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BIO89-100 Demonstrated Robust Reductions in Liver Fat, Improved Metabolic Parameters, Favorable Tolerability and Potential for Weekly (QW) or Every 2 Weeks (Q2W) Dosing in a Phase 1b/2a Placebo-Controlled, Double-Blind, Multiple Ascending Dose Study in NASH.

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Abstract

Background:
Fibroblast growth factor 21 (FGF21) is an endogenous metabolic hormone that regulates carbohydrate, lipid and energy metabolism. FGF21 analogs have demonstrated capability to improve both hepatic and metabolic abnormalities in NASH. BIO89-100 is a long-acting glycoPEGylated FGF21 analog, with promising tolerability and pharmacodynamic effects and the only FGF21 analog with potential for once Q2W dosing.
Methods:
This Phase 1b/2a trial enrolled 81 NASH subjects with liver fat ≥10% by MRI-PDFF. Subjects were randomized to 12 weeks of treatment with BIO89-100 at one of 6 doses or placebo. Key endpoints were safety, tolerability, pharmacokinetics, change in liver fat content as measured by MRI-PDFF and liver and metabolic markers.
Results:
Baseline characteristics were similar between groups. At week 13, all BIO89-100 dose groups showed significant relative reductions in MRI-PDFF; decreased liver fat was accompanied by a corresponding decrease in liver fat volume. Significant decreases in ALT were observed, as well as reductions in levels of PRO-C3. Metabolic benefits of BIO89-100 included a favorable effect on lipids along with increases in adiponectin. There were no deaths, drug-related serious adverse events, hypersensitivity reactions or adverse effects on blood pressure or heart rate reported.
Conclusion:
Treatment with BIO89 100 for 12 weeks resulted in robust, clinically meaningful improvements in liver fat and volume and markers of liver stress and fibrosis. Additionally metabolic improvements in lipid profiles and adiponectin were observed. Moreover, treatment was associated with a favorable safety and tolerability profile. These data support the further investigation of BIO89-100 in NASH and other metabolic diseases.

Keywords: Fibroblast growth factor 21; Non-alcoholic steatohepatitis; metabolic parameters

Abbreviations: FGF21; NASH; MRI-PDFF; BIO89-100

Funding and Conflicts of Interest

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