



**358**

**First-in-Class Treatment for  
Hyperinsulinemic Hypoglycemia**

*January 31, 2017*

# Forward-Looking Statement

Certain statements contained herein including, but not limited to, expected licensing transactions, statements related to anticipated timing of initiation and completion of clinical trials, anticipated size of clinical trials, therapeutic and market potential of XOMA's product candidates, the manufacture of our product candidates, the expansion of our endocrine program, regulatory approval of unapproved product candidates, sufficiency of our cash resources and anticipated levels of cash utilization, or that otherwise relate to future periods are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934.

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# Patients Need 358 to Succeed!

**Jim R. Neal, Chief Executive Officer and Member of the Board of Directors**



## Highlights from Proof-of-Concept 358 Studies

- Proof-of-concept established in 14 CHI and 13 PBS patients
- 358 treatment clearly increases glucose levels and reduces hypoglycemia
- Other met objectives enable initiation of multi-dose studies
- Multi-dose protocol approved in UK for CHI patients aged 2 and older

# CHI Disease Burden is Significant in Neonatal and Pediatric Population

## Disease Burden

- Major emotional burden on families
- Parents in constant fear of hypoglycemic attacks
  - Constant monitoring of blood glucose
  - Irreversible brain damage and permanent developmental issues may result



## Economic Burden

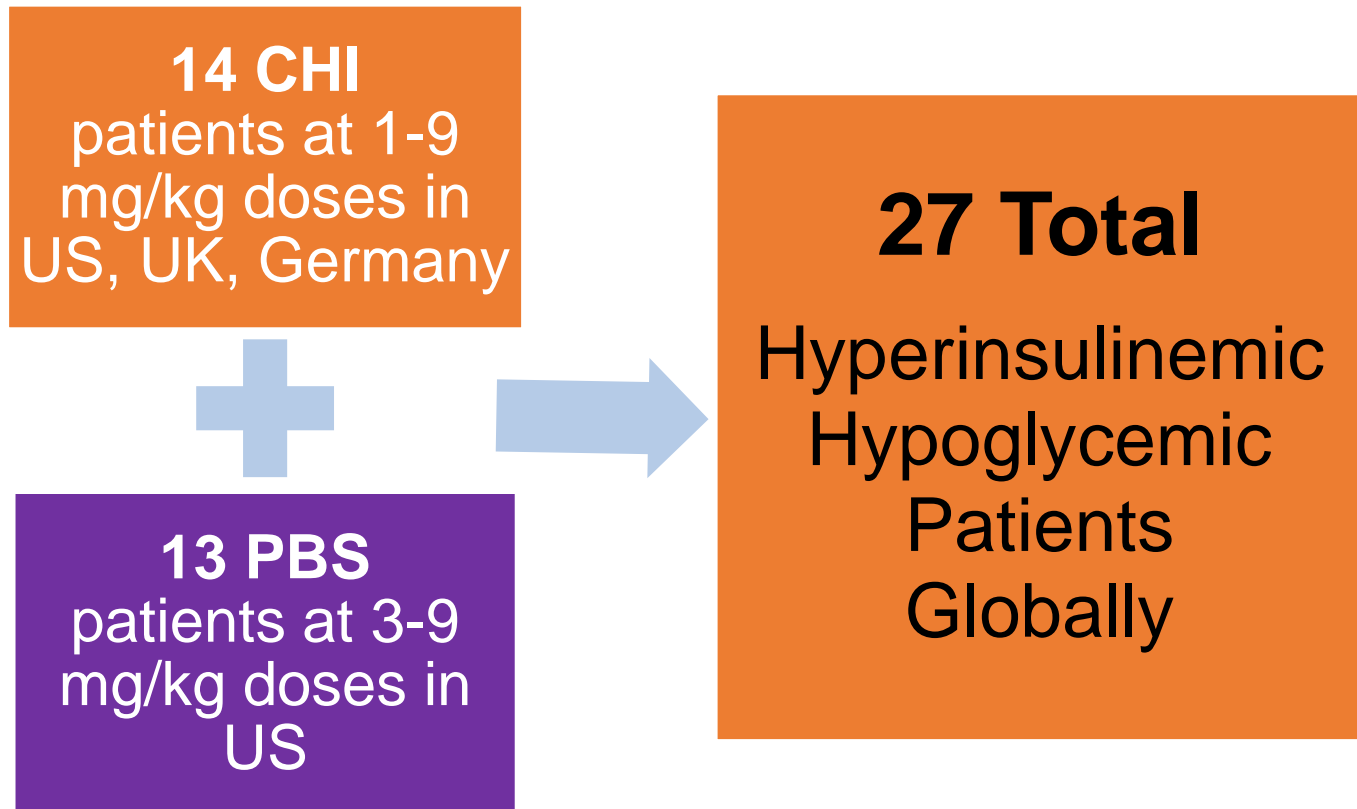
- Medical Treatment: **\$150,000 / year**
- Cost of Nursing Care: **\$200,000 / year**
- In event of pancreatectomy: **\$1,000,000**
  - Type 1 diabetics post-pancreatectomy

## Healthcare System Burden

- Patients may require medical treatment for many years
- Significant costs incurred over patient's lifetime
- Long-term care requirements: epilepsy, permanent brain damage
- CHI centers of excellence: 5 in U.S., 8 outside U.S.

# The Global Phase 2 Patient Data Set

**Triple the N described in mid-September and well-distributed across both indications and dose levels**



# Low Blood Sugar is the Major Problem *and* Unmet Need in these Hyperinsulinemic Disorders

- Hypoglycemia is commonly defined as glucose values  $<70$  mg/dL
- Glucose levels were monitored, often in parallel, by:
  - bedside glucometer
  - serum laboratory
  - Continuous Glucose Monitoring (CGM)

## By CGM:

- CGM durations of blood glucose below 70 mg/dL for  $\geq 2$  hr/day is abnormal<sup>1</sup>
- An improvement of  $\sim 50\%$  is considered “clinically meaningful”<sup>2</sup>

1. Accuracy of Continuous Glucose Monitoring Measurements in Normo-Glycemic Individuals. PLOS One October 7, 1-13, 2015. JDRF, Diabetes Care 33:1297, 2010. Brynes AE, Brit JAKintola, A.A. Accuracy of Continuous Glucose Monitoring Measurements Nutr 93:179, 2005

2. CHI Key Opinion Leaders and Principal Investigators

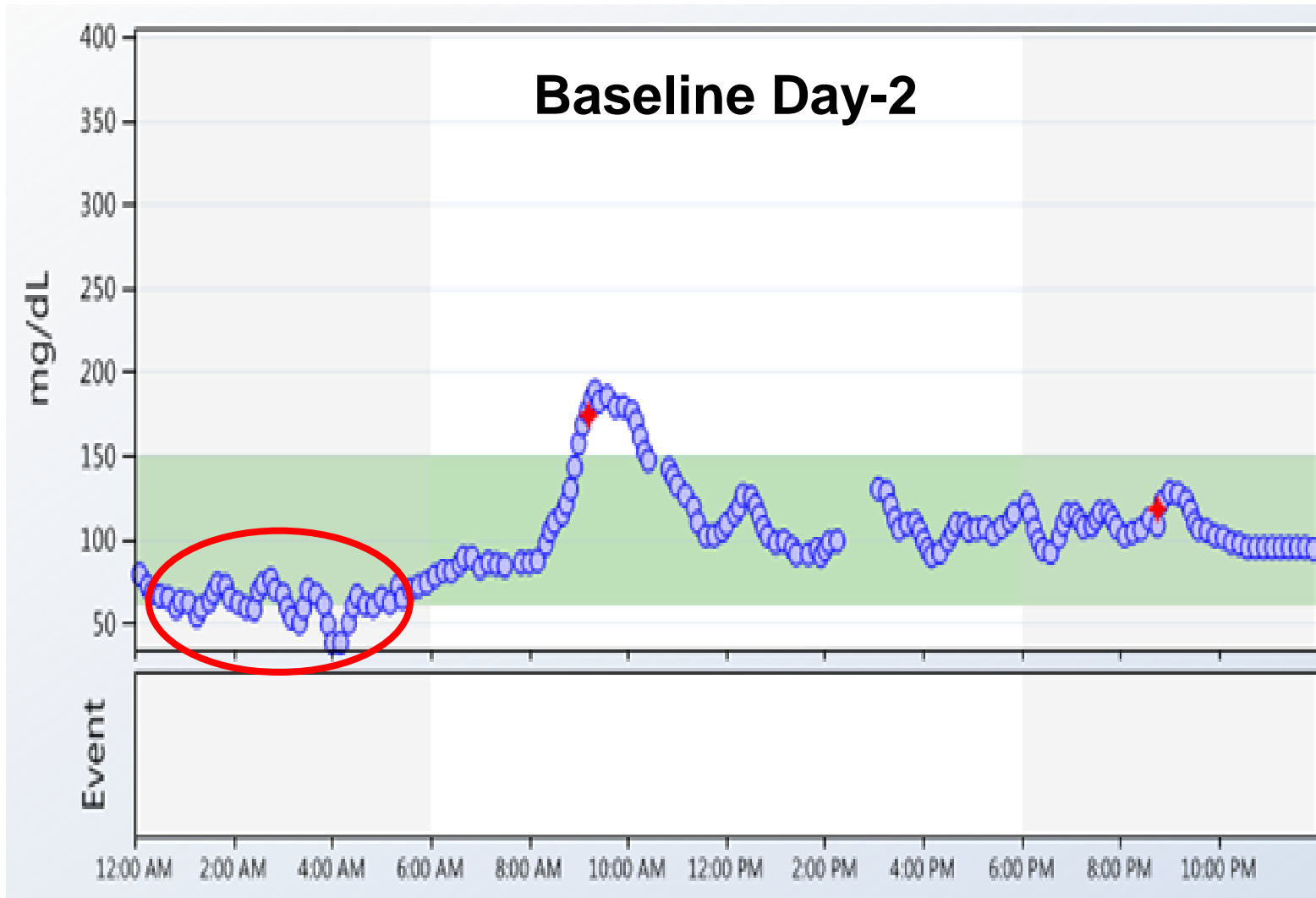
**CHI**

# Enrolled Adolescent & Adult Patients were Consistent with CHI Disease Population

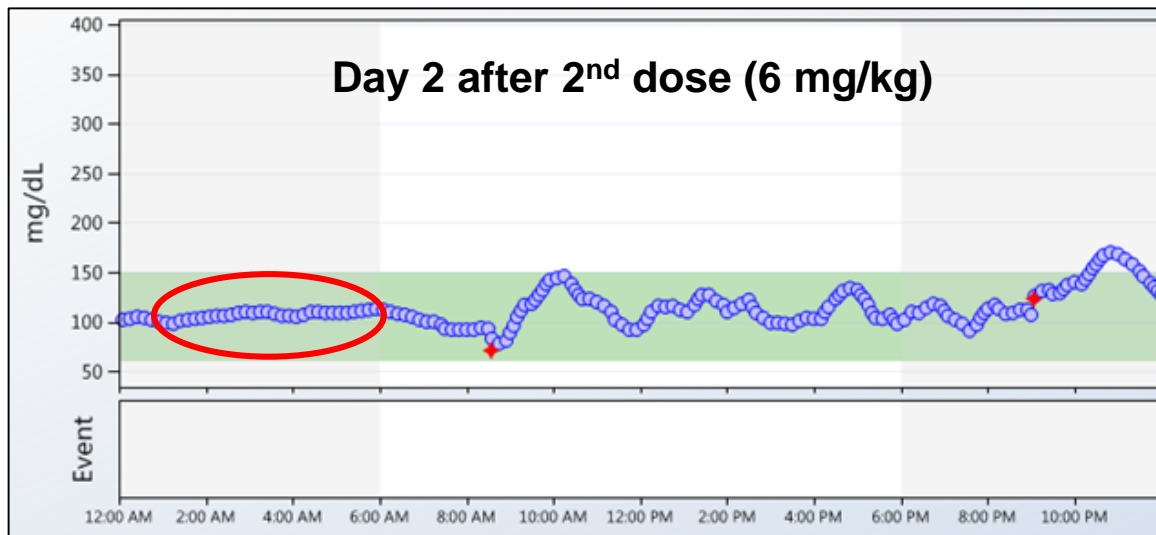
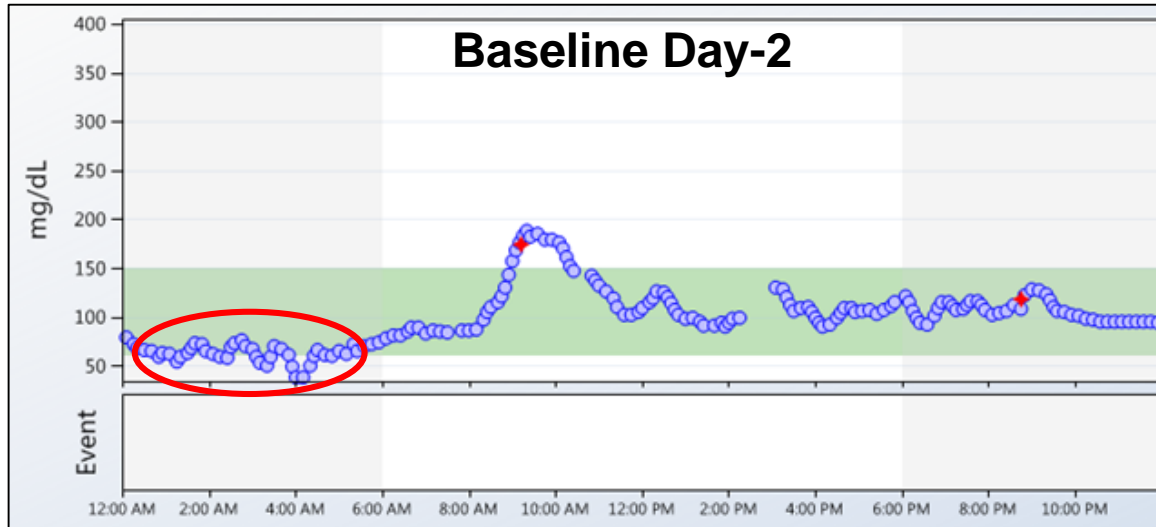
- **6 Females + 8 Males**
- **Aged 12-37**
- **CHI mutation profile consistent with disease population**
  - Majority K-ATP mutations
- **Washed out of pre-existing drugs (e.g. diazoxide, octreotide) and studied in-unit for 4 baseline days and 12 days post-358**



# Nighttime hypoglycemia is common in CHI. For example, the 24hr CGM profile of a 12 year-old CHI Patient



# Normalization of Glycemia in the 12 year-old CHI Patient Following 358 dosing

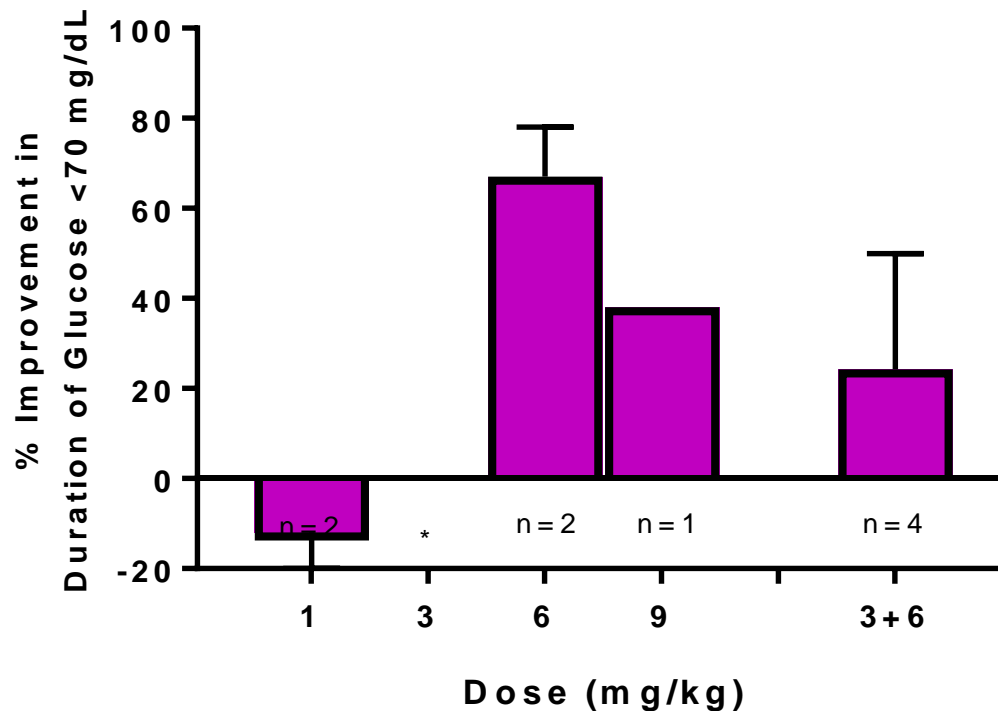


★ = calibration

# 358 Reduced Duration of Hypoglycemia by 25% - 70%

9/14 Patients with baseline durations of 24hr CGM  $<70$  mg/dL for  $\geq 120$  min  
Change in Post-358 Days 2,4,6 vs Non-challenge Baseline Days -2 & -1

Duration of Hypoglycemia ( $<70$  mg/dL)



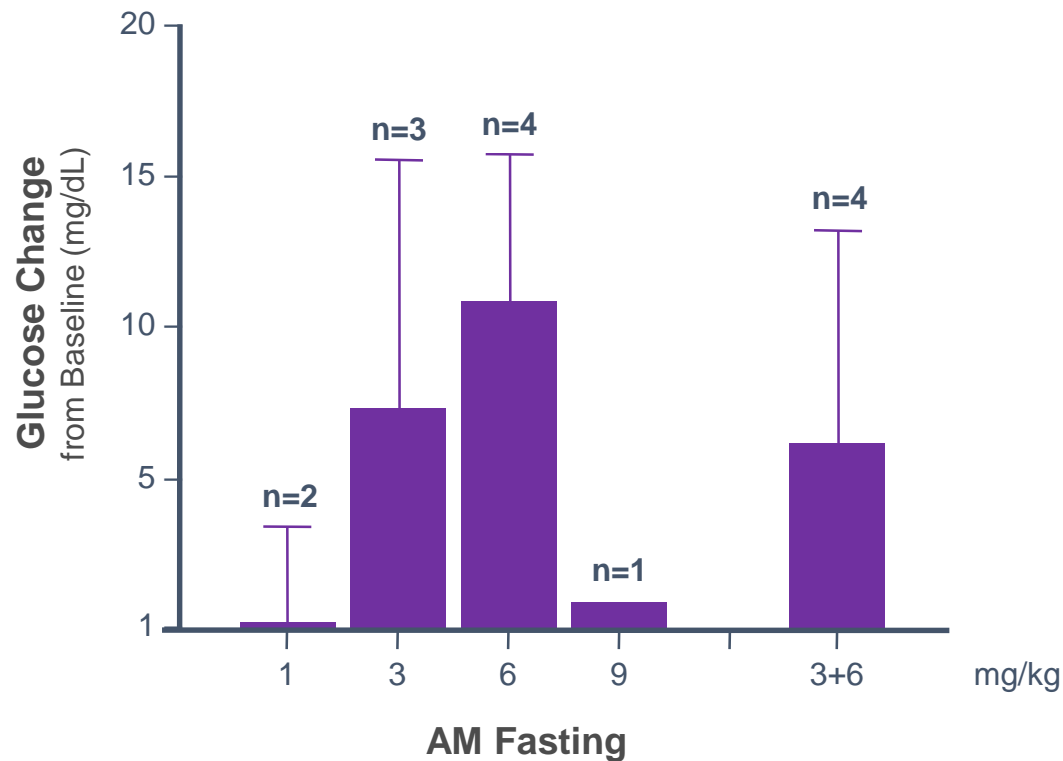
\* Excluded from analysis as they did not meet this CGM criteria

# Improvement of the AM Fasting Glucose Level is a Goal in CHI Management

- **Overnight fasting glucose measurements are a common laboratory test**
- **Hyperinsulinemic patients tend to have low fasting blood glucose values**

# 358 Treatment Increased AM Fasting Glucose Levels in CHI Patients

Change Post-358 on Days 2,4,6 vs Baseline Days -2 & -1  
(mean bedside glucose, all patients)



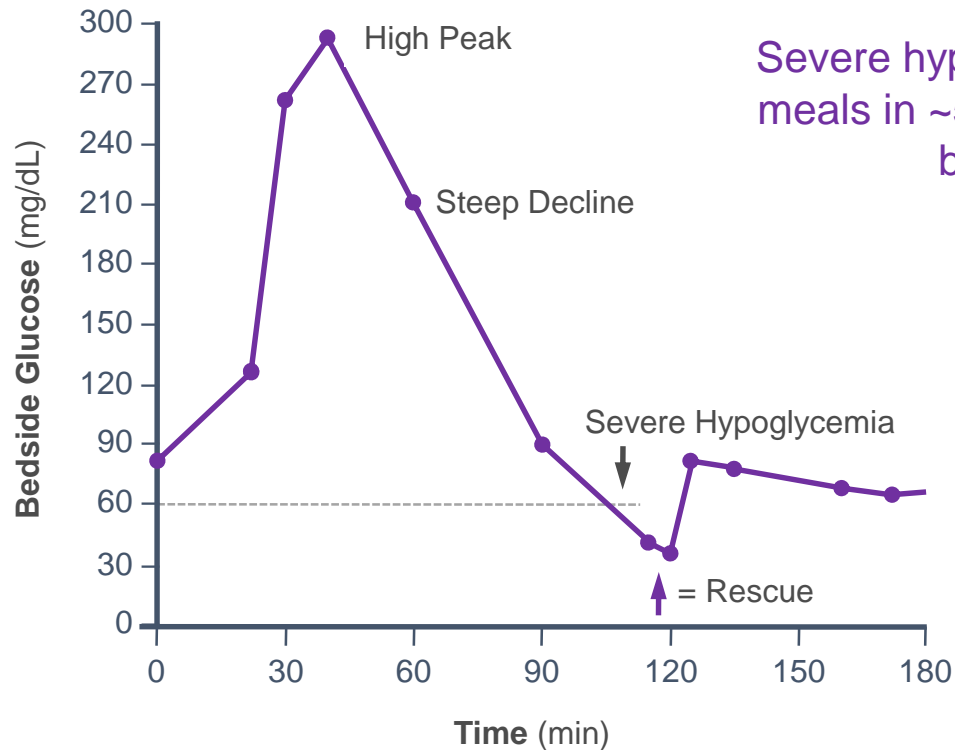
# Completed CHI Studies Support Advancement to Repeat Dose Protocol Phase

- **Single-dose data in CHI patients established a beneficial dose range with predictable pharmacokinetics and acceptable safety**
- **Program is ready for advancement to a repeat-dose phase**
  - Experience with relevant endpoints
  - Protocol involving 3-month dosing of CHI patients aged 2 and up is completing all regulatory approvals in UK

**PBS**

# Post-meal Glycemic Crashes are the Major Issue in Hyperinsulinemic PBS Patients

## Typical Profile of Blood Glucose vs Time Post-Meal



Severe hypoglycemic risk following meals in ~5% of Roux-en-Y gastric bypass patients

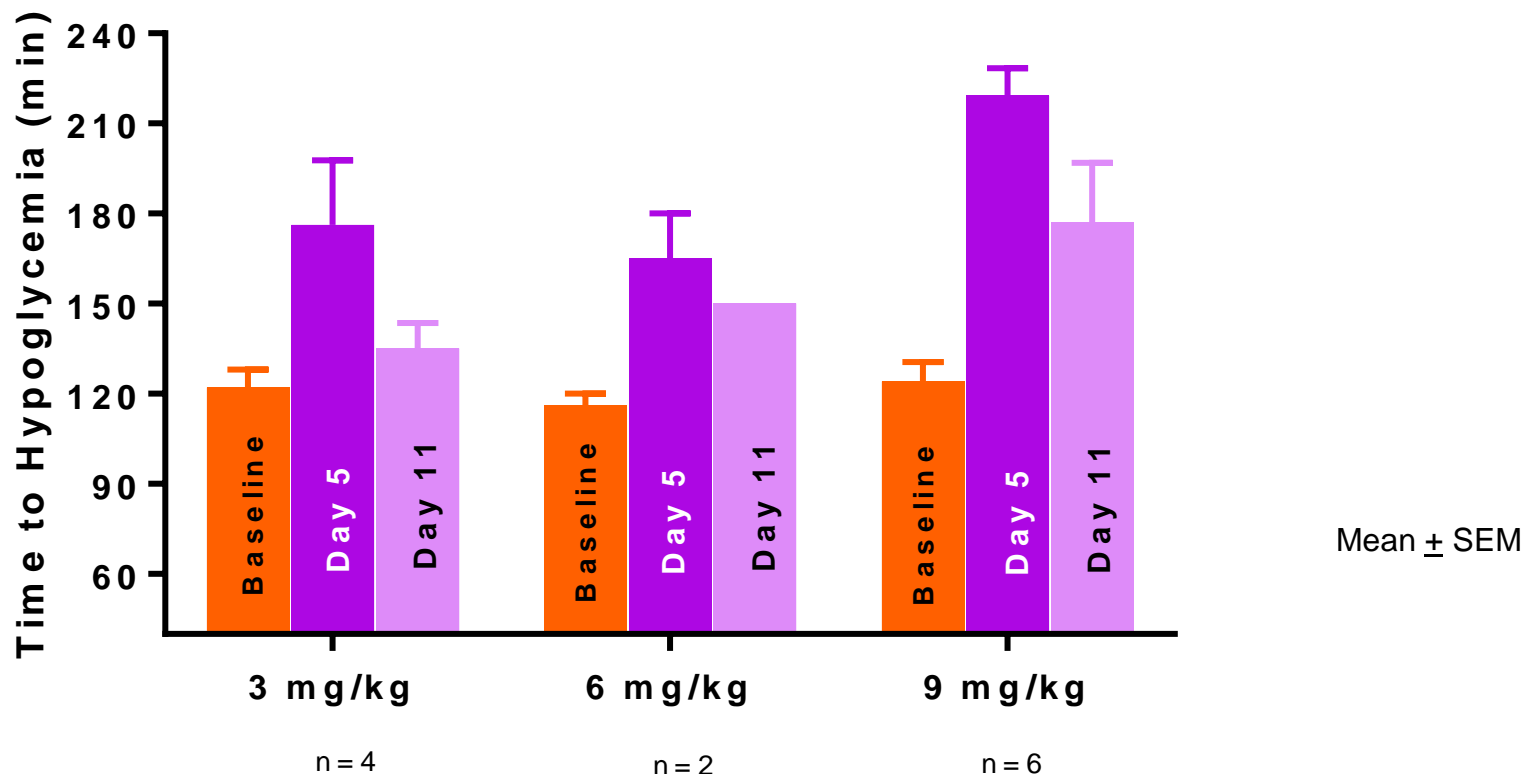


# Enrolled Patients were Representative of Typical PBS Patients

- **12 Females + 1 Male**
- **Aged 42-68**
- **Body weight 62-112 kg**
- **Washed out of pre-existing drugs (e.g. diazoxide, octreotide, acarbose) and studied in-unit for 4 baseline days and 12 days post-358**

# 358 Significantly Improves Glucose Control in PBS Patient Meal-Challenge Tests

## Meal Test Duration



*Duration of Meal Tolerance and Magnitude of Improvement Increase with Increasing Dose*

# Nighttime Hypoglycemia is Evident in PBS, too, and is Meaningfully Improved in the Majority Following 358

9 mg/kg Cohort, 4 baseline days vs 4 post-358 Days 3-6

Patient #	Avg Glucose (mg/dL)	
	Baseline	Post-X358
1002	87	82
1003	68	79
3005	71	81
4002	64	76
4003	61	73
4004	68	93

Also, the duration of hypoglycemia at nighttime was reduced ~50% in all these patients

# Completion of Single-dose Phase Enables Further Development

- **Single-dose data in PBS patients established a broad active dose range. Pharmacokinetics mimic healthy volunteers and there were no drug-related safety issues**
- **Program is ready for advancement to a repeat-dose phase**
  - Experience with relevant endpoints
- **Next step: Initiating repeat-dose protocol under US IND**

# Achievement of 358 Proof-of-Concept in CHI & PBS

- ✓ **Administration of 358 resulted in clinically meaningful improvement in glucose levels:**
  - improved AM fasting glucose levels
  - reduced daily periods of hypoglycemia
  - improved time to hypoglycemia in meal tests in PBS
  - correction of nighttime hypoglycemia
- ✓ **The post-358 improvement occurs in a majority of the patients treated at 3-9 mg/kg doses**
- ✓ **The duration of action ranged 1-2 weeks**
- ✓ **Additional serum markers in PBS & CHI affirm attenuated insulin action following 358 treatment**

# Phase 2 Safety Summary

# Safety Findings Support Further Clinical Development

**Across all Phase 1 and Phase 2 Trials 358 was determined to be generally safe and well-tolerated**

*In the Phase 1 healthy volunteer studies of ascending single doses of 358 ( N=22)*

- No deaths and no serious adverse events
- No clear positive anti-drug antibody titers seen
- No clinically significant changes in laboratory parameters, ECGs, physical examinations or vital signs.

*In the CHI and PBS studies (N=27)*

- All patients completed studies. No deaths. 2 serious adverse events unrelated to study drug. 1 serious adverse event related to study drug but consistent with pre-trial history.
- No clear positive anti-drug antibody titers seen
- No clinically significant changes in laboratory parameters, ECGs, physical examinations or vital signs.

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**Thank You**