89bio Initiates Phase 3 ENLIGHTEN-Fibrosis Trial of Pegozafermin in Non-Cirrhotic Metabolic Dysfunction-Associated Steatohepatitis (MASH) Patients with Fibrosis

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—Co-primary endpoints in ENLIGHTEN-Fibrosis assessed at week 52 will potentially support accelerated approval in non-cirrhotic MASH (fibrosis stage F2-F3) patients—

—ENLIGHTEN-Cirrhosis, the second trial in the program, is planned to evaluate patients with compensated cirrhosis (F4) and is expected to initiate in the second quarter of 2024—

SAN FRANCISCO, March 12, 2024 (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 initiation of its Phase 3 ENLIGHTEN Program evaluating the efficacy and safety of pegozafermin in patients with metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH). ENLIGHTEN-Fibrosis, the first of two Phase 3 trials in the program, has initiated and is evaluating non-cirrhotic MASH patients with fibrosis stage F2-F3.

"The ENLIGHTEN-Fibrosis trial is designed to build on the robust anti-fibrotic and metabolic effects observed across non-cirrhotic MASH patients treated with pegozafermin in the Phase 2b ENLIVEN trial," 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 investigator of the ENLIGHTEN program. "There is a critical need for a therapeutic option that improves liver health and provides anti-fibrotic benefits for MASH patients with fibrosis."

ENLIGHTEN-Fibrosis is a global Phase 3, randomized, double-blind, placebo-controlled trial of pegozafermin for the treatment of patients with biopsy-confirmed non-cirrhotic MASH. Approximately 1,000 patients are expected to be randomized in a 1:1:1 ratio to receive either 30mg of pegozafermin administered weekly, 44mg administered every two weeks, or placebo. The co-primary endpoints are a one-point or greater improvement in fibrosis with no worsening of MASH, and MASH resolution with no worsening of fibrosis. The co-primary endpoints will be assessed at week 52 and are intended to support a filing for accelerated approval in the U.S. and conditional approval in Europe in non-cirrhotic patients. Patients are expected to continue to be treated beyond the 52-week assessment through outcomes to support full approval.

"We are excited to initiate our first Phase 3 trial in MASH for pegozafermin, a leading and potentially best-in-class FGF21 analog, which strikes the right balance of sustained efficacy, favorable tolerability, and dosing convenience," said Hank Mansbach, Chief Medical Officer of 89bio. "ENLIGHTEN-Fibrosis aims to enroll MASH patients, including those on background GLP-1-based therapies, where pegozafermin has demonstrated additional anti-fibrotic and metabolic effects. We remain on track to initiate our second Phase 3 trial in MASH patients with compensated cirrhosis in the second quarter of 2024."

Key secondary endpoints include additional histological endpoints, noninvasive tests (NITs) and metabolic and lipid assessments. The trial is designed to employ a three-panel consensus biopsy reading methodology, which was successfully utilized in the ENLIVEN trial. Patients will self-administer pegozafermin using the planned commercial liquid formulation delivered as a single subcutaneous injection.

About Metabolic dysfunction-associated steatohepatitis (MASH)
MASH, formerly known as nonalcoholic steatohepatitis (NASH), is a more advanced form of metabolic dysfunction-associated steatotic liver disease (MASLD) which is a chronic, progressive disease in which fat accumulates in the liver, ultimately leading to scarring or fibrosis. Fibrosis damages the liver and can lead to more severe liver-related complications, including cirrhosis, liver failure, and hepatocellular cancer (HCC) and is associated with increased risk for cardiovascular disease. In later stages, MASH can cause cirrhosis, which increases the risk for serious intervention such as a liver transplant, with MASH being a leading cause of liver transplants among adults. Most people with MASH experience few or no symptoms until they've progressed to an advanced stage, and as a result, the disease often goes undetected for years, or even decades.

About The ENLIGHTEN Program
The ENLIGHTEN program is comprised of two Phase 3 global, multi-center, randomized, double-blind, placebo-controlled trials, evaluating the efficacy and safety of pegozafermin in patients with MASH. The ENLIGHTEN-Fibrosis study, the first of two Phase 3 trials in the program, is expected to enroll approximately 1,000 patients with non-cirrhotic MASH (fibrosis stage F2-F3) to evaluate the efficacy and safety of pegozafermin. The co-primary endpoints measured at week 52 are a one-point improvement in fibrosis with no worsening of MASH and MASH resolution with no worsening of fibrosis, assessed at week 52. ENLIGHTEN-Cirrhosis, the second of the two Phase 3 trials in the program, is expected to evaluate the efficacy and safety of pegozafermin in MASH patients with compensated cirrhosis (F4).

About pegozafermin
Pegozafermin is a specifically engineered glycoPEGylated analog of fibroblast growth factor 21 (FGF21) being developed for the treatment of metabolic dysfunction-associated steatohepatitis (MASH) and severe hypertriglyceridemia (SHTG). FGF21 is an endogenous hormone that has broad effects such as regulating energy expenditure, glucose and lipid metabolism. In clinical trials, pegozafermin has demonstrated direct anti-fibrotic and anti-inflammatory effects on the liver, as well as reduced triglyceride levels, improved insulin resistance and glycemic control, and continued to demonstrate a favorable safety and tolerability profile. The FDA granted pegozafermin Breakthrough Therapy designation (BTD) for the treatment of MASH with fibrosis. Pegozafermin is advancing into the Phase 3 ENLIGHTEN trial program for MASH and is being studied in the Phase 3 ENTRUST trial for SHTG.

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 metabolic dysfunction-associated steatohepatitis (MASH) 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, statements regarding the therapeutic potential and utility, efficacy and clinical benefits of pegozafermin, the safety and tolerability profile of pegozafermin, trial designs, clinical development plans and timing for pegozafermin, including the anticipated design of the ENLIGHTEN-Fibrosis and ENLIGHTEN-Cirrhosis trials and timing of initiation of the ENLIGHTEN-Cirrhosis trial and the possibility of obtaining accelerated approval in non-cirrhotic MASH (fibrosis stage F2-F3) patients using co-primary endpoints in ENLIGHTEN-Fibrosis trial. 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 Securities and Exchange Commission (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 design of the ENLIGHTEN-Fibrosis and ENLIGHTEN-Cirrhosis trials and initiation of the ENLIGHTEN-Cirrhosis trial; expectations regarding the timing and outcome of the ENTRUST 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; receipt of BTD for pegozafermin in MASH may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA; 89bio's substantial dependence on the success of its lead product candidate; competition from competing products; 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 Annual Report on Form 10-K for the year ended December 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.

Investor Contact:
Annie Chang
89bio, Inc.
investors@89bio.com

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

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