89bio Announces Additional Data from the ENLIVEN Phase 2b Trial of Pegozafermin in Patients with Compensated Cirrhotic (F4) Nonalcoholic Steatohepatitis (NASH) at AASLD The Liver Meeting® 2023

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—Reductions in key non-invasive tests (NITs) of liver inflammation and fibrosis support previously demonstrated fibrosis improvements across compensated cirrhotic (F4) patients at week 24—

—A responder analysis suggests that responses in NITs were correlated with fibrosis improvement—

—Pegozafermin continued to demonstrate a best-in-class tolerability profile—

SAN FRANCISCO, Nov. 12, 2023 (GLOBE NEWSWIRE) -- 89bio, Inc. (Nasdaq: ETNB), a clinical-stage biopharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of liver and cardiometabolic diseases, today announced additional data from a post-hoc analysis of the ENLIVEN Phase 2b trial evaluating treatment with pegozafermin in a subgroup of patients with F4 NASH. These data were featured in an oral presentation during the AASLD The Liver Meeting®, being held in Boston, Massachusetts.

“Patients with NASH and compensated cirrhosis face a critical imperative to mitigate the risk of decompensation, necessitating therapies that halt or even reverse the progression of fibrosis,” Dr. Hank Mansbach, Chief Medical Officer of 89bio commented. “While the cohort of F4 patients in ENLIVEN was relatively small, we were encouraged by data suggesting that pegozafermin could potentially provide benefits to these patients by addressing both liver pathology and the metabolic irregularities that may contribute to the disease. We plan to initiate our Phase 3 program in the first half of next year pending feedback from regulatory agencies which is expected this quarter.”

The ENLIVEN Phase 2b trial enrolled 14 patients who initially met the study histological inclusion criteria of fibrosis F2 or F3 and were subsequently re-classified as having F4 fibrosis by the consensus panel. The 14 patients’ baseline characteristics were generally consistent with a well-compensated F4 population featuring higher percentage of patients with diabetes, higher PRO-C3, increased liver stiffness as measured by VCTE, and lower platelet counts.

Treatment with pegozafermin led to clinically meaningful improvements in liver specific biomarkers of stiffness and fibrosis (Pro-C3, FAST, VCTE, FIB-4), inflammation (ALT and AST), and other key non-invasive markers.

Table 1. Liver Non-Invasive Tests (NITs) Results [marker of]

	Placebo (n=2)	Pegozafermin (n=11)
ALT [liver damage][1]	-41%	-53%
AST [liver damage] [1]	-1%	-31%
Pro-C3 [collagen deposition][1]	19%	-5%
VCTE [liver stiffness][2]	-0.8kPa	-2.7kPa
FAST [liver stiffness][2]	8%	-46%
FIB-4 [liver fibrosis][2]	12%	-11%

[1]LS mean change from baseline; [2]Median change from baseline

In a responder analysis, a significant proportion of patients identified as responders through NITs at the 24-week mark also exhibited histologically confirmed fibrosis improvement. These data, while preliminary, suggest a potential correlation between NIT-based improvements and histological measures of fibrosis reduction.

Five out of 11 pegozafermin-treated patients experienced at least one-stage improvement in liver fibrosis with no worsening of NASH by week 24 (45%) compared with zero out of one patient on placebo. Additionally, as previously reported, nine out of the 11 pegozafermin-treated patients had fibrosis improvement (82%) compared with zero out of one patient on placebo.

Safety and tolerability in the F4 patients was consistent with the favorable profile observed with the primary analysis of ENLIVEN reported earlier this year and prior studies in the pre-cirrhotic patient population. Across dose groups, the most frequently reported treatment-related adverse events were Grade 1 or 2 diarrhea and injection site reaction.

A copy of the AASLD presentation will be accessible under “Scientific Publications” in the pipeline section of 89bio’s website.

About pegozafermin
Pegozafermin is a specifically engineered glycoPEGylated analog of fibroblast growth factor 21 (FGF21) being developed for the treatment of nonalcoholic steatohepatitis (NASH) and severe hypertriglyceridemia (SHTG). FGF21 is a promising therapeutic target since it is an endogenous hormone that has broad effects such as regulating energy expenditure, glucose and lipid metabolism. In clinical trials, pegozafermin has demonstrated direct anti-fibrotic and anti-inflammatory effects on the liver, as well as reduced triglyceride levels, improved insulin resistance and glycemic control, and continued to demonstrate a best-in-class safety and tolerability profile. The U.S. Food and Drug Administration (FDA) granted pegozafermin

Breakthrough Therapy designation (BTD) for the treatment of NASH with fibrosis. Pegozafermin is currently being evaluated in the Phase 2b ENLIVEN trial for the treatment of NASH and the Phase 3 ENTRUST trial for the treatment of SHTG.

About ENLIVEN
ENLIVEN is a multicenter, randomized, double-blind, placebo-controlled Phase 2b trial designed to evaluate the safety and efficacy of weekly or every-two-week dosing of pegozafermin for the treatment of patients with biopsy confirmed NASH and NAS ≥ 4 for 48 weeks. In the trial, 192 patients were dosed with pegozafermin 44mg Q2W, 30mg QW, 15mg QW, or placebo. Primary outcomes measured were proportion of participants with resolution of NASH without worsening of fibrosis and proportion of participants with ≥1 stage decrease in fibrosis stage with no worsening of NASH at week 24. Secondary measures included change from baseline in liver fat, liver enzymes, noninvasive markers of liver fibrosis, glycemic control, lipoproteins, and body weight as well as safety and tolerability measures. Trial patients are being treated in a blinded extension phase for 24 weeks for a total treatment period of 48 weeks, with some placebo patients re-randomized to receive pegozafermin in the extension phase. ENLIVEN achieved high statistical significance on primary histology endpoints and statistical analysis with 30mg QW and 44mg Q2W dosing at week 24 and the results were published in the *New England Journal of Medicine*. To learn more about the clinical trial, visit clinicaltrials.gov: NCT04929483.

About 89bio
89bio is a clinical-stage biopharmaceutical company dedicated to the development of best-in-class therapies for patients with liver and cardiometabolic diseases who lack optimal treatment options. The company is focused on rapidly advancing its lead candidate, pegozafermin, through clinical development for the treatment of nonalcoholic steatohepatitis (NASH) and severe hypertriglyceridemia (SHTG). Pegozafermin is a specifically engineered, potentially best-in-class fibroblast growth factor 21 (FGF21) analog with unique glycoPEGylated technology that optimizes biological activity through an extended half-life. Pegozafermin has been granted Breakthrough Therapy Designation for the treatment of NASH with fibrosis from U.S. Food and Drug Administration (FDA). The company is headquartered in San Francisco. For more information, visit www.89bio.com or follow the company on LinkedIn.

Forward-looking Statements
Certain statements in this press release may constitute "forward-looking statements" within the meaning of the federal securities laws, including, but not limited to, statements regarding the therapeutic potential and utility, efficacy and clinical benefits of pegozafermin, the safety and tolerability profile of pegozafermin, the potential correlation between responses in NITs and fibrosis improvement and the timing for feedback from regulatory agencies. Words such as "may," "might," "will," "objective," "intend," "should," "could," "can," "would," "expect," "believe," "design," "estimate," "predict," "potential," "anticipate," "goal," "opportunity," "develop," "plan" or the negative of these terms, and similar expressions, or statements regarding intent, belief, or current expectations, are forward looking statements. While 89bio believes these forward-looking statements are reasonable, undue reliance should not be placed on any such forward-looking statements, which are based on information available to us on the date of this release. These forward-looking statements are based upon current estimates and assumptions and are subject to various risks and uncertainties (including, without limitation, those set forth in 89bio's filings with the Securities and Exchange Commission (SEC)), many of which are beyond 89bio's control and subject to change. Actual results could be materially different. Risks and uncertainties include: expectations regarding the initiation of the Phase 3 trial in NASH; expectations regarding the timing and outcome of the ENTRUST Phase 3 trial in SHTG; 89bio's ability to execute on its strategy; positive results from a clinical study may not necessarily be predictive of the results of future or ongoing clinical studies; receipt of BTD for pegozafermin in NASH may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA; 89bio's substantial dependence on the success of it lead product candidate; competition from competing products; the impact of general economic, health, industrial or political conditions in the United States or internationally; the sufficiency of 89bio's capital resources and its ability to raise additional capital; and other risks and uncertainties identified in 89bio's Annual Report on Form 10-K for the year ended December 31, 2022 and other subsequent disclosure documents filed with the SEC. 89bio claims the protection of the Safe Harbor contained in the Private Securities Litigation Reform Act of 1995 for forward-looking statements. 89bio expressly disclaims any obligation to update or alter any statements whether as a result of new information, future events or otherwise, except as required by law.

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