XERIS PHARMACEUTICALS

XeriSol™ Glucagon for Congenital Hyperinsulinism

September 2015

GLUCAGON

- increase glucose levels by stimulation of liver glycogenolysis
- 5-10µg/kg/h
- stimulate the beta cell to secrete insulin (Insulinsekretagogue)

side effects:

- Nausea, vomiting,
- reduced pancreatic enzyme secretion,
- reduced myocardial kontraction,
- Tachyphylaxis
- Erythema necrolyticum migrans

GLUCAGON: WATER CREATES THE PROBLEM

- Poor stability
- Poor solubility

↓

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

↓

- Poor products
- Poor access
- Poor compliance

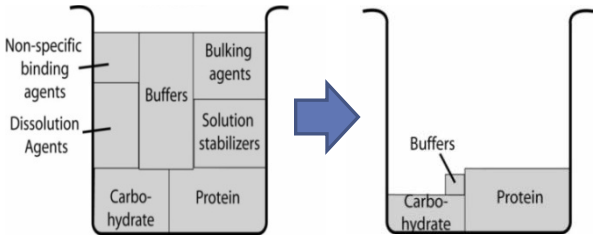
SOLUTION – REPLACE THE WATER!

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



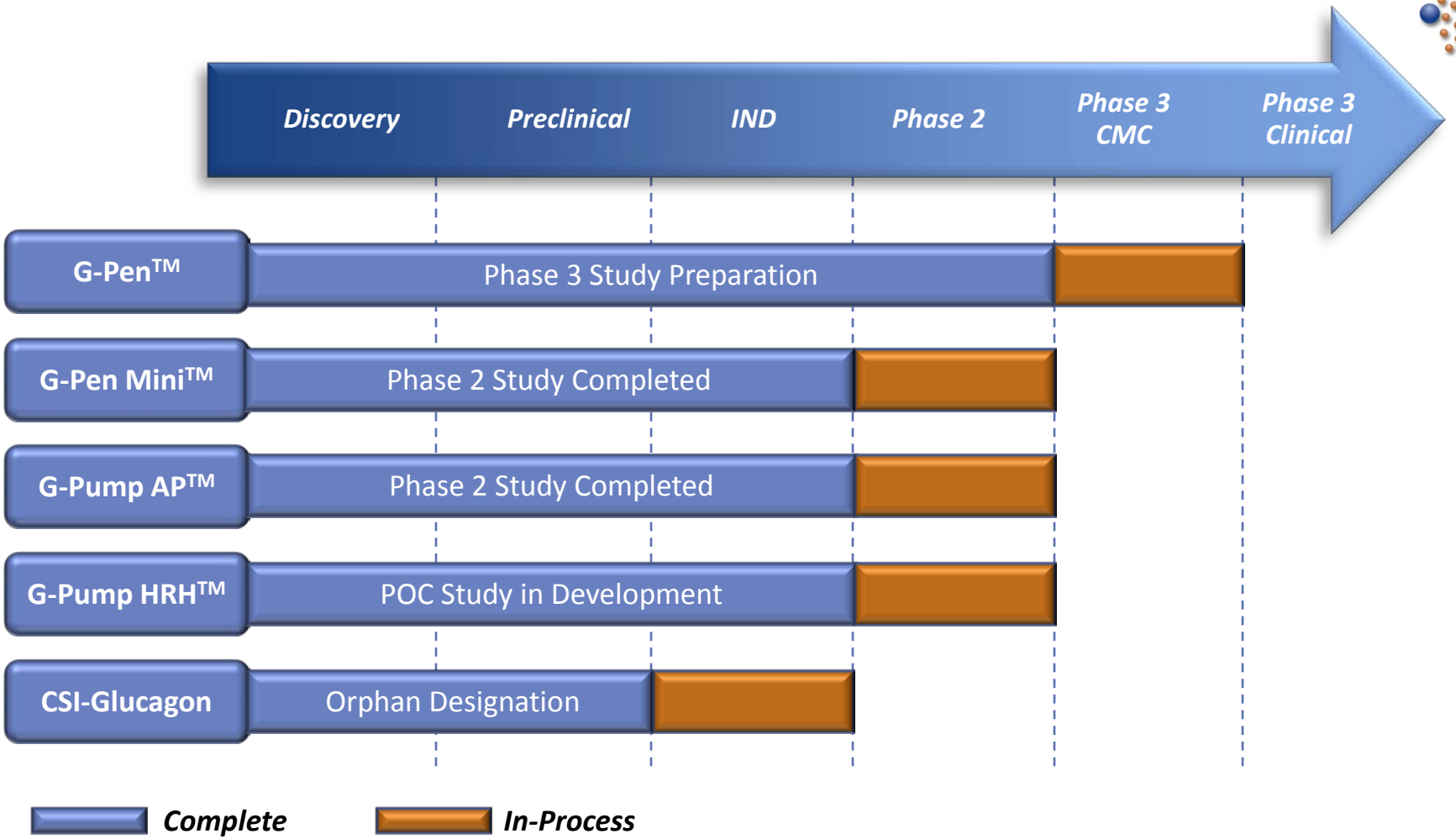
Simplifying the formulation
Can eliminate many ingredients often required in water-based formulations

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

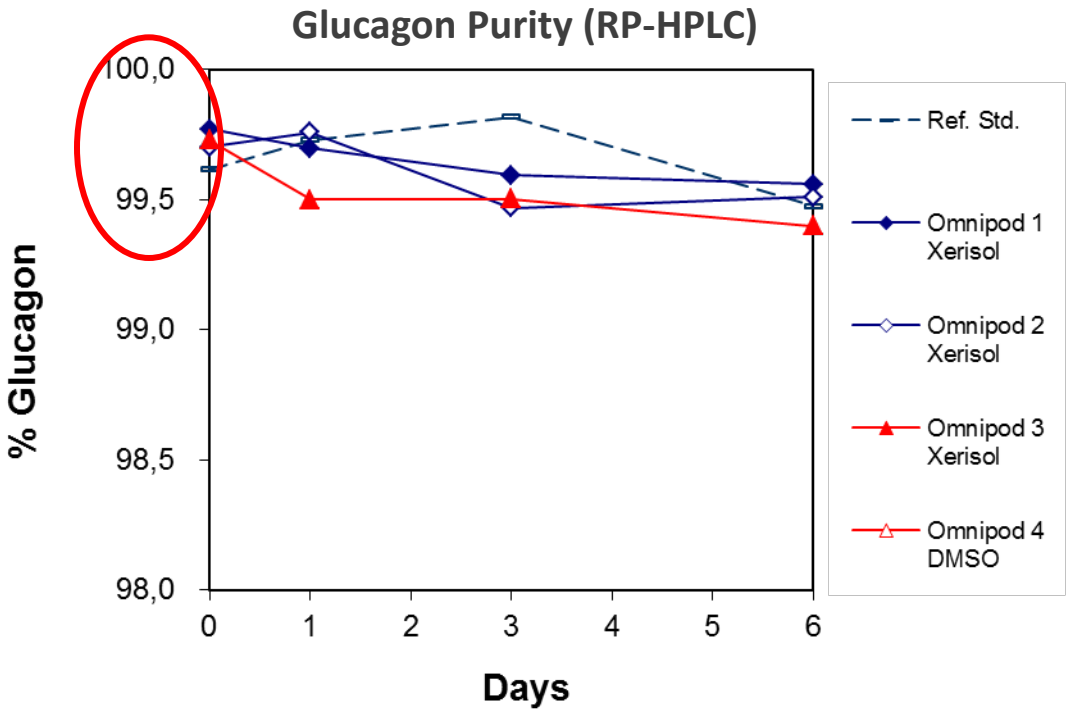
Intellectual Property
Xeris has intellectual property at each step of formulation

GLUCAGON PRODUCTS IN DEVELOPMENT

GLUCAGON PRODUCTS DEVELOPMENT STATUS



EXCELLENT STABILITY IN OMNIPOD® INFUSION PUMPS AT 37° C

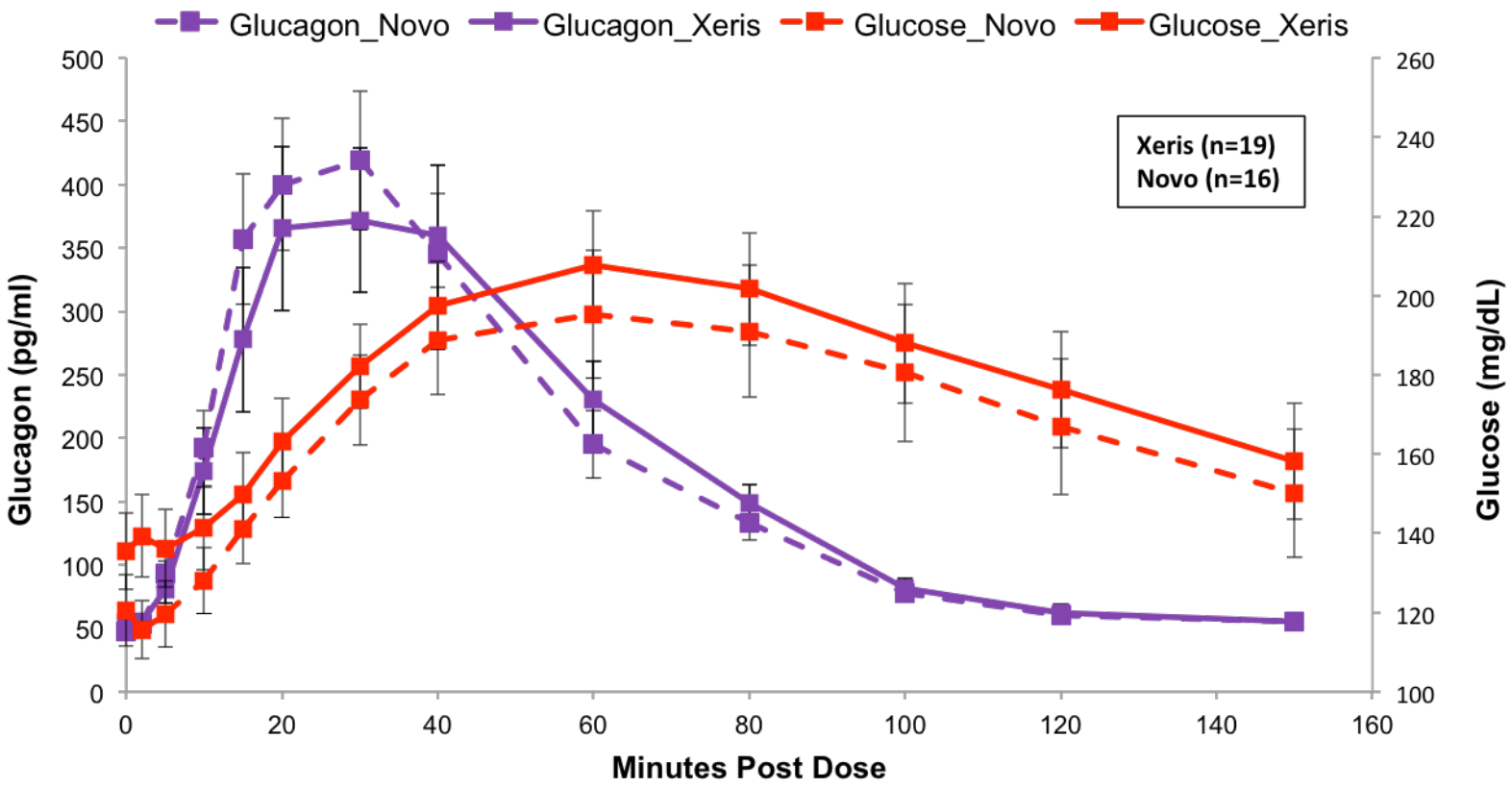


Study Highlights

- XeriSol™ Glucagon remained clear and free of particulates over 6 days inside the OmniPod® stored at 37°C
- No significant abnormalities observed in UV spectrum from 350 – 650 nm
- RP-HPLC and SE-HPLC showed high glucagon purity maintained over 6 days inside the OmniPod® stored at 37°C
- Minor and insignificant leachables detected

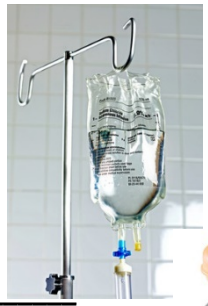
XERISOL GLUCAGON IS EQUALLY EFFECTIVE AS NOVO GLUCAGEN® WHEN DELIVERED FROM AN OMNIPOD® PUMP

Mean (± SEM) Plasma Glucose and Glucagon Concentrations after a Single Dose of Xeris or Novo Glucagon (2.0 µg/kg, ~ 150 µg)



Xeris glucagon was stored for 5 months as a liquid, Novo GlucaGen® reconstituted immediately prior to use!!

GLUCAGON INFUSION IS STANDARD OF CARE IN HOSPITAL



Cook Children's Medical Center - glucagon experience

»10 patients using current

»7 patients treated with glucagon during stabilization pre-surgery – (4 focal, 3 diffuse)

	Mean	Range
Birth weight (Kg)	4.3	3.1 -5.3
Age at start of glucagon(days)	21	3 - 45
Dose of glucagon (mcg/kg/hr)	10	7.9 – 13
Max GIR pre glucagon(mg/kg/min)	23	14 – 41
Min GIR on glucagon(mg/kg/min)	7.2	1.8 – 8
Duration of glucagon(days)	9.4	4 - 15

~75% reduction in GIR

»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 on a 4.1mg/kg/min GIR

Similar experience in other HI centers globally

GLUCAGON

Mohnike et al. 2008 Retrospective Study

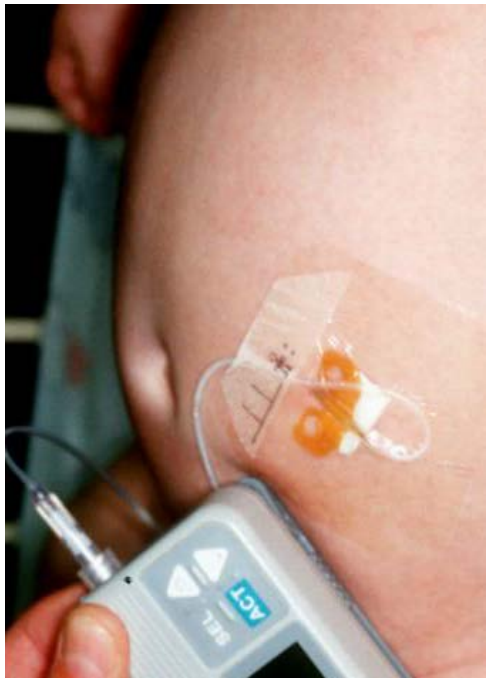
	No operation			Glucagon after operation		Preoperative glucagon			
Patient	1	2	3	4	5	6	Tec 1	Tec 2	Tec 3
Gender	F	F	M	F	M	M	M	F	F
Histologic type; age at pancreatic surgery	No surgery	No surgery	No surgery	Diffuse 3 weeks	Diffuse, repeated pancreatic operations at age 33 and 88 days, 2.5 years	Diffuse	Focal 4 months	Diffuse 5 months	Focal 6.5 months
Mutation in ABCC8 (SUR1)	Not tested	Not tested	R1437Q paternal allele only	1672-9T>A/ 2698-2A>G	DelF 1388/3992-9 G>A	4481 G>A paternal allele only	One allele D1471N	50T>C/ 2394-1G>A	Not tested
Gestation age, weeks	40	Full term	40	37	Information not available	38	40	40	30
Birth weight, g	4,280	Information not available	3,110	3,820	3,544	3,955	3,600	4,800	1,870
Age of initial hypoglycemia, h	36	Seizures at 2 months of age	24	4	72	Birth	24	6	18
Presenting blood glucose, mmol/l	1.1	1.5	1.3	0.9	1.1	1.3	0.5	0.8	0.8
Insulin at hypoglycemia, mU/l	26.0	8.8	5.6	218.0	Information not available	50.0	19.0	419.0	14.5
Glucose infusion rate, mg/kg/min	16.0	7.0	20.0	14.0	Information not available	14.0	20.0	26.0	14.0
Maximum dose of octreotide, µg/kg/day	15	10	15	None	20	8	35	10	30
Age at start; maximum dose of s.c. glucagon, mg/kg/day	46 days; 0.026	5.5 months; 0.24	165 days; 0.8	120 days; 0.4	0.1	43 days; 0.41	27 days; 0.25	42 days; 0.26	112 days; 0.46
Discharge from hospital with glucagon	8 weeks	Transferred to local hospital on combination therapy and then home	25 weeks	10 weeks	3 months	No	8 weeks	No	No
Blood glucose <2.6 mmol/l during s.c. glucagon	None	None	None	None		Information not available	<3 times/ month	5 times/ month	None
Duration of glucagon treatment	4 years	>4 months	6 weeks	1.3 years	2 years	10 days	2.5 months	3.5 months	Days
Age at last presentation	5 years	9.5 months	8 months	1.5 years	10 years	6.5 months	7 years	6 years	2 years
Erythema necrolyticum	No	No	No	No	No	No	No	Yes	Yes

Tec = Glucagon-Technosphere™.

THE PROMISE OF SC GLUCAGON AS LONG-TERM TREATMENT FOR CHI

Mohnike et al. 2008 Retrospective Study

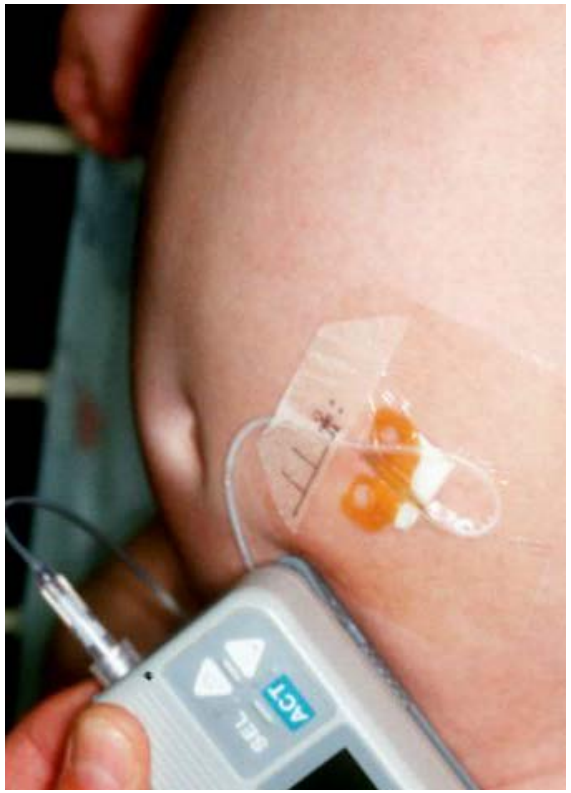
- SC glucagon continued for 1-4 years in 3 of 6 children without further symptomatic hypoglycemia, convulsions or unconsciousness
- Central glucose infusions significantly reduced or eliminated in all 9 children.



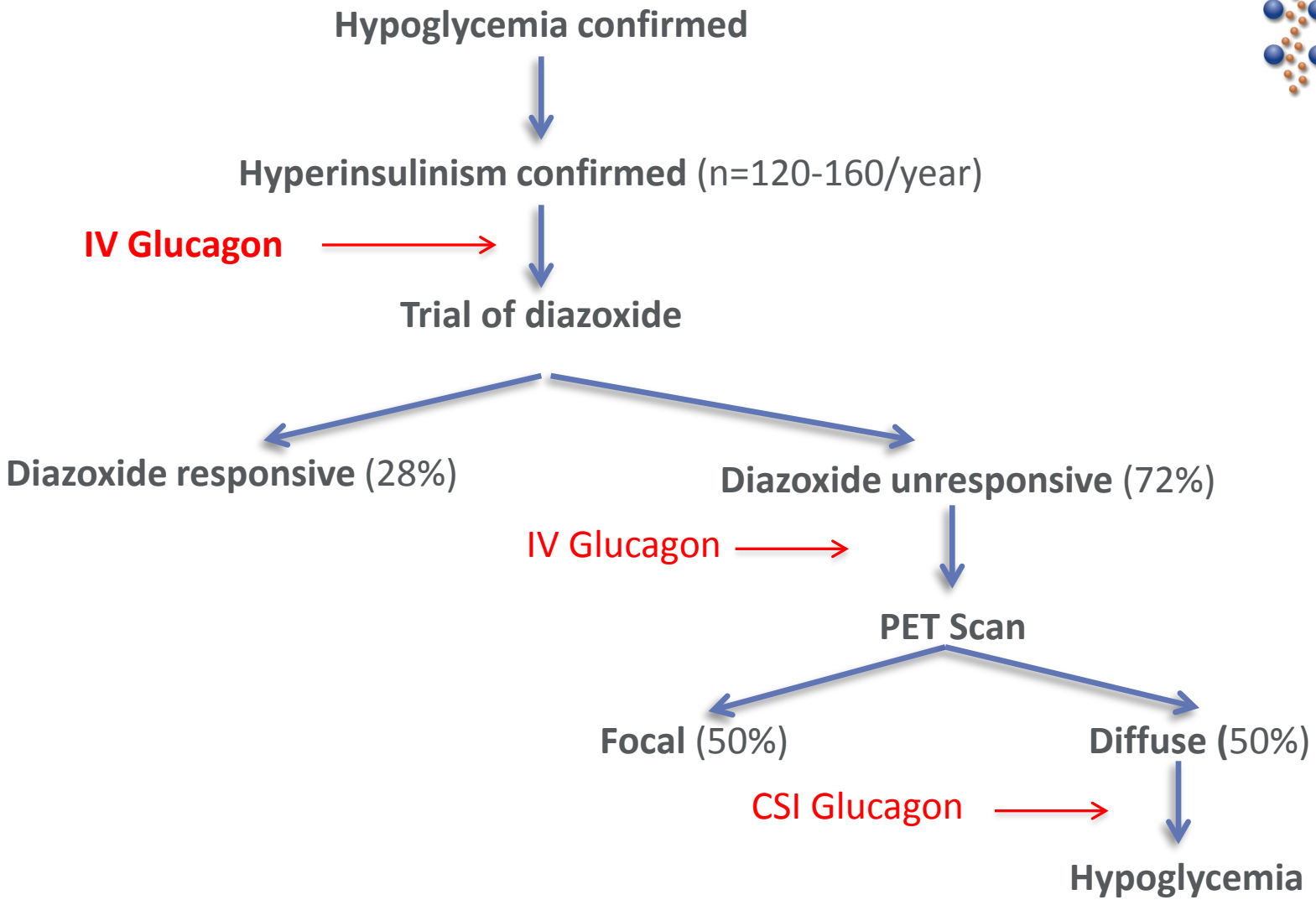
THE PROMISE OF SC GLUCAGON AS LONG-TERM TREATMENT FOR CHI

Mohnike et al. 2008 Retrospective Study

- 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)



CURRENT OFF-LABEL USE OF GLUCAGON



PROGRAM SUMMARY

- Orphan Product Designation received from FDA and EMA
- $2M NIH-NIDDK grant received
  - Collaboration with Drs. Thornton (Cook Children's) and DeLeon (CHOP)
  - Funds juvenile toxicology study
  - Funds short-term clinical trial in US centers
- Significant leverage from other glucagon programs
  - Non-clinical chronic toxicology program
- Pre-IND interaction with FDA
  - Filing IND in October 2015
- Short-term POC clinical trial to start in 1Q16

XERIS PHARMACEUTICALS

XERISOL GLUCAGON FOR CONGENITAL HYPERINSULINISM

September 2015

PRESENTATION OVERVIEW

- XeriSol Technology Overview
- Xeris Glucagon Programs
- Current Off-Label Use of Glucagon
- Continuous Subcutaneous Infusion (CSI) Glucagon for Treatment of CH
- CSI Clinical Development Plans