89bio Presents Positive Results from ENTRIGUE Phase 2 Trial of Pegozafermin in Patients with Severe Hypertriglyceridemia (SHTG) at European Society of Cardiology Congress 2022

August 26, 2022

-Results featured in a late-breaking oral presentation-

-Treatment with pegozafermin demonstrated consistent and significant benefit in triglyceride (TG) reduction as well as improvements in liver fat and glycemic control-

-Positive data support the advancement into a Phase 3 trial in SHTG-

SAN FRANCISCO, Aug. 26, 2022 (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 the presentation of data from ENTRIGUE, its Phase 2 proof-of-concept trial of pegozafermin in severe hypertriglyceridemia (SHTG) at the European Society of Cardiology (ESC) Congress 2022. Deepak L. Bhatt, MD, MPH, Brigham and Women's Hospital and Harvard Medical School, presented the data during the Late-Breaking Science Innovations in Drug Treatment session at the Congress, in Barcelona, Spain and virtually on August 26-29, 2022. A copy of the oral presentation will be accessible under "Scientific Publications" in the pipeline section of 89bio's website.

"These data build on the growing body of evidence demonstrating that treatment with pegozafermin can significantly reduce triglycerides (TG), reduce atherogenic lipoproteins, and improve liver fat and glycemic control markers in patients with SHTG," said Hank Mansbach, Chief Medical Officer of 89bio. "Consistent with prior studies, pegozafermin was generally well-tolerated with a favorable safety profile across different doses. We believe pegozafermin has the potential to become an important treatment for cardio-metabolic and liver diseases, and we look forward to advancing it into a Phase 3 trial in SHTG in the first half of 2023."

The Phase 2 trial, ENTRIGUE, met its primary endpoint of statistically significant reductions in median TGs from baseline in patients across all dose groups treated with pegozafermin compared to placebo after 8 weeks. Significant reductions in TGs were observed consistently across all prespecified patient subgroups. The trial also met a variety of secondary endpoints, including improvements in atherogenic lipoproteins, metabolic measures and liver fat.

Median Percent Change in Triglycerides from Baseline at Week 8

Dosing group	**Median TG reduction**
Placebo (n=18)	-12%
9mg QW (n=16)	-57%***
18mg QW (n=17)	-56%***
27mg QW (n=18)	-63%***
36mg Q2W (n=16)	-36%*

* p<0.05; *** p<0.001 versus placebo based on Wilcoxon Rank-Sum Test

"These data highlight pegozafermin's unique and differentiated profile as this is the first study to systematically measure and show significant improvements in liver fat in severe hypertriglyceridemia patients," said Dr. Bhatt. "Furthermore, the robust and consistent results observed across multiple metabolic measures and patient subgroups – which represent the patients we see every day in the clinic – demonstrate pegozafermin's potential to address the critical need for severe hypertriglyceridemia treatment options that not only reduce triglycerides but also improve broader cardio-metabolic risks."

In a sub study of treated patients who were evaluated with magnetic resonance imaging – proton density fat factor (MRI-PDFF), robust reductions in liver fat from baseline were observed at week 8 across all dose groups versus placebo (n=23 with baseline and follow-up imaging). Further, 88% of treated patients vs. 0% of placebo patients achieved a ≥30% reduction in liver fat from baseline and 24% of treated patients vs. 0% of placebo patients achieved normalized levels of liver fat at week 8.

Pegozafermin treatment also resulted in clinically meaningful improvements in non-HDL-C and apo-B, a key marker of cardiovascular risk and a direct measure of the number of atherogenic particles. New analyses show reductions in both apo-B subtypes, apoB48 and apoB100, which suggests that pegozafermin reduces atherogenic lipoproteins and chylomicrons.

Mean Percent Change in non-HDL-C and ApoB Subtypes (mg/dL) from Baseline at Week 8

Dosing Group	Non-HDL-C	Apo-B100	Apo-B48
Placebo	-3%	-0.6%	25%

9mg QW	-14%	-7%	-49%*
18mg QW	-22%**	-12%*	-28%
27mg QW	-29%***	-15%*	-59%*
36mg Q2W	-9%	0.8%	-2%

*p<0.05; ** p<0.01; *** p<0.001 versus placebo based on MMRM analysis

Patients treated across all doses with pegozafermin also saw improvements in apolipoprotein C3 (ApoC3) levels. Patients in the highest dosing group saw a 50% percent decrease in median ApoC3 (mg/dL) levels from baseline at week 8 (p<0.001).

Dr. Bhatt receives research funding from 89bio, which funding is provided to Brigham and Women's Hospital.

About ENTRIGUE
ENTRIGUE is a randomized, double-blind, placebo-controlled trial that enrolled a total of 85 SHTG patients either on stable background therapy (55% - statin/statin combos, and/or prescription fish oil, and/or fibrates) or not on any background therapy treated weekly or every two weeks with pegozafermin. The trial enrolled an advanced population with high risk of cardiovascular disease as evidenced by mean baseline values of treated patients with TGs of 733 mg/dL, non-HDL-C of 211 mg/dL, 43.5% with HbA1c ≥6.5%, and, in the subgroup of patients undergoing MRI-PDFF, liver fat content of 20.1%.

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. Pegozafermin is currently being evaluated in the Phase 2b ENLIVEN trial in NASH and is expected to move into Phase 3 program for SHTG in 2023.

Recent Phase 2 data with pegozafermin in SHTG patients demonstrated significant and clinically meaningful reductions in triglycerides as well as improvements in other cardiometabolic measures. Additionally, Phase 1b/2a data with pegozafermin in biopsy-confirmed NASH patients demonstrated clinically meaningful changes on histology endpoints and non-invasive measures of total liver health as well as many of the underlying metabolic comorbidities commonly associated with NASH.

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 with operations in Herzliya, Israel. 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, clinical development plans and timing for pegozafermin, including the Phase 2b ENLIVEN trial and the timing for the initiation of the Phase 3 trial in SHTG. 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 initiation of the Phase 3 trial in SHTG; positive results from a clinical study may not necessarily be predictive of the results of future or ongoing clinical studies; expectations regarding pegozafermin's potential to address need for SHTG treatment options; 89bio's substantial dependence on the success of it lead product candidate; competition from competing products; 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 June 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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