89bio Presents New Analysis of Data from Phase 2 ENTRIGUE Trial of Pegozafermin in Patients with Severe Hypertriglyceridemia (SHTG) at American College of Cardiology's Annual Scientific Session Together with World Congress of Cardiology

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– Post hoc analysis data demonstrated pegozafermin treatment significantly reduced triglycerides and other atherogenic lipids in patients with SHTG regardless of their background lipid-modifying therapy status –

SAN FRANCISCO, March 04, 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 the presentation of additional data from the Phase 2 ENTRIGUE trial of pegozafermin in patients with severe hypertriglyceridemia (SHTG) at the American College of Cardiology's 72 nd Annual Scientific Session & Expo Together with World Congress of Cardiology (ACC.23/WCC). The presentation featured results of a post hoc analysis exploring the effect of pegozafermin treatment on lipids among study participants based on their background lipid-modifying therapy (LMT) status. These results were presented by Deepak L. Bhatt, M.D., M.P.H., Director of Mount Sinai Heart and the Dr. Valentin Fuster Professor of Cardiovascular Medicine at the Icahn School of Medicine at Mount Sinai, and a copy of the poster is accessible under "Scientific Publications" in the pipeline section of 89bio's website.

"We are encouraged by this additional data from the Phase 2 ENTRIGUE trial demonstrating significant reductions in triglycerides and a positive impact on atherogenic lipids with pegozafermin when added to background therapy, including high intensity statins, in patients with SHTG," said Hank Mansbach, Chief Medical Officer of 89bio. "The overall positive ENTRIGUE data continues to support the advancement of pegozafermin into a pivotal Phase 3 program in SHTG. As the only FGF21 analog in development for the treatment of SHTG, we believe with its compelling and differentiated profile, pegozafermin could become an important new cardiometabolic medicine."

The company previously announced that the randomized, double-blind ENTRIGUE trial met the primary endpoint of statistically significant reductions in median TGs from baseline in patients treated with 27mg of pegozafermin given weekly compared to placebo after 8 weeks (62% vs. 5% increase, for patients not on background therapy; p=0.013, and 68% vs. 18% for patients on background therapy; p=0.012). Significant reductions in TGs were observed consistently across all prespecified patient subgroups. The trial also met numerous secondary endpoints, including improvements in atherogenic lipoproteins, metabolic measures and liver fat. Approximately 50% of patients in ENTRIGUE were on concomitant lipid-modifying therapy, which is representative of the real-world setting. Pegozafermin was generally safe and well-tolerated.

Of the 85 ENTRIGUE study participants randomized and treated with pegozafermin or placebo, 55% were on background lipid-modifying therapy (45% on statin therapy of which 55% were on high intensity statins, 14% on prescription fish oil, and 7% on fibrates). Results of the post hoc analysis of lipid effects of pegozafermin among study participants based on their lipid-modifying background therapy status demonstrated that pegozafermin significantly reduced TG and other atherogenic lipids after eight weeks of therapy. Pegozafermin also led to reductions in TGs among patients on background high-intensity statins compared with placebo.

Median Percent Change in TG from Baseline at Week 8

N= (placebo, pegozafermin pooled)	Placebo	Pegozafermin	27 mg QW
Background Therapy			
Yes (n=11, 34)	**-18%**	**-59%****	**-68%******
No (n=6, 30)	**5%**	**-51%*****	**-62%*******
High Intensity Statins			
Yes (n=4,16)	**-6%**	**-58%**	**-72%**

p value vs placebo for change from baseline based on Wilcoxon Rank-Sum Test
**p=0.001, ***p=0.004, ****p=0.012, *****p=0.013

As previously reported, pegozafermin-treated patients reached their initial treatment goal (i.e., a reduction in their TG level to less than 500 mg/dL) irrespective of background therapy. In the overall study population, 80% of those treated with pegozafermin reached their initial treatment goal compared with 29% of those on placebo (p<0.001). Among those on lipid-modifying background therapy, the comparable figures were 85% and 46%, respectively (p<0.05); among those not on background therapy, the comparable figures were 73% and 0%, respectively (p<0.01).

Treatment with pegozafermin also led to improvements in non-HDL cholesterol irrespective of background therapy; however, among study participants on background therapy those decreases were more robust. Improvements in apolipoprotein B (apo-B), a key marker of cardiovascular risk and a direct measure of the number of atherogenic particles, were observed irrespective of background therapy, and there were no significant changes in levels of LDL-cholesterol across the participants.

Median Percent Change in Non-HDL Cholesterol, Apo-B, and LDL-cholesterol from Baseline at Week 8

Dosing Group	**Non-HDL Cholesterol**	**Apo-B**	**LDL-Cholesterol**

Placebo (Overall Population)	-1%	1%	9%
Overall Pegozafermin Treated Population	-18%*	-11%*	10%
Placebo (Patients on Background Therapy)	-7%	-1%	11%
Pegozafermin Treated Patients on Background Therapy	-29%	-18%	2%

*p<0.05 versus placebo based on MMRM analysis

“This new analysis builds on the growing body of evidence demonstrating that treatment with pegozafermin can significantly reduce triglycerides and improve markers of atherogenic risk across a wide variety of patients with SHTG,” said Dr. Bhatt. “These findings are encouraging given the critical need for new therapeutic options that not only reduce triglyceride levels but also improve broader cardiometabolic risks for patients with SHTG regardless of their lipid-modifying treatment status.”

Dr. Bhatt receives research funding from 89bio.

About ENTRIGUE
The randomized, double-blind, placebo-controlled ENTRIGUE trial enrolled 85 patients with 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 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, a severe form of elevated serum triglycerides, is a rare but harmful and underappreciated condition that affects up to 4 million people in the United States. SHTG is commonly associated with obesity, metabolic syndrome, insulin resistance, type 2 diabetes mellitus and non-alcoholic fatty liver disease (NAFLD). SHTG increases the risk of atherosclerotic cardiovascular events and acute pancreatitis, which is the primary consideration driving the urgent need to treat these patients. The current standard of care for SHTG includes lifestyle changes and medications that include fish oils (icosapent ethyl and omega-3 ethyl esters), fibrates, niacin and statins. However, studies have shown that these therapies only have a modest effect on triglycerides, with as many as 50% of people with SHTG unable to achieve a treatment goal of a triglyceride level less than 500 mg/dL on treatment. These therapies do not provide broader metabolic benefits and may even worsen other risk factors for cardiovascular disease.

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 an endogenous hormone that modulates important drivers of lipid metabolism and NASH including triglyceride reduction, glycemic control, steatosis, inflammation and fibrosis. Pegozafermin was specifically engineered using a unique glycoPEGylated technology to extend the half-life while maintaining potency.

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 non-alcoholic 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. 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, the therapeutic potential and clinical benefits of pegozafermin, the safety and tolerability profile of pegozafermin and 89bio’s clinical development plans for 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 initiation of the first 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; 89bio’s substantial dependence on the success of it lead product candidate; competition from competing products; expectations regarding FDA approval and feedback; the effect of the COVID-19 pandemic on 89bio’s clinical trials and business operations, and 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 September 30, 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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