**Background**

- Pegozafermin (PGZ), a long-acting fibroblast growth factor 21 (FGF21) analog, was evaluated in NASH patients with proven F2/F3 fibrosis (ENLIVEN trial) for efficacy/safety. This study demonstrated the benefit of PGZ in both hepatic and extra-hepatic parameters, including histologic improvements.
- Glucagon-like peptide-1 receptor agonists (GLP-1 therapy), approved for T2DM and obesity, decrease hepatic steatosis and inflammation and are currently being investigated as a treatment for MASH.
- We previously showed at 24 weeks PGZ on top of GLP-1 therapy (compared to GLP-1 therapy alone), improved markers of fibrosis and inflammation, and reduced liver fat and triglyceride levels.

- There were 41 patients on background GLP-1 therapy randomized to placebo or PGZ in the 48-week Safety Analysis Set (SAS); 36 in the Full Analysis Set (FAS).

**Objective**

- To investigate the efficacy/safety of PGZ when added to existing background GLP-1 therapy over the course of 48 weeks.

**Methods**

- **ENLIVEN Trial Design**

  - **Main Study** (24 weeks)
    - Placebo (QW or Q2W)
    - Pegozafermin 30mg QW
    - Pegozafermin 60mg QW
  - **Blinded Extension Phase** (24 weeks)
    - Placebo (QW or Q2W)
    - Pegozafermin 30mg QW
    - Pegozafermin 60mg QW

- **Primary Analysis Population**
  - F2-F3 NASH; NAS ≥ 4

<table>
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<th>Parameter</th>
<th>Mean or %</th>
<th>Placebo (n=13)</th>
<th>PEGOZAFERMIN 15mg QW (n=26)</th>
<th>PEGOZAFERMIN 30mg QW (n=26)</th>
<th>Placebo (QW or Q2W)</th>
<th>PEGOZAFERMIN 15mg QW (QW or Q2W)</th>
<th>PEGOZAFERMIN 30mg QW (QW or Q2W)</th>
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<tr>
<td>BMI (kg/m²)</td>
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<td>HbA1c, ≥ 6.5%</td>
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**Baseline Characteristics of Subjects on Background GLP-1 Therapy Compared to Overall ENLIVEN Study Population**

- **F Sustain Improvements over a Wide Range of Liver NITS**
  - **Long-term Treatment with PGZ on Top of GLP-1 Therapy**
    - There with no treatment-related AE discontinuations.

**Results**

- **Sustained Benefits on Fibrosis Markers Were Observed with PGZ vs. Placebo in Patients on Background GLP-1 Therapy at Week 48**
  - MRI-PDFF:n=18; ALT, Pro-C3 and ELF:n=10
  - PGZ/GLP-1: MRI-PDFF n=22; ALT, Pro-C3 and ELF n=10
  - Placebo/GLP-1: MRI-PDFF n=25; ALT, Pro-C3 and ELF n=25

- **Sustained Benefits on Fibrosis Markers Were Observed with PGZ vs. Placebo in Patients on Background GLP-1 Therapy at Week 48**

**Conclusions**

- **Safety and Tolerability**
  - An acceptable safety and tolerability profile was retained when PGZ was added to background GLP-1 therapy. There with no treatment-related AE discontinuations.

- **Patients on background GLP-1 therapy were more likely to be obese, have Type 2 diabetes, hypertension and HbA1c ≥ 6.5%.
- Addition of PGZ therapy to GLP-1 background therapy provided more extensive benefit versus GLP-1 alone as measured by NITs for liver fat, inflammation and fibrosis.
- Benefits of PGZ treatment were sustained over the course of 48 weeks.
- PGZ, on top of GLP-1 therapy, continues to demonstrate a favorable safety and tolerability profile.