kg/min

The Potential of SC Glucagon As long-term Treatment for CHI

- Mohnike K et al. Horm Res. 2008;70(1):59-64.
- SC glucagon continued for 1-4 years in 3 of 6 children without further symptomatic hypoglycemia, convulsions or unconsciousness;
- Central glucose infusions significantly reduced or eliminated in all 9 children;
- Glucagon treatment initiated to manage recurrent hypoglycemia after subtotal pancreatectomy in 2 of 9 children;
- Pancreatectomy or subsequent resurgeries avoided in 5 of the 9 children;
- Octreotide was reduced to 8-15 µg/kg/day – considerably lower than if it were given alone, without glucagon (15-60 µg/kg/day)

Xeris Phase 2 CHI Clinical Trial (NCT02937558)

- XSGO-CH01: A Phase 2 Proof-of-Concept Study of CSI Glucagon (Continuous Subcutaneous Glucagon Infusion) to Prevent Hypoglycemia with Lower Intravenous Glucose Infusion Rates in Children up to One Year of Age with Congenital Hyperinsulinism
- Congenital Hyperinsulinism, or CHI, is a condition caused by several genetic defects that result in severe, persistent hypoglycemia in infants and children, which can lead to significant morbidity and mortality.
- In the fourth quarter of 2016, we initiated a randomized controlled Phase 2 clinical trial at four CHI centers of excellence in the United States, with interim efficacy results from subjects are expected in the second half of 2018.
- While the study is blinded, the protocol allows physicians to use continuous subcutaneous infusion glucagon in an open-label extension phase as appropriate. During one observation, the open-label data showed use of continuous subcutaneous infusion of glucagon enabled the reduction of the IV glucose infusion rate by a clinically significant 65%.

Xeris Phase 2 CHI Clinical Trial (NCT02937558)

- To date, continuous subcutaneous glucagon has been observed to be well-tolerated and in this clinical trial there have been no unanticipated adverse events or reported SAEs.

- We expect the randomized controlled data from this clinical trial will support initiation of a pivotal phase 3 program for continuous subcutaneous infusion of glucagon. Following consultation with FDA, we expect to initiate in the first half of 2019.

Thank You!

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