Data from 89bio's ENLIVEN Phase 2b Trial of Pegozafermin in Patients with Nonalcoholic Steatohepatitis (NASH) Published in The New England Journal of Medicine and Simultaneously Presented in a Late-breaker Session at the EASL International Liver Congress

June 24, 2023

– ENLIVEN results demonstrated that treatment with pegozafermin 30mg weekly and 44mg every-two-week doses resulted in statistically significant changes on both primary histology endpoints –

– New data showed pegozafermin resulted in significant benefit across several key sub populations of NASH patients, and that adding pegozafermin to patients taking GLP-1 therapies improved key NASH measures –

– Discussions with regulatory agencies regarding advancement into Phase 3 trials in NASH planned for the second half of 2023 –

SAN FRANCISCO, June 24, 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 cardio-metabolic diseases, today announced that data from the Phase 2b ENLIVEN trial evaluating treatment with pegozafermin in patients with nonalcoholic steatohepatitis (NASH) were published online in the *New England Journal of Medicine* (*NEJM*). The data were simultaneously presented in a late-breaking oral session today at the European Association for the Study of the Liver (EASL) Congress 2023 in Vienna, Austria and were also selected for inclusion in the Best of EASL Congress summary.

The published manuscript titled "A Randomized, Controlled Trial of the FGF21 Analog Pegozafermin in NASH" is available online. A copy of the EASL oral presentation will be accessible under "Scientific Publications" in the pipeline section of 89bio's website.

"As a physician, I know how important it is to provide patients with therapies that can be impactful across a broad population of individuals with NASH, especially ones that can easily blend into their daily lives," said Rohit Loomba, M.D., MHSc, chief of the Division of Gastroenterology and Hepatology at University of California San Diego School of Medicine, and lead study author who presented the data at EASL. "It's both incredibly encouraging and exciting to see the positive, consistent results from this research across all aspects – efficacy, safety, tolerability, and dosing convenience."

The randomized, double-blind, placebo-controlled 24-week Phase 2b ENLIVEN trial evaluated 219 adult patients of whom 192 had biopsy-confirmed fibrosis stages F2-F3 NASH and NAS ≥ 4 for 24 weeks. In this trial, treatment with 44mg every-two-week (Q2W) and 30mg (QW) dosing groups resulted in statistically significant changes on both primary histology endpoints demonstrating at least one-stage fibrosis improvement without worsening of NASH (27% and 26%, respectively) at 3.5 times the placebo rate (7%) and NASH resolution without worsening of fibrosis (26% and 23%, respectively), between 12 to 14 times the placebo rate (2%). Treatment with pegozafermin also led to clinically meaningful changes compared to baseline in liver fat and other key non-invasive tests (NITs) of liver inflammation and fibrosis. Improvements were observed in HbA1c, adiponectin and across lipid markers that are important factors for an effective treatment for NASH. In addition, reductions in liver and spleen volume were observed. The trial included 14 biopsy confirmed NASH patients with compensated cirrhosis (F4 patients) who were not part of the primary analysis, but continued in the study, 12 of which underwent a follow-up biopsy at Week 24. Five out of eleven of these patients treated with pegozafermin had fibrosis improvement ≥1 stage without worsening of NASH.

"NASH is highly associated with metabolic syndrome and increased cardiovascular risk, driving its impact far beyond the liver. Data from ENLIVEN show the promise of FGF21 analogs and potential of pegozafermin as a mainstay treatment for NASH, given it addresses both liver pathology and the underlying metabolic overload that drives it," said Arun J. Sanyal, M.D., Interim-Chair of the Division of Gastroenterology, Hepatology and Nutrition at Virginia Commonwealth University / VCUHealth. "I am thrilled to see the strong efficacy data across the two FDA approvable histology endpoints, potential to benefit patients already on GLP-1 therapies, and the impressive results across markers of total liver health, which is critically important for this patient population."

New results presented at EASL showed:

- Patients on GLP-1 treatment who received pegozafermin saw broad incremental benefits across liver markers of fibrosis, including the Enhanced Liver Fibrosis (ELF) Test, Vibration-controlled transient elastography and the FibroScan-AST (FAST) score. Improvements were observed in liver fat, ALT levels as well as metabolic (HbA1c) markers.
- Across all patients, treatment with pegozafermin demonstrated statistically significant improvements on additional NITs for hepatic inflammation and fibrosis, including ELF, FIB-4 index and FAST. These data were consistent with previously reported markers and further build on the positive impact of pegozafermin on NITs.
- Treatment with pegozafermin was consistent and showed significant benefit in achieving fibrosis improvement across several key sub populations including type 2 diabetes status, fibrosis stage (F2 or F3), and ALT levels.
- There were no clinically relevant changes observed on vital signs, bone biomarkers or dual x-ray absorptiometry (DEXA) scans.

"Publication in an esteemed peer-reviewed journal like the *New England Journal of Medicine* validates the importance of these data, including the strong histology endpoints and impressive results seen across markers of total liver health in the overall study population and in patients on background GLP-1 therapies," said Hank Mansbach, Chief Medical Officer of 89bio. "These data support advancement into Phase 3 development and we look forward to upcoming conversations with regulatory agencies to help inform this next step."

Pegozafermin demonstrated a favorable safety and tolerability profile consistent with prior studies. Across dose groups, the most common adverse events (AEs) were Grade 1 or 2 gastrointestinal events (diarrhea, nausea and increased appetite), most of which were mild to moderate in nature. No clinically relevant effects on DEXA scans, bone biomarkers or vital signs were noted. No drug-induced liver injury, tremor or hypersensitivity reactions were reported.

About pegozafermin
Pegozafermin is a specifically engineered glycoPEGylated analog of fibroblast growth factor 21 (FGF21) being developed for the treatment of non-alcoholic steatohepatitis (NASH) and severe hypertriglyceridemia (SHTG). FGF21 is a promising therapeutic target for NASH and SHTG since it is an endogenous hormone that functions as a master metabolic regulator with broad effects on energy expenditure and glucose and lipid metabolism. Enhancing the activity of FGF21 has been shown to reduce hepatic steatosis, inflammation, and triglyceride levels, as well as improve insulin resistance and glycemic control. 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 fibrosis stage F2 - F3 NASH and NAS ≥ 4 for 48 weeks. In the trial, 219 patients were randomized and dosed with pegozafermin 44mg Q2W, 30mg QW, 15mg QW, or placebo; 27 patients were prospectively excluded from the primary analysis population based on fibrosis stage or NAS score resulting in 192 patients in the full analysis set.

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 24 weeks. 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.

In the ENLIVEN trial, biopsies were scored independently by three pathologists on the NAS components and fibrosis using the NASH-CRN criteria. Pathologists were blinded to the clinical trial participant, treatment, and study timepoint. There was protocol-specific training before and during the study to improve concordance between readers. The scores from each reader were then compared by an algorithm. If all three agreed on the score, that was recorded as the final score. If there was disagreement, the mode was selected and if that was not available the median or consensus call score was recorded. On average, full agreement or mode determined the final score for more than 95% of the biopsies.

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 therapeutic candidate, pegozafermin, through clinical development for the treatment of non-alcoholic steatohepatitis (NASH) and severe hypertriglyceridemia (SHTG). 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, efficacy and clinical benefits of pegozafermin, the safety and tolerability profile of pegozafermin, pegozafermin as a potentially differentiated treatment for NASH, 89bio's clinical development plans for pegozafermin, including commencement of a Phase 3 trial based on results from the Phase 2b ENLIVEN trial, the potential dosing regimen of pegozafermin, if approved, and the relationship between the results from the positive data from Phase 2b ENLIVEN trial and results of future clinical studies. 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 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 clinical benefit and safety of pegozafermin; expectations regarding the timing for discussions with regulatory agencies; 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; 89bio's substantial dependence on the success of it lead product candidate; competition from competing products; expectations regarding FDA approval and feedback; 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.

Investor Contact:
Ryan Martins
Chief Financial Officer
investors@89bio.com

PJ Kelleher
LifeSci Advisors, LLC
+1-617-430-7579
pkelleher@lifesciadvisors.com

Media Contact:
Sheryl Seapy
Real Chemistry
sseapy@realchemistry.com