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

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—With the initiation of ENLIGHTEN-Cirrhosis, pegozafermin is the first FGF21 analog to enter a Phase 3 trial in MASH patients with compensated cirrhosis (F4)—

—Regression of fibrosis by histology at month 24 will serve as the basis for potential accelerated approval with clinical outcomes to support the potential for confirmatory or full approval—

SAN FRANCISCO, May 14, 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 ENLIGHTEN-Cirrhosis, a Phase 3 trial of pegozafermin in patients with MASH with compensated cirrhosis (F4).

"MASH patients with compensated cirrhosis are in critical need of effective therapies that can halt and ideally reverse the progression of fibrosis to prevent the onset of liver decompensation," said Arun J. Sanyal, MBBS, M.D., Director of the Stravitz-Sanyal Institute for Liver Disease and Metabolic Health, Virginia Commonwealth University. "Due to its demonstrated anti-fibrotic benefits, pegozafermin has the potential to be uniquely positioned to meet the needs of compensated cirrhotic MASH patients and could reduce the risk of decompensation. I look forward to evaluating the potential benefits of pegozafermin in this Phase 3 trial given the severity of symptoms this patient population experiences."

ENLIGHTEN-Cirrhosis is a global Phase 3, randomized, double-blind, placebo-controlled trial evaluating pegozafermin for the treatment of MASH patients with compensated cirrhosis (F4). The trial will enroll approximately 760 patients, who will be randomized in a 1:1 ratio to either receive 30mg of pegozafermin administered weekly or a placebo. The interim analysis primary endpoint of fibrosis regression is defined as improvement in fibrosis from F4 to an earlier stage. A subset of the 760 patients will be evaluated at 24 months to assess fibrosis regression, potentially supporting an accelerated approval filing in the United States and conditional approval in Europe. The trial will continue to monitor all participants until a pre-defined number of clinical outcome events are observed. The primary endpoint for the final analysis will be a clinical outcome composite and is expected to form the basis for confirmatory or full approval for MASH patients at both stage F4 and as well as stages F2-F3. Based on prior discussions and alignment with regulatory agencies on the modified definitions of cirrhosis clinical outcome events, the timeline for reaching the expected number of events could be expedited compared to previous Phase 3 trials that have been conducted in MASH patients with compensated cirrhosis.

"Initiating the ENLIGHTEN-Cirrhosis trial marks a significant milestone for pegozafermin as it becomes the first FGF21 analog to enter a Phase 3 trial in MASH patients with compensated cirrhosis," said Hank Mansbach, Chief Medical Officer of 89bio. "Regulatory agencies have aligned on a potential accelerated approval pathway based on histological evidence showing regression of fibrosis. In our Phase 2b ENLIVEN trial, we observed not only improvements in key non-invasive markers of liver inflammation and fibrosis, but specific improvements in fibrosis based on histology among patients treated with pegozafermin. We are eager to build on these results in our comprehensive global Phase 3 trial involving a larger number of patients."

Key secondary endpoints include noninvasive tests (NITs) evaluating liver health and metabolic markers. The trial is designed to employ a three-panel consensus biopsy reading methodology, which was successfully utilized in the Phase 2b 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, also known as nonalcoholic steatohepatitis (NASH), is a chronic and progressive condition that represents a severe form of metabolic dysfunction-associated steatotic liver disease (MASLD). It is characterized by fat accumulation in the liver, which causes inflammation and can ultimately lead to scarring or fibrosis. By 2030, it is projected to affect over 27 million people in the U.S. The disease is categorized based on the extent of liver fibrosis. In cases of advanced fibrosis, the treatment goal is to improve liver health, reverse fibrosis, and prevent the progression of the disease and related complications such as cirrhosis and cardiovascular risks. Estimates suggest that approximately 20% of patients with MASH may develop cirrhosis, a serious condition that significantly impairs liver function. Cirrhosis can lead to life-threatening complications from esophageal varices, ascites, or hepatocellular carcinoma. Patients may ultimately require a liver transplant to avoid death from liver failure.

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 trial, the first of two Phase 3 trials in the program, will 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, for which demonstration of an effect on each is needed to support regulatory approval, 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 two Phase 3 trials in the program, will 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. Pegozafermin received Breakthrough Therapy designation (BTD) status from the U.S. Food and Drug Administration (FDA) and Priority Medicines (PRIME) status from the European Medicines Agenda (EMA) for the treatment of MASH with

fibrosis. Pegozafermin is being studied in 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 and enrollment in the ENLIGHTEN-Cirrhosis trial and the possibility of obtaining accelerated approval in the United States and conditional approval in Europe in compensated cirrhosis (F4) MASH patients using regression of fibrosis by histology at month 24 in ENLIGHTEN-Cirrhosis 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; 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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2024 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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