A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Avexitide in Post-Bariatric Hypoglycemia (LUCIDITY)

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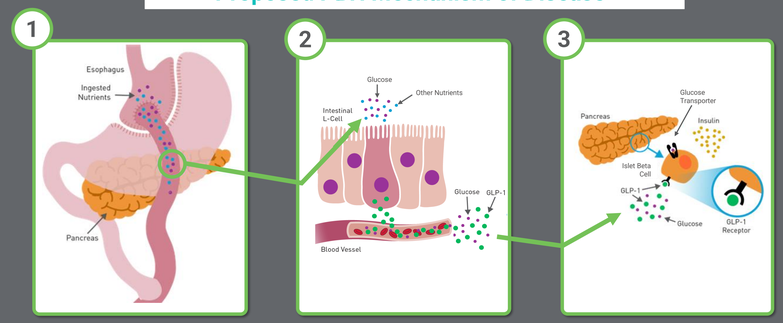
ABSTRACT # 0062

BACKGROUND

- Post-bariatric hypoglycemia (PBH) is an increasingly recognized and potentially serious complication of bariatric surgery that typically occurs ~1-3 years postoperatively[1]
- Increased levels of the incretin gut hormone glucagon-like peptide-1 (GLP-1) due to altered nutrient transit lead to exaggerated postprandial insulin secretion and severe hypoglycemia, typically multiple times daily[2]
- Physical activity[4] and stress[5] may also trigger PBH symptoms
- Currently, there are no treatments approved for PBH
- Avexitide is a first-in-class GLP-1 receptor antagonist designed to competitively inhibit GLP-1-mediated insulin secretion and stabilize glucose levels

Proposed PBH Mechanism of Disease[3]



Altered Nutrient Transit due to anatomical changes associated with bariatric surgery (e.g., Roux-en-Y gastric bypass)

Increased GLP-1 Secretion by intestinal L-cells due to increased delivery of nutrients to the distal jejunum and proximal ileum

Hyper-Secretion of Insulin driven by GLP-1 leading to hypoglycemia with potentially severe symptoms and consequences

Proposed Avexitide Mechanism of Action

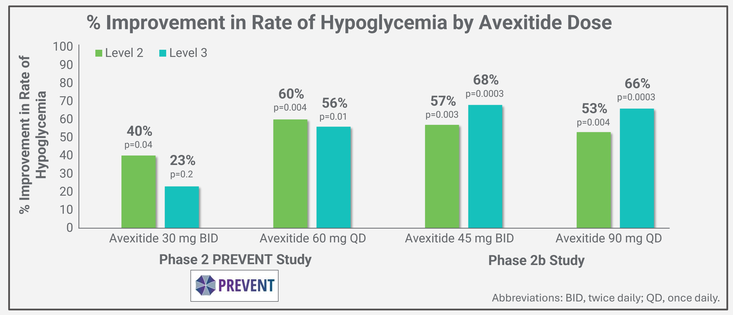
Stabilized Glucose Levels with Avexitide
GLP-1 Receptor Antagonist

OBJECTIVE

Describe the design of a phase 3 trial assessing avexitide in PBH

AVEXITIDE PHASE 2[6] & 2b[7] CLINICAL TRIAL RESULTS

- Avexitide demonstrated statistically significant reductions in hypoglycemic events in phase 2 and 2b clinical trials



- Avexitide was generally well tolerated in both trials
- No clinically relevant increases were observed in fasting and peak postprandial plasma glucose levels

STUDY DESIGN

- LUCIDITY will be a phase 3, randomized, double-blind, placebo-controlled study conducted at approximately 20 U.S. sites
- Approximately 75 participants will be randomized 3:2 to receive either 90 mg of avexitide subcutaneously once daily or placebo
- After completion of the 16-week double-blind treatment period, participants may be eligible to enroll in an open-label extension (OLE) period to receive avexitide
- Plans for post-trial access to avexitide for participants who complete the OLE period are in development

Key Trial Entry Criteria

- Has undergone Roux-en-Y gastric bypass (RYGB) at least 12 months prior to screening visit
- Has a clinical diagnosis of PBH
- Has at least 3 discrete hypoglycemic events during the 3-week run-in period despite adhering to consistent dietary management
  - At least 2 of the qualifying events must be Level 2 or greater in severity, and at least 1 event must be adjudicated by the independent EAC as Level 3 (per American Diabetes Association & European Association for the Study of Diabetes)*

*Level 2 hypoglycemia, glucose <54mg/dL as measured by SMBG; Level 3 hypoglycemia, severe event characterized by altered mental and/or physical functioning that requires assistance for treatment of hypoglycemia.

CONCLUSION

- The phase 3 LUCIDITY study will evaluate the efficacy and safety of avexitide, a first-in-class GLP-1 receptor antagonist in PBH
- Initiation of the LUCIDITY study is planned for Q1 2025 with topline data anticipated in 2026

Study Objectives

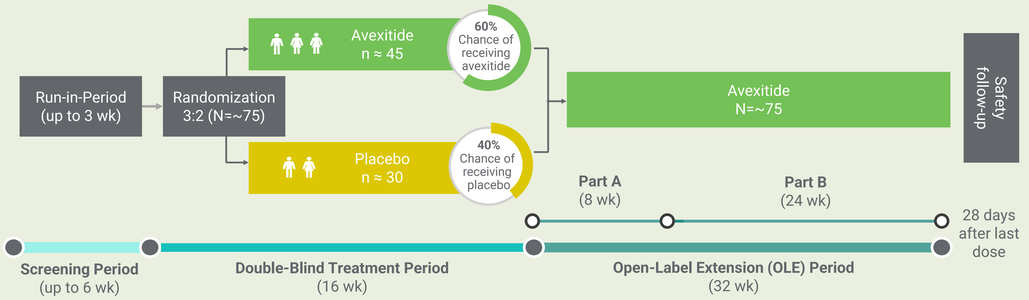
Primary Objectives

- Assess reduction in the composite of Level 2 and Level 3 hypoglycemic events as measured by self-monitoring blood glucose (SMBG) and adjudication committee
- Evaluate the safety and tolerability of avexitide

Secondary and Tertiary Objectives

- Further evaluate the efficacy of avexitide compared to placebo on additional measures of hypoglycemia as measured by blinded continuous glucose monitoring (blinded CGM)
- Further evaluate the long-term safety of avexitide
- Evaluate effects of avexitide on participant quality of life

LUCIDITY Phase 3 Study Design



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Disclosures
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