Pegzaférmin Led to Significant Metabolic Benefits, in Addition to Robust Beneficial Effects on the Liver, in an Open-label Cohort of a Phase 1b/2 Study in Subjects with Non-alcoholic Steatohepatitis (NASH)


INTRODUCTION

FGF21 is an endogenous hormone regulating carbohydrate, lipid and energy metabolism.

FGF21 analogs have demonstrated improvements in both liver and extra-hepatic metabolic derangements in NASH.

Pegzaférmin (previously BIO89-100), a long-acting glycoPEGylated recombinant human FGF21 analog in development for NASH, significantly improved liver and cardiovascular parameters, and demonstrated favorable safety and tolerability, in a Phase 1b/2a study in NASH.

BACKGROUND

- Obesity, insulin resistance, type 2 diabetes mellitus (T2DM) and dyslipidemia are common associations with NAFLD/NASH.
- Metabolic disorders are key drivers of NASH and significant risk factors for cardiovascular (CV) morbidity and mortality in NASH patients, that increases with advancing fibrosis.
- White treatments for NASH would ideally address both liver injury and metabolic perturbations in this population. Treatment of metabolic (such as increased liver cholesterols) has been a drawback in several NASH drug development programs.

OBJECTIVE

The objective of this open-label, 20-week study was to examine the effect of pegzaférmin (PGZ) on extra-hepatic metabolic parameters in a biopsy-proven NASH population.

METHODS

Phase 1b/2a NASH Trial Design – Open-Label Cohort

RESULTS

Baseline Characteristics

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>PGZ QW 27mg (SC) (n=20)</th>
<th>p value for change from baseline</th>
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<tbody>
<tr>
<td>Mean age (y)</td>
<td>58.4</td>
<td>🟢***&lt;0.001</td>
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| BMI (kg/m²) | 31.9 | 🟢3.2%
| Weight (kg) | 104.6 | 🟢3.9%
| %F2/%F3 | 35%/65% | 🟢0.5%
| Type 2 Diabetes | 85% | 🟢26%
| HDL-C (mg/dL) | 43.4 | 🟢20%
| Non-HDL-C (mg/dL) | 125.9 | 🟢26%
| LDL-C (mg/dL) | 92.0 | 🟢18%
| HDL (mg/dL) | 40.6 | 🟢8.6%
| Adiponectin (μg/dL) | 3.95 | 🟢20%

Pegzaférmin Demonstrated Clinically Meaningful Improvement on HbA1c and Adiponectin with Notable Body Weight Reduction

- Patients with baseline HbA1c ≥6% at Week 20:
  - Total patient population (n=19): -26%
  - Total patient population (n=18): -28%
- Patients with baseline HbA1c ≥6% and ≥2 point improvement in NAS at Baseline:
  - Total patient population (n=10): -17%

CONCLUSIONS

- In a cohort of mostly diabetic NASH subjects with advanced fibrosis, many of whom were on treatment for diabetes, hyperlipidemia or both, PGZ (27 mg QW for 20 weeks) led to meaningful reductions in extra-hepatic metabolic parameters:
  - Significant improvement in serum lipids (TG, LDL-C, non-HDL-C, HDL-C, HbA1c, adiponectin and body weight)
  - Marked improvement in serum lipids and HbA1c on top of treatment for hyperlipidemia or diabetes
- These benefits were additive to robust beneficial effects on liver histology and favorable safety and tolerability, and suggest a potential of PGZ to protect subjects with NASH not only from liver related outcomes, but also from CV risk.

- PGZ is currently being evaluated in NASH subjects (NAS ≥ 4, F2-F3) in the ongoing Phase 2b ENLIVEN study. NCT04929483

*Subjects who completed treatment (N=19)