Clinical Development of Avexitide for Hyperinsulinemic Hypoglycemia
AVEXITIDE (EXENDIN 9-39)

First-in-class GLP-1 Receptor Antagonist with Inverse Agonist Properties

• N-terminus 31-amino-acid fragment of exendin-4, a 39 amino-acid naturally occurring peptide

• Investigational product in development by Eiger BioPharmaceuticals for the treatment of hyperinsulinemic hypoglycemia (HI)

• 39 patients with HI have received avexitide by continuous IV infusion under 3 proof-of-concept studies conducted at CHOP

• Eiger has developed a stable, sterile solution formulation for subcutaneous injection (SC avexitide injection).

• 63 adults have received avexitide SC injection to date
  - 40 healthy volunteers
  - 23 patients with post-bariatric hypoglycemia, of which 18 patients self-injected avexitide once or twice daily for 28 days
AVEXITIDE TARGETS THE GLP-1 RECEPTOR

Inhibition of GLP-1 Receptor Signaling Reduces Fasting and Postprandial Hyperinsulinemia

Preclinical studies in a mouse model of $K_{ATP}^1$ and in pancreatic islets from patients with HI$^2$ have demonstrated critical role of GLP-1r in $K_{ATP}^1$ and elucidated Avexitide’s mechanism of action:

- Avexitide binds to the GLP-1r
- Competes with endogenous GLP-1 at the receptor (antagonist)
- Prevents basal GLP-1r signaling (inverse agonist)
- Reduces cAMP-mediated insulin release
- Reduces fasting and postprandial hyperinsulinemia
- Represents a targeted therapeutic approach

# PROOF OF CONCEPT DEMONSTRATED IN MULTIPLE CLINICAL TRIALS

Intravenous and Subcutaneous Administration in Patients with Hyperinsulinemnic Hypoglycemia

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Formulation*</th>
<th>Dosing Duration</th>
<th>Patient Number and Age Cohort</th>
<th>Hyperinsulinemnic Hypoglycemia Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV Infusion</td>
<td>Lyophilized Formulation</td>
<td>Single Dose</td>
<td>10 adolescent &amp; adult</td>
<td>Congenital Hyperinsulinism</td>
</tr>
<tr>
<td></td>
<td>Lyophilized Formulation</td>
<td>Single Dose</td>
<td>16 children</td>
<td>Congenital Hyperinsulinism</td>
</tr>
<tr>
<td></td>
<td>Lyophilized Formulation</td>
<td>Single Dose</td>
<td>13 neonates &amp; infants</td>
<td>Congenital Hyperinsulinism</td>
</tr>
<tr>
<td></td>
<td>Lyophilized Formulation</td>
<td>Single Ascending Dose</td>
<td>8 adults</td>
<td>Post-bariatric Hypoglycemia</td>
</tr>
<tr>
<td>SC Injection</td>
<td>Lyophilized Formulation</td>
<td>Single Ascending Dose</td>
<td>8 adults</td>
<td>Post-bariatric Hypoglycemia</td>
</tr>
<tr>
<td></td>
<td>Lyophilized Formulation; 15 patients</td>
<td>Multiple Ascending Dose</td>
<td>20 adults</td>
<td>Post-bariatric Hypoglycemia</td>
</tr>
<tr>
<td></td>
<td>Solution Formulation; 5 patients</td>
<td>Up to 3 Days Twice Daily Injection</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Solution Formulation</td>
<td>Single Ascending Dose; Multiple Ascending Dose; 3 Days Twice Daily Injection</td>
<td>40 adults</td>
<td>Healthy Volunteers</td>
</tr>
<tr>
<td></td>
<td>Solution Formulation</td>
<td>28 Days Outpatient Administration; Once and Twice Daily Injection</td>
<td>18 adults</td>
<td>Post-bariatric Hypoglycemia</td>
</tr>
</tbody>
</table>

*Lyophilized Formulation = lyophilized elexitide reconstituted prior to intravenous or subcutaneous administration; Solution Formulation = stable, sterile solution formulation of elexitide for subcutaneous injection.
CONCLUSIONS

• Avexitide is a first-in-class GLP-1 receptor antagonist with inverse agonist properties

• The GLP-1 receptor plays an important role in the mechanisms mediating $K_{\text{ATP}}$HI

• Three Proof of Concept studies of Avexitide in $K_{\text{ATP}}$HI at CHOP (IV infusion; n=39)
  - Demonstrated reduction in fasting and postprandial hyperinsulinemic hypoglycemia

• Eiger has developed a stable, solution formulation of avexitide for subcutaneous injection (SC avexitide injection) and has evaluated this formulation in 63 adults

• SC avexitide injection has been well-tolerated with no treatment-related SAEs or withdrawals

• Future investigations in patients with $K_{\text{ATP}}$ HI may employ SC avexitide injection
COMMITTED TO RARE DISEASES