XERIS PHARMACEUTICALS

CSI GLUCAGON™ FOR TREATMENT OF SEVERE, PERSISTENT HYPOGLYCEMIA

CHI Annual Conference

Galloway, NJ

August 16-17, 2014

HYPOGLYCEMIA AND GLUCAGON

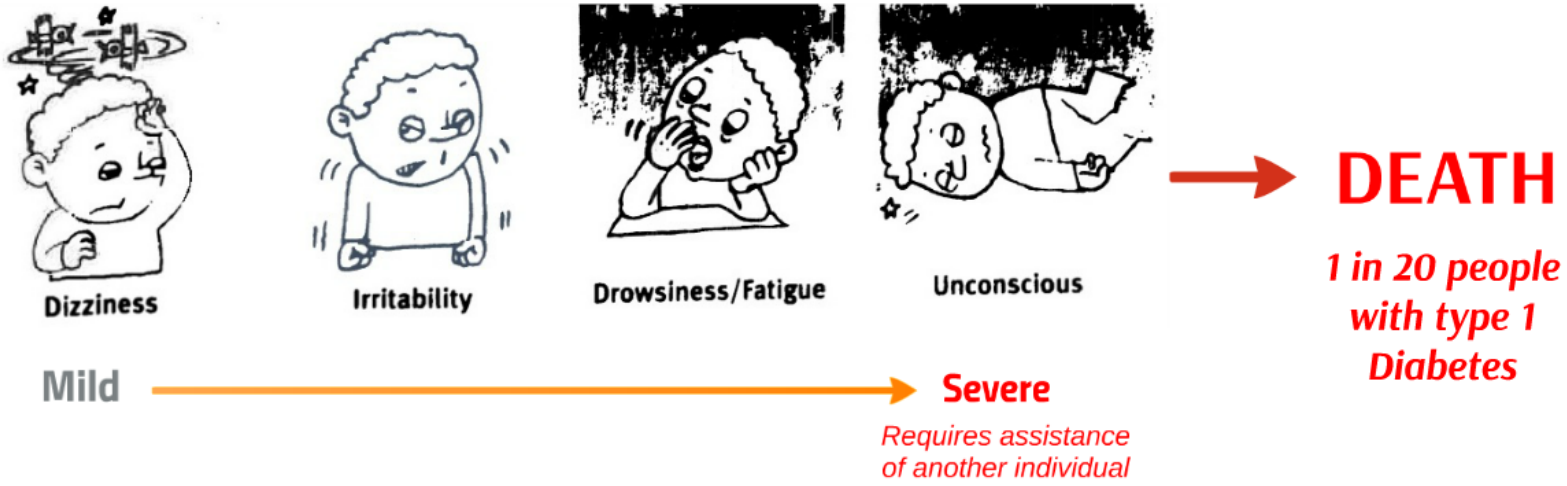
- Hypoglycemia – the unmet need
- Glucagon's role in treatment of hypoglycemia…historically limited….why?
- How room temperature stable glucagon is meeting the need
- Xeris' CSI (Continuous Subcutaneous Infusion) Glucagon™ development program for HI

OUR COMPANY

- Located in Austin Texas
- Office & laboratory facilities on north side of University of Texas campus
- Currently 15 employees and contractors
- CMC, toxicology, regulatory & drug development experience
- Our r&D efforts are focused on formulation discovery and screening in house – e.g. room temperature stable monomeric insulin
- Raising $5M to fund development programs

3208 Red River Street, 3rd Floor
Austin, Texas

HYPOGLYCEMIA - GLUCAGON VS. INSULIN



Glucagon - the counter-regulatory hormone to insulin

- Natural hormone responsible for raising blood sugar
- Works in tandem with insulin to regulate blood sugar
- Only outpatient treatment for severe hypo (emergency rescue)

UNMET NEED: HYPOGLYCEMIA

G-Pen™
Severe Hypo

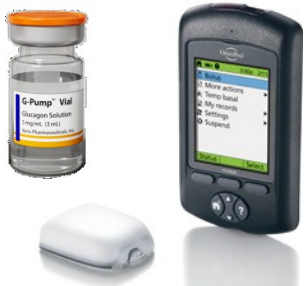
G-Pump–AP™
Bionic Pancreas

G-Pen Mini™
Moderate hypo

XeriSol Glucagon (5 mg/ml)

G-Pump–HRH™
High-Risk Hypo

CSI Glucagon™
Congenital Hyperinsulinism



SIZE OF PROBLEM – LARGE FOR DIABETES

Piper has Type 1 diabetes.*

One in twenty people like Piper will die from low blood sugar.

* From NY Times ad placed by the JDRF

Severe Physical & Emotional Burden

- Diabetics live with the fear of hypoglycemia on a daily basis
- Parents worried about their kids at night when risk of hypoglycemia is greatest
- Lack of easy treatments for severe/moderate hypoglycemia makes social interaction (sleepovers, camping trips, etc.) difficult for kids, leading to isolation and stigma
- Latest report from ADA Working Group on Hypoglycemia demonstrates significant morbidities and mortality associated with hypoglycemia

21M diagnosed diabetics

8.1 undiagnosed

(CDC 2014)

6M insulin dependent

300M hypo events/yr

3.3M severe events/yr

SIZE OF PROBLEM – SMALL NUMBERS FOR HI, BUT SEVERE AND PERSISTENT PROBLEM

Piper has Congenital Hyperinsulinism…..

Approximately 30% of HI kids will suffer some neurological dysfunction from their severe, persistent hypoglycemia

Est. 170 diagnosed annually in US

50% Focal

95% surgical cure

50% Diffuse

50% Diazoxide Rx

50% Surgical Rx or Medical Mgt.

90% of pancreatectomies lead to insulin dependence

by age 14

Severe Physical , Emotional Burden

- **Parents worry about their kids 24/7** - risk of hypoglycemia is constant
- Kids live with the fear of hypoglycemia on a daily basis
- Lack of care-giver and patient- friendly treatments for HI makes social interaction (sleepovers, camping trips, etc.) difficult for kids, leading to isolation and stigma
- Staggering financial impact on families

GLUCAGON'S HISTORICALLY LIMITED ROLE IN TREATING HYPOS – ITS INSTABILITY WATER!

- Poor stability
- Poor solubility

↓

- Complicated formulations
- Reconstitution/Refrigeration
- Large volumes, painful

↓

- Poor products
- Poor access
- Poor compliance

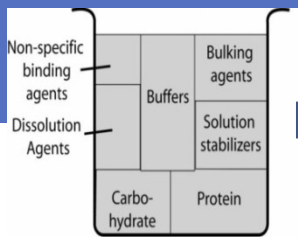
XERIS' SECRET SAUCE – REMOVE THE WATER!

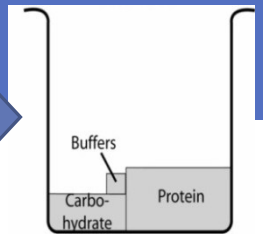
FORMULATE
Simplify the formulation

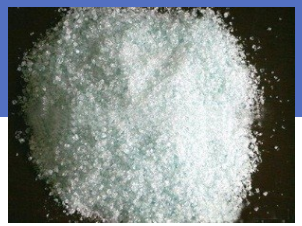
DRY
Dry down to a powder

MIX
Add non-water, bio-compatible solvent/diluent

PACKAGE
Package in auto-injectors, pens & pumps





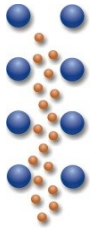


Simplifying the formulation
Can eliminate many ingredients often required in water-based formulations

Co-formulation
Process allows two drugs to be combined in the same formulation in a way not before possible

Intellectual Property
Xeris has intellectual property at each step of formulation

EARLY PROOF OF CONCEPT FOR MEDICAL MANAGEMENT OF HI HYPOS WITH GLUCAGON



Previous Use of Glucagon in treating severe, persistent hypoglycemia with HI

- **Mohnike et al. 2008** reported a retrospective review of 9 HI patient cases where continuous subcutaneous (SC) glucagon was used as a treatment option (1 – 3 mg/day), with or without concomitant octreotide and IV glucose.

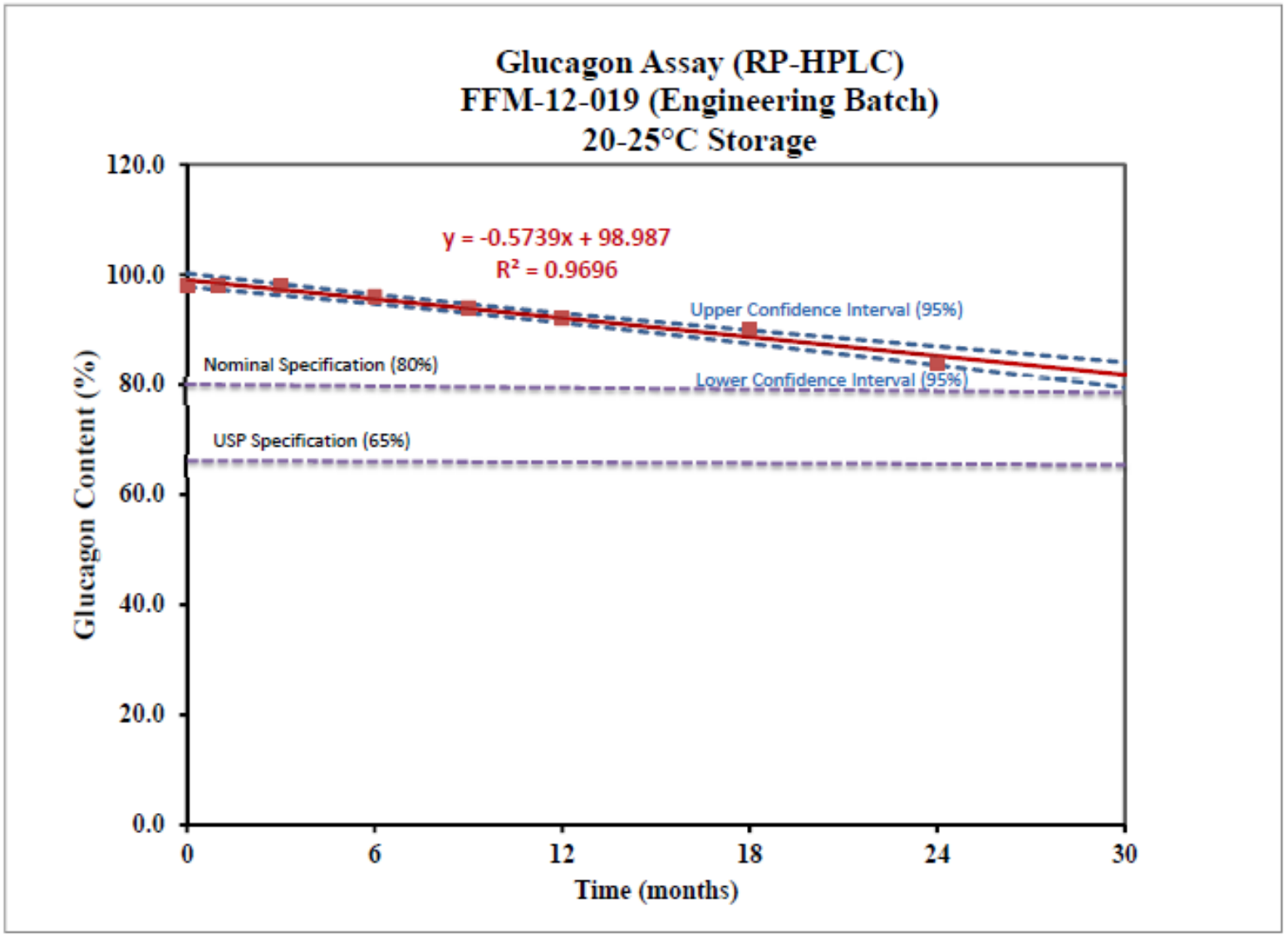
The objectives of using continuous SC glucagon were to:

- Stabilize blood glucose levels for several weeks without the use of high-volume dextrose infusions administered via a central catheter, which often causes bloating, and
- Avoid pancreatectomy or resurgeries (further reduction of pancreatic tissue) in patients with diffuse HI.

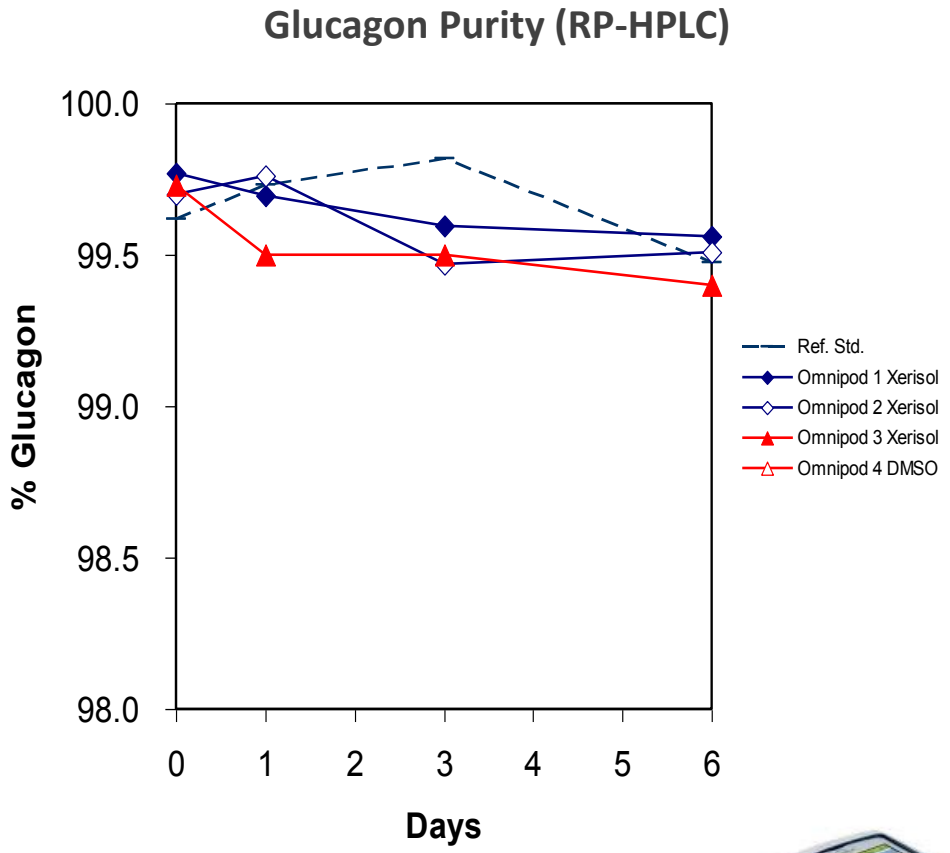
OUTCOMES WITH SC GLUCAGON

- Central glucose infusions significantly reduced or eliminated in all 9 children
- SC glucagon continued in 3 of 6 children for 1-4 years without further symptomatic hypoglycemia, convulsions or unconsciousness
- Glucagon treatment was initiated to manage recurrent hypoglycemia after subtotal pancreatectomy in 2 of 9 children
- Pancreatectomy or resurgeries were avoided in 5 of 9 children
- Octreotide was reduced to 8-15 µg/kg/day – considerably lower than if given alone, without glucagon (15-60 µg/kg/day)
- An experimental, stabilized glucagon (glucagon Technospheres™ suspension) was IRB approved and used successfully in 3 children – a peek at the future

G-PEN™ STABILITY @ ROOM TEMPERATURE



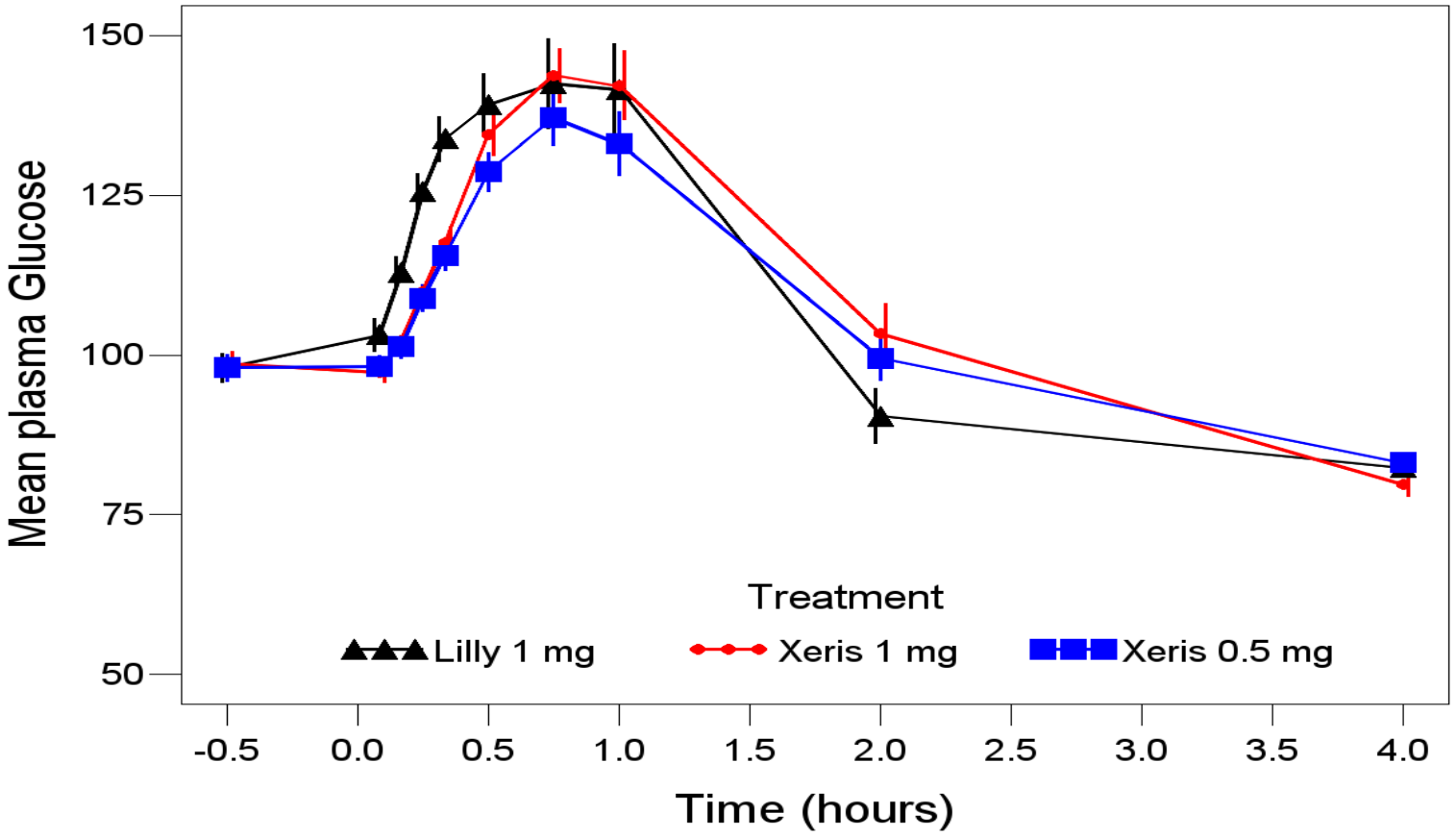
CSI GLUCAGON™ STABILITY IN OMNIPOD® PATCH-PUMP



Study Highlights

- Testing with both RP-HPLC and SE-HPLC showed high glucagon purity maintained over 6-days inside the OmniPod® stored at 37C
- G-Pump™ Glucagon remained clear and free of particulates over 6 days inside the OmniPod® stored at 37C
- No significant findings observed in UV spectrum from 350 – 650 nm

POSITIVE PHASE 2 PHARMACODYNAMIC RESULTS

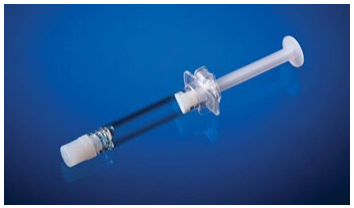


» ***No Statistically Significant Differences*** in AUC, T_{MAX}, and C_{MAX} (full dose)

CSI GLUCAGON™ + OMNIPOD™ PATCH PUMP FOR HI

CSI Glucagon™

West



OmniPod™

Insulin Management System

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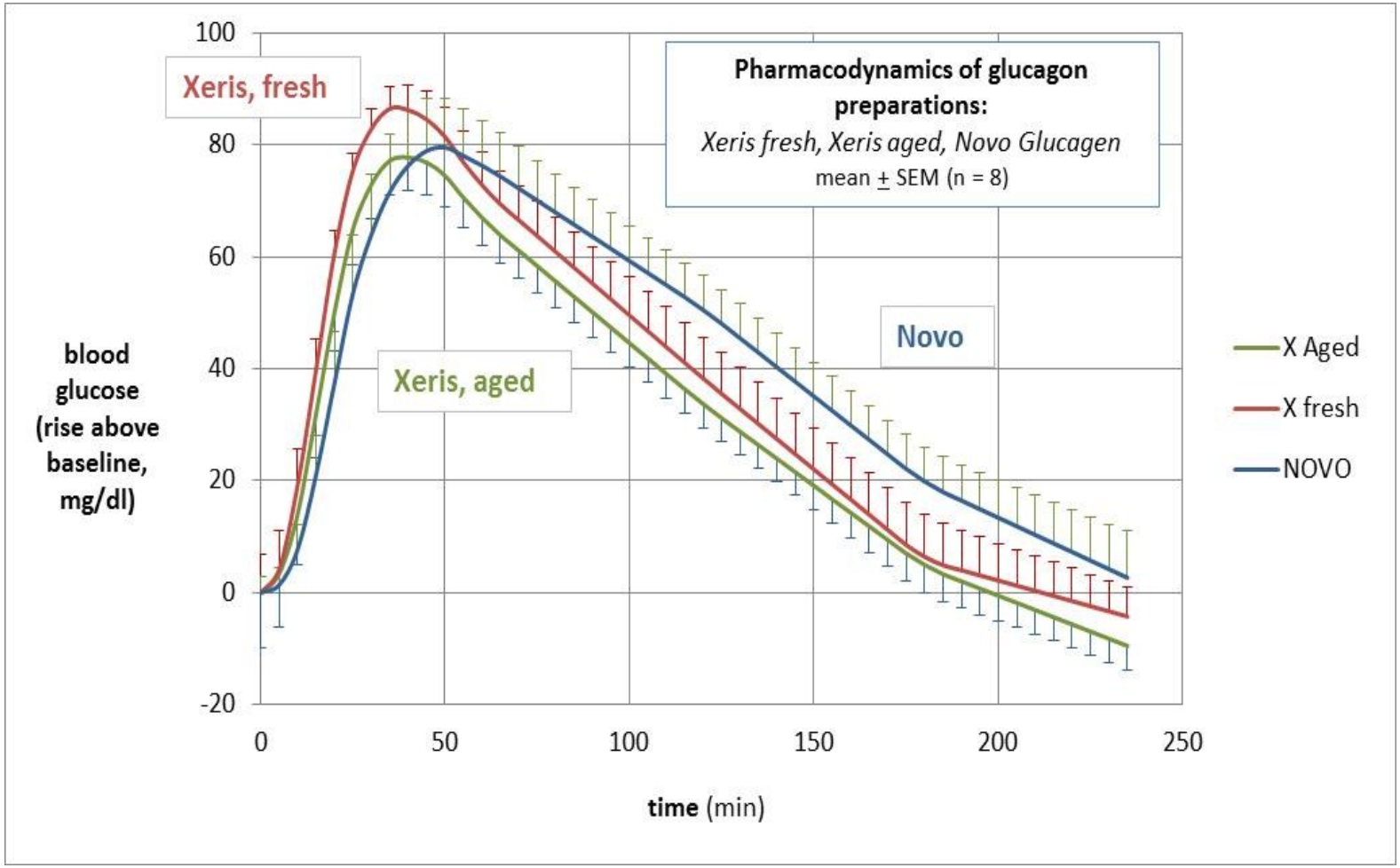
PIG PK/GLUCODYNAMICS STUDY DESIGN

- Conducted at OHSU Legacy Research Institute
- Flurane anesthetized female Yorkshire Pigs (35-50 kg)
- Insulet OmniPod® inserted on abdominal skin
- 2 µg/kg of:
  - Xeris fresh Glucagon (N=8)
  - Xeris 7-day aged Glucagon (N=8)
  - Novo GlucaGen® (N=8)
- Blood obtained at baseline and 10 points over 2 hours
- Serum collected for glucose and glucagon analysis

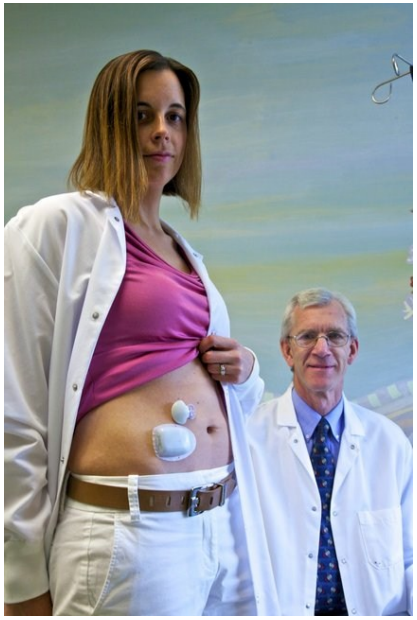
CSI GLUCAGON™ PIG STUDY



G-PUMP™ GLUCAGON CLINICAL PLAN

Phase 2a Inpatient Dose-Ranging Study

- 18 diabetic patients on insulin clamp
- Three randomized micro-doses of G-Pump™ Glucagon from OmniPod® pump *on same day*
  - Ward et al glycogen depletion study
- Same doses with Novo GlucaGen® comparator on Day 2
- ***Enrollment completed!***

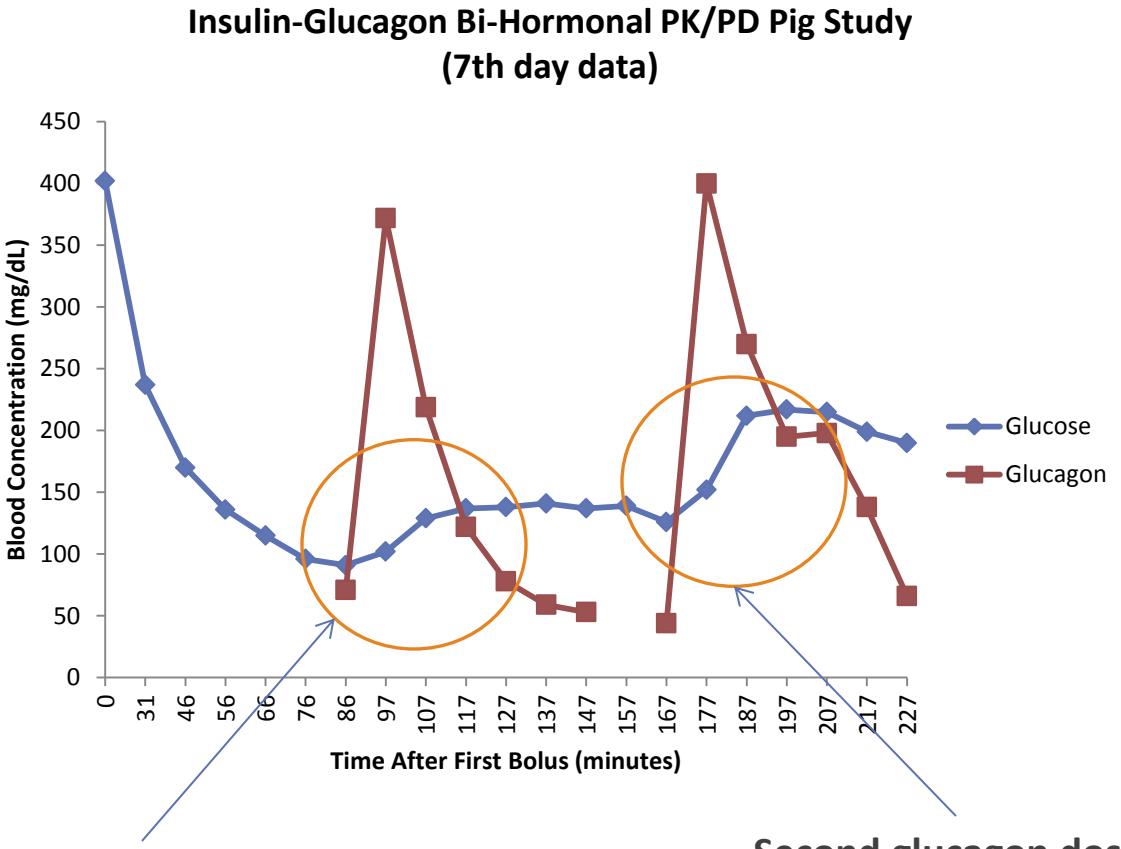


Phase 2b Outpatient Closed-Loop (Hotel Study)

- 30-hour closed-loop study with CGM, insulin pump, glucagon pump, OHSU adaptive control algorithm
- Hotel near OHSU campus with nurse nearby
- Amendment to Castle/Ward open IDE

JDRF

BI-HORMONAL PUMP PK/PD DATA



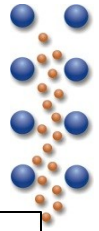
First glucagon dose
boosts blood glucose

Second glucagon dose
boosts blood glucose

Study Highlights

- Study conducted in diabetic pigs by Dr. Edward Damiano at Boston University
- Xeris glucagon administered via pump strapped to pig
- Glucagon subjected to higher temp and agitation for 7 days
- Basal insulin + bolus at T = 0 starts to bring glucose down
- Demonstrated glucose boosting effect at 7 days not possible with Lilly glucagon

A SAFETY-EFFICACY CLINICAL TRIAL WITH CSI GLUCAGON™ DELIVERED AS A CONTINUOUS, SUBCUTANEOUS INFUSION WITH AN OMINIPOD® PUMP IN PEDIATRIC PATIENTS WITH HI



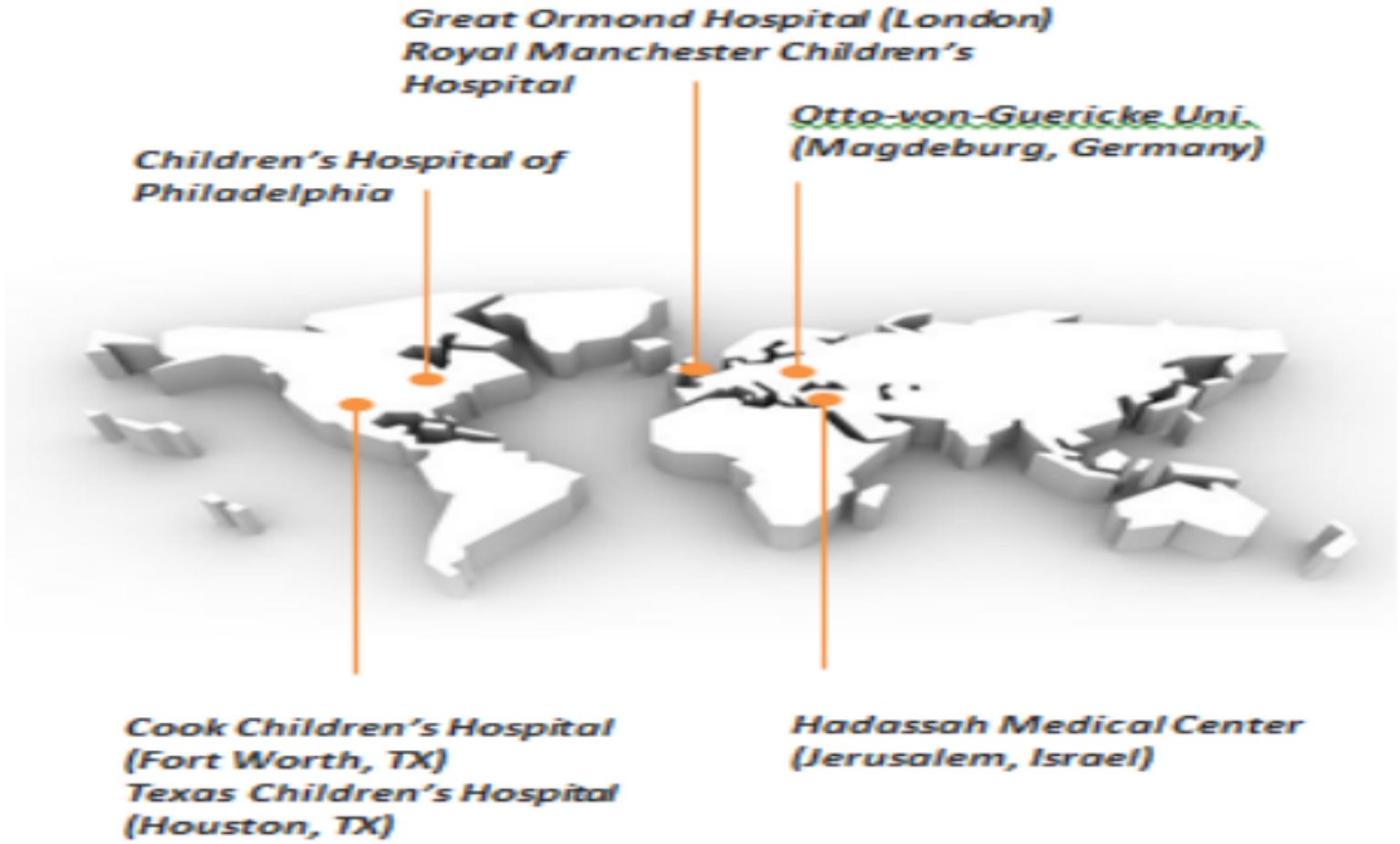
- The study contemplates an approximately 3-4-day **in-patient phase** in which CSI Glucagon™ is integrated into a medical management program with IV glucose and/or somatostatin to stabilize a patient's blood glucose levels.
- Medical management goals are:
  - To decrease IV glucose feeds and/or somatostatin utilization (both of which have their own adverse effects),
  - To increase fasting intervals.

Out-patient Phase

Patient will be discharged to an out-patient setting – once goals are met for the remainder of the 180-day period.

Patient will continue on CSI Glucagon™ indefinitely after 180 days, if clinical goals continued to be met until sufficient complex carbohydrates can be integrated into their diet, whereupon glucagon treatment can be tapered and eventually discontinued.

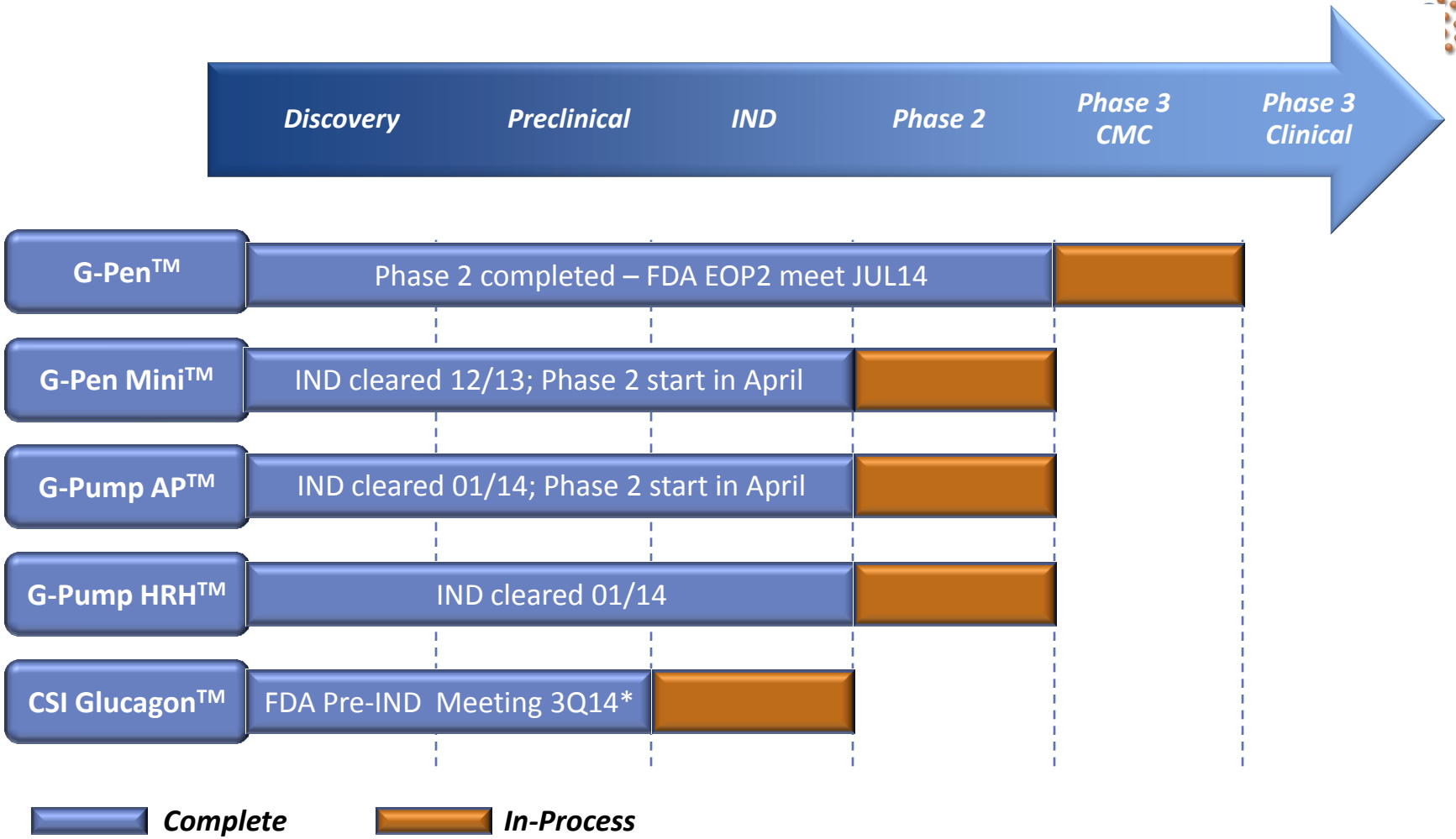
CLINICAL SITES FOR EARLY 2015 HI TRIAL



THE POTENTIAL FOR CSI GLUCAGON™ IN TREATING HI

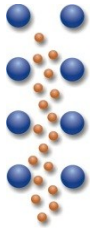
	Current Std. of Care	Potential with Pump-G
In Patient		
Medical Mgt. of Blood Glucose	Octreotide and dextrose feed	↓↓ or discontinued
Surgery	Unchanged	↓ - more parents may elect for medical management not surgery
Time in hospital	Unchanged	↓ - faster to stable glucose levels and discharge to out-patient care
Costs	Unchanged	↓ - faster to medical management and discharge
Out Patient		
Medical Mgt	Octreotide and Dextrose Feed	Reduced or never started
Risk of severe hypos	Unchanged	↓↓
Quality of life	Unchanged	↑↑
Costs	Unchanged	↓↓

GLUCAGON DEVELOPMENT STATUS



***Orphan Drug designation application submitted to FDA June 2014; European Medicines Agency July 2014**

PEER-REVIEWED VALIDATION



MGH 1811

NIDDK
NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Baylor College of Medicine

OHSU

JDRF

Joslin Diabetes Center

BU
BOSTON UNIVERSITY

Texas Diabetes Institute
University Health System

Sir Frederick Banting Legacy Foundation

EPILEPSY FOUNDATION
Not another moment lost to seizures

epilepsy therapy project

Stronger Together

$5.7M received in non-dilutive research and development grants

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A PARENT & PATIENT-FRIENDLY SOLUTION FOR THE HI COMMUNITY