89bio Publishes Positive Results from Phase 2 ENTRIGUE Trial of Pegozafermin in Patients with Severe Hypertriglyceridemia (SHTG) in Nature Medicine

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– Published data showed consistent and significant reductions in triglycerides, atherogenic lipoproteins and liver fat, and pegozafermin's favorable safety and tolerability profile –

– SHTG Phase 3 ENTRUST trial initiated in May 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 cardiometabolic diseases, today announced that the previously reported positive data from the Phase 2 ENTRIGUE trial of pegozafermin in patients with severe hypertriglyceridemia (SHTG) were published online in *Nature Medicine.*

As previously announced, ENTRIGUE met its primary endpoint of demonstrating statistically significant reductions in median triglycerides (TGs) from baseline in pegozafermin-treated patients across all dose groups compared to placebo after eight weeks of treatment. Significant reductions in TGs were observed consistently across all prespecified patient subgroups, including those on lipid-modifying background therapies. Additionally, the ENTRIGUE trial met multiple secondary endpoints, showing that treatment with pegozafermin led to improvements in atherogenic lipoproteins, metabolic measures, liver fat, and markers of liver inflammation.

"People with SHTG have a greater risk for acute pancreatitis, which is the leading cause for gastrointestinal-related hospitalization in the United States and can lead to organ failure and death. As current therapies rarely address the range of needs of patients with SHTG, innovative medicines that not only reduce TGs but also lower other lipid levels and improve co-existing cardiometabolic conditions are urgently needed," said Deepak L. Bhatt, M.D., M.P.H., Director of Mount Sinai Heart[1] and lead author of the *Nature Medicine* paper. "Results from ENTRIGUE highlight the therapeutic potential of pegozafermin to significantly reduce TGs, as well as improve the overall lipid profile, liver fat, and broader cardiometabolic parameters. These encouraging data underscore the promise of pegozafermin for patients with SHTG and strengthen the emerging evidence of the benefit associated with TG reduction."

Data from the ENTRIGUE trial show pegozafermin significantly reduced TGs after only eight weeks of treatment across all dose groups, with placebo-corrected changes from baseline ranging from -29% to -53%. In pooled data across all doses, pegozafermin lowered TG levels to less than 500 mg/dL in 80% of patients compared to 29% of patients on placebo. The trial also demonstrated that pegozafermin had positive effects on atherogenic lipids, including improvements in levels of non-HDL-C and apolipoprotein B (ApoB), across the majority of patients. Importantly, reductions in both triglycerides and atherogenic lipoproteins occurred regardless of whether patients were on lipid-modifying background therapy. Additionally, robust reductions in liver fat were observed across all dose groups, as evaluated with magnetic resonance imaging – proton density fat factor (MRI-PDFF), including 88% of patients who achieved a ≥30% reduction in liver fat from baseline and 24% who achieved normalized levels of liver fat after 8 weeks of treatment. Pegozafermin was well tolerated with a favorable safety profile across doses.

"Pegozafermin is the only fibroblast growth factor 21 (FGF21) analog in development for the treatment of SHTG, and we believe it represents a highly differentiated option based on its broad metabolic effects, potential favorable impact on risk of acute pancreatitis and a safety profile that is supportive of adoption and compliance," said Hank Mansbach, Chief Medical Officer of 89bio. "The publication of positive Phase 2 data from both our SHTG and NASH programs in highly regarded scientific journals, *Nature Medicine*, and the *New England Journal of Medicine*, demonstrates the strength of pegozafermin data generated to date and its potential as a future meaningful treatment option."

About ENTRIGUE
The randomized, double-blind, placebo-controlled ENTRIGUE trial enrolled 85 patients with severe hypertriglyceridemia (SHTG) either on stable background therapy or not on any background therapy who were treated weekly or every two weeks with pegozafermin. The trial enrolled an advanced population with a high risk of cardiovascular disease as evidenced by mean baseline values of triglycerides (TGs) of 733 mg/dL and non-HDL-C of 211 mg/dL; 43.5% had HbA1c ≥6.5%, and, in the subgroup of patients undergoing MRI-PDFF, liver fat content was 20.1%.

About severe hypertriglyceridemia (SHTG)
SHTG is a lipid abnormality characterized by severely elevated triglyceride (TG) levels (> 500mg/dL) and associated with an increased risk for acute pancreatitis and atherosclerotic cardiovascular diseases. It is an underappreciated condition that affects up to four million people in the United States with an urgent need for treatments that can effectively reduce TG levels and improve comorbidities. Patients with SHTG have multiple co-morbid metabolic disorders such as dyslipidemia (up to 65%), Type 2 diabetes mellitus (up to 70%) and non-alcoholic fatty liver disease (NAFLD; up to 100%). The current standard of care for SHTG includes lifestyle changes and medications that include fish oils, fibrates, niacin and statins. However, studies have shown that these therapies only have a modest effect on triglycerides and do not provide broader metabolic benefits and it is estimated that ~50% of treated patients (~900,000 in the United States) are unable to bring their triglyceride levels below 500 mg/dL.

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.

About 89bio
89bio is a clinical-stage biopharmaceutical company dedicated to the development and commercialization of innovative therapies for the treatment of liver and cardiometabolic diseases. The company's lead product candidate, pegozafermin, is currently being developed for the treatment of NASH and 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, clinical benefits and adoption of pegozafermin, the safety and tolerability profile of pegozafermin and the risk/benefit profile of pegozafermin. 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 Phase 3 ENTRUST 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; 89bio's substantial dependence on the success of its lead product candidate; competition from competing products; expectations regarding FDA approval and feedback; 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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2023 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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[1] Dr. Bhatt is the Dr. Valentin Fuster Professor of Cardiovascular Medicine at the Icahn School of Medicine at Mount Sinai and as primary investigator of the ENTRIGUE trial, receives research funding from 89bio.