89bio Reports Positive Topline Results from ENTRIGUE Phase 2 Trial of Pegozafermin in Patients with Severe Hypertriglyceridemia (SHTG)

June 28, 2022

- Trial met primary endpoint demonstrating statistically significant and clinically meaningful reductions across all doses (63% at the 27mg QW dose; p<0.001) in triglycerides (TG) from baseline; results were consistent in patients on or not on background therapy -

- Observed significant and potent reductions in atherogenic lipids (non-HDL-C and apo B), liver fat, and improvements in liver enzymes and glycemic control markers -

- ENTRIGUE results support 89bio's transition to a late-stage development company; Phase 3 expected to initiate in first half of 2023 -

- Conference call and webcast today at 1:30 p.m. PST/4:30 p.m. EST -

SAN FRANCISCO, June 28, 2022 (GLOBE NEWSWIRE) -- 89bio, Inc. (Nasdaq: ETNB), today announced positive topline results from ENTRIGUE, the Phase 2 proof-of-concept study evaluating pegozafermin for the treatment of severe hypertriglyceridemia (SHTG). Treatment with pegozafermin resulted in clinically meaningful and significant reductions in triglycerides (TG) from baseline across all doses (with a 63% reduction in the highest dosing group; p<0.001) and various subgroups, statistically significant improvements in key markers of cardiovascular risk (non-HDL-C and apo B), reductions in liver fat, and improvements in glycemic control markers.

"There is a critical need for SHTG treatment options that not only reduce triglycerides but also address broader cardiometabolic risks including hepatic steatosis and improve insulin sensitivity" said Deepak L. Bhatt, MD, MPH, Executive Director of Interventional Cardiovascular Programs, Brigham and Women's Hospital Heart & Vascular Center, Professor of Medicine, Harvard Medical School. "Treatment with pegozafermin demonstrated impressive triglyceride reduction coupled with meaningful reductions in non-HDL-C and improvements in cardiometabolic parameters. Taken together, pegozafermin's profile in ENTRIGUE shows great potential to uniquely address the key needs for patients with SHTG."

Results showed statistically significant reductions in median TGs from baseline across all dose groups treated with pegozafermin, compared to placebo after 8 weeks. Additionally, results were consistent in patients not on background therapy or on background therapy (consistent results on statins or statin combos, prescription fish oils, and fibrates) and across various subgroups, including those with the greatest disease burden, such as Type 2 diabetes and baseline TG levels ≥750 mg/dL.

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

Median Percent Change in Triglycerides from Baseline at Week 8

Dosing group	**Patients on background therapy[1]**	**Patients not on background therapy**
Placebo	-18%	5%
9mg QW	-59%	-50%
18mg QW	-56%	-59%
27mg QW	-68%	-62%
36mg Q2W	-45%	-21%

1. Background therapy defined as concomitant lipid modifying therapy
Patients on background therapy: placebo (n=11), 9mg QW (n=8), 18mg QW (n=9), 27mg QW (n=10), 36mg Q2W (n=8)
Patients not on background therapy: placebo (n=6), 9mg QW (n=8), 18mg QW (n=8), 27mg QW (n=6), 36mg Q2W (n=8)

Responder analysis on primary endpoint of TG reduction demonstrated:

- A significantly higher proportion of patients reached the initial treatment goal of reducing TG <500 mg/dL on pooled

pegozafermin vs. placebo (80% vs. 29%; p<0.001).

- Treatment with 27mg QW resulted in a significantly higher proportion of patients achieving TG normalization (<150 mg/dL) vs. placebo (31% vs. 0%; p<0.05) and
- Greater proportion of patients achieved significant TG reduction of ≥ 50% from baseline vs. placebo (75% vs. 6%; p<0.001).

Pegozafermin treatment also resulted in significant improvements compared to placebo (mean percent change from baseline) and clinically meaningful changes on an absolute basis in non-HDL-C and apo B that are key markers of cardiovascular risk (absolute change from baseline of 55 mg/dL and 22 mg/dL in non-HDL-C and apo B respectively with 27mg QW dose). Patients treated across all doses with pegozafermin also demonstrated an improvement in HDL-C and no change in LDL-C vs. placebo.

Mean Percent Change in non-HDL-C and apo B from Baseline at Week 8

Dosing group	**non-HDL-C**	**apo B**
Placebo	-3%	-1%
9mg QW	-14%	-11%
18mg QW	-22%**	-14%*
27mg QW	-29%***	-18%**
36mg Q2W	-9%	-1%

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

Pegozafermin treatment resulted in a mean relative reduction in liver fat from baseline at week 8 across all dose groups versus placebo in the substudy of patients with magnetic resonance imaging – proton density fat factor (MRI-PDFF) and the results are summarized in the table below.

Mean Relative Reduction in Liver Fat vs. Baseline at Week 8 in Substudy

Dosing group	**MRI-PDFF**
Placebo (n=6)	-5%
9mg QW (n=3)	-55%*
18mg QW (n=5)	-38%
27mg QW (n=7)	-44%
36mg Q2W (n=2)	-37%

* p<0.05 versus placebo based on ANCOVA analysis

- A significant proportion of patients responded to therapy with up to 88% and 41% of treated patients vs. 0% of placebo patients achieving a ≥30% or a ≥50% reduction in liver fat versus baseline, respectively.
- Results also demonstrated a significant reduction in liver enzymes and an improvement in glycemic control markers in pegozafermin treated patients.

Pegozafermin continues to be generally well tolerated with a favorable safety profile across doses consistent with prior studies. In ENTRIGUE, the most commonly reported treatment-related adverse events were nausea, diarrhea, and injection site reactions, all which were classified as mild or moderate. No tremors or transaminase elevation adverse events were observed. There were no drug-related serious adverse events and two Grade 2 treatment-related discontinuations.

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 liver fat content of 20.1%.

Hank Mansbach, Chief Medical Officer of 89bio, commented, “We are extremely pleased by the robust and consistent results observed across multiple measures and patient subgroups in this study. These results add to the body of evidence demonstrating pegozafermin’s unique and differentiated profile based on broad metabolic effects and a favorable safety/tolerability profile. These positive data support the advancement into a Phase 3 trial in SHTG based on regulatory precedent, which we plan to initiate in the first half of 2023. These results also build confidence in our ongoing Phase 2b ENLIVEN trial in NASH with data expected in the first quarter of 2023.”

Rohan Palekar, Chief Executive Officer of 89bio, added, “SHTG remains a significant market opportunity with a large patient population who are underserved with the existing therapeutic options. In market research, physicians have indicated a strong preference for a drug that could address the metabolic co-morbidities, especially the liver fat benefit seen in a majority of these patients. We believe the results from ENTRIGUE position pegozafermin as potentially the first FGF21 analog to market and to become an important metabolic drug for treatment of cardio-metabolic and liver disease.”

Today’s Conference Call Information

89bio will host a conference call and webcast at 1:30 p.m. PST / 4:30 p.m. EST today, June 28, 2022. Analysts and investors can participate in the conference call by dialing (1-877-704-4453) or domestic callers and +1 (1-201-389-0920) for international callers, using the conference ID 13730718.

The webcast can be accessed live here and on the Events & Presentations page in the Investors section of the 89bio website, www.89bio.com. The webcast will be archived on the company's website for at least 30 days after the conference call.

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 NASH including glycemic control, steatosis, inflammation and fibrosis. Pegozafermin was specifically engineered using a unique glycoPEGylated technology to extend the half-life while maintaining potency. Recent 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, in patients with NASH as well as many of the underlying metabolic comorbidities commonly associated with NASH. Pegozafermin is currently being evaluated in the Phase 2b ENLIVEN trial in NASH.

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 is focused on rapidly advancing its lead candidate, pegozafermin, through clinical development for the treatment of non-alcoholic steatohepatitis (NASH) and severe hypertriglyceridemia (SHTG). 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 for the treatment of SHTG, the efficacy and safety of pegozafermin, pegozafermin's potential as a compelling treatment option for SHTG, the expected timing of the initiation of the Phase 3 trial in SHTG, the expected timing of data from the ongoing Phase 2b ENLIVEN trial in NASH and the relationship between the results from the positive data from Phase 2 ENTRIGUE trial and results of future or ongoing clinical studies, including the ongoing Phase 2b ENLIVEN trial in NASH. Words such as "may," "might," "will," "objective," "intend," "should," "could," "can," "would," "expect," "believe," "design," "estimate," "predict," "potential," "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: positive results from a clinical study may not necessarily be predictive of the results of future or ongoing clinical studies; and other risks and uncertainties identified in 89bio's Annual Report on Form 10-K for the year ended December 31, 2021, its Quarterly Report on Form 10-Q for the quarter ended March 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

Source: 89bio, Inc.