89bio Announces New Positive Long-Term Data from the ENLIVEN Phase 2b Trial of Pegozafermin in Patients with Nonalcoholic Steatohepatitis (NASH)

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—Data at week 48 demonstrated that treatment with pegozafermin led to sustained statistically significant improvements across liver fat and non-invasive tests (NITs) of liver injury/inflammation and fibrosis in NASH patients with fibrosis stage F2-F3—

—Subgroups of patients treated with pegozafermin on background GLP-1-based therapies and patients with compensated cirrhosis (F4) each showed robust benefits at week 48—

—Pegozafermin continued to demonstrate a favorable safety and tolerability profile consistent with previously reported data—

SAN FRANCISCO, Nov. 27, 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 positive topline data from the blinded extension phase of its Phase 2b ENLIVEN trial evaluating treatment with pegozafermin in patients with nonalcoholic steatohepatitis (NASH). At week 48, both the 30mg weekly (QW) and 44mg every-two-week (Q2W) dosing schedules of pegozafermin demonstrated statistically significant improvements across key markers of liver health. The benefits observed at week 48 were consistent with the results observed at week 24, indicating sustained benefits over time.

“We are very encouraged by these long-term efficacy and tolerability data which establish pegozafermin as the first FGF21 analog candidate to demonstrate positive, sustained benefits over a 48-week period in patients with advanced NASH,” said Hank Mansbach, Chief Medical Officer of 89bio. “Notably, we observed consistent and robust benefits in F2-F3 NASH patients, as well as in subgroups of patients receiving concurrent GLP-1 therapy and F4 patients with compensated cirrhosis, validating pegozafermin’s anti-fibrotic effects across a broad spectrum of patients. The sustained improvement in observed key liver health markers could lead to greater histological response rates, which we will aim to confirm in Phase 3 development. We are working with the regulatory agencies and look forward to providing additional details of our Phase 3 NASH program before the end of this year."

ENLIVEN Extension Data
Patients in ENLIVEN continued in a blinded extension phase for an additional 24 weeks (Extension Phase) past the primary endpoint at week 24 (Main Study), for a total treatment period of 48 weeks. A subset of patients in the placebo arm of the Main Study (n=19) were re-randomized to receive pegozafermin 30mg weekly (QW) during the Extension Phase. The efficacy endpoints assessed in the Extension Phase included liver fat, non-invasive markers of fibrosis and inflammation, and metabolic markers. Per the protocol, these patients did not undergo biopsies at week 48.

Table 1. Extension Phase Data at Week 48: Liver NITs Results [marker of]

F2-F3 Patients	**Placebo**	**Pegozafermin**	
		30mg QW	**44mg Q2W**
	(n=35)[1, 2]	**(n=50)[2]**	**(n=45)[2]**
MRI-PDFF [liver fat] [4]	-11%	-60%**	-47%*
ALT [liver injury/inflammation][3]	-11%	-42%***	-35%**
AST [liver injury/inflammation][3]	-4%	-39%***	-36%***
ELF score [liver fibrosis][3]	+0.1	-0.3**	-0.4***
Pro-C3 [collagen deposition][3]	+5%	-15%***	-14%***
VCTE (kPa) [liver stiffness][4]	-0.8	-2.9*	-1.3
FAST [liver fibrosis][3]	-4%	-59%***	-51%***

***p<0.001, **p<0.01, *p<0.05 versus placebo. [1] Dataset excludes 19 placebo patients who were re-randomized to pegozafermin 30mg QW in the Extension Phase. [2] Extension data at week 48 represents patients who entered the blinded Extension Phase. [3] Least Square (LS) mean change from baseline. [4] Median change from baseline.

Treatment Effects Were Robust and Consistent across Patient Sub-groups
Patients on Background GLP-1 Therapy:
Consistent with results observed in the Main Study, patients on background GLP-1 therapy who received pegozafermin continue to derive a greater benefit on markers of liver fibrosis, liver injury/inflammation, liver fat and lipids, compared to patients who continued GLP-1 therapy in the placebo group. Patients entering ENLIVEN on background GLP-1 therapies were required to have been on a stable regimen for at least six months.

Table 2. Extension Phase Data at Week 48: Patients on Background GLP-1, Liver NITs and Lipids Results [marker of]

	Placebo (n=12)	**Pegozafermin[3]**

		(n=26)
MRI-PDFF [liver fat][2]	-34%	-53%
ALT [liver injury/inflammation][1]	-15%	-44%
AST [liver injury/inflammation] [1]	-11%	-42%
ELF score [liver fibrosis] [1]	0	-0.5
Pro-C3 [collagen deposition][1]	-9%	-19%
VCTE (kPa) [liver stiffness] [2]	-3.2	-2.2
FAST [liver fibrosis] [1]	-43%	-52%
Triglycerides [lipids][2]	-12%	-22%
LDL-C [lipids][2]	-5%	-14%

[1] LS mean change from baseline. [2] Median change from baseline. [3] Patients dosed with pegozafermin 30mg QW or 44mg Q2W.

Compensated Cirrhosis (F4) Patients:
Biopsy-confirmed compensated cirrhosis F4 patients who had previously demonstrated histological response and improvement across NITs at week 24 continued to demonstrate robust and sustained improvements in non-invasive measures at week 48.

Table 3. Extension Phase Data at Week 48: F4 Patients, Liver NITs Results [marker of]

	Pegozafermin[3] (n=12)
ALT [liver injury/inflammation][1]	-58%
AST [liver injury/inflammation][1]	-38%
ELF score [liver fibrosis][1]	-0.5
Pro-C3 [collagen deposition][1]	-20%
VCTE (kPa) [liver stiffness][2]	-1.1
FAST [liver fibrosis][1]	-42%

[1] LS mean change from baseline. [2] Median change from baseline. [3] Patients dosed with pegozafermin 15mg QW, 30mg QW or 44mg Q2W.

Patients Re-randomized from Placebo to Pegozafermin:
The patients re-randomized to receive 30mg QW during the Extension Phase demonstrated robust improvements in NITs of liver fibrosis, liver injury/inflammation, and liver fat following 24 weeks of treatment with pegozafermin after experiencing minimal to no change during the first 24 weeks on placebo. Patients in the re-randomized group serve as their own control and thus provide independent compelling evidence of pegozafermin's rapid and robust therapeutic effects.

Pegozafermin continued to demonstrate a favorable safety and tolerability profile at week 48, consistent with previously reported data. The most common treatment-emergent adverse events were Grade 1 or 2 gastrointestinal events. Incidence rates of adverse events remained generally stable between week 24 and week 48 with no new patients on pegozafermin reporting diarrhea or nausea during the Extension Phase. At week 48, no clinically meaningful or statistically significant changes in bone mineral density or bone biomarkers were observed relative to placebo. No clinically meaningful or statistically significant changes in blood pressure or heart rate were observed relative to placebo.

About pegozafermin
Pegozafermin is a specifically engineered glycoPEGylated analog of fibroblast growth factor 21 (FGF21) being developed for the treatment of nonalcoholic steatohepatitis (NASH) 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 U.S. Food and Drug Administration (FDA) granted pegozafermin Breakthrough Therapy designation (BTD) for the treatment of NASH with fibrosis. Pegozafermin is advancing into a Phase 3 trial for NASH and is being studied in the Phase 3 ENTRUST trial for SHTG.

About ENLIVEN
ENLIVEN was a multicenter, randomized, double-blind, placebo-controlled Phase 2b trial designed to evaluate the safety and efficacy of weekly or every-two-week dosing of pegozafermin for the treatment of patients with biopsy confirmed NASH and NAS ≥ 4 for 48 weeks. In the trial, 192 patients were dosed with pegozafermin 15mg QW, 30mg QW and 44mg Q2W, or placebo. Primary outcomes measured were proportion of participants with resolution of NASH without worsening of fibrosis and proportion of participants with ≥1 stage decrease in fibrosis stage with no worsening of NASH at week 24. Secondary measures included change from baseline in liver fat, liver enzymes, noninvasive markers of liver fibrosis, glycemic control, lipoproteins, and body weight as well as safety and tolerability measures. Patients who entered the blinded extension phase were subsequently treated for an additional 24 weeks for a total treatment period of 48 weeks. Some patients who were on placebo (n=19) were re-randomized to receive pegozafermin in the extension phase. Key endpoints in the extension phase include liver fat and non-invasive markers of liver fibrosis and inflammation. ENLIVEN achieved high statistical significance on primary histology endpoints with 30mg QW and 44mg Q2W dosing at week 24 and the results were published in the *New England Journal of Medicine*. To learn more about the clinical trial, visit clinicaltrials.gov: NCT04929483.

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 nonalcoholic 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. Pegozafermin has been granted Breakthrough Therapy designation for the treatment of NASH with fibrosis from U.S. Food and Drug Administration (FDA). 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, including the relationship between the results from the Phase 2 ENLIVEN trial and potential results of future clinical studies such as whether sustained improvement in key liver health markers observed could lead to greater histological efficacy, the safety and tolerability profile of pegozafermin, trial designs, clinical development plans and timing for pegozafermin, including the ENTRUST Phase 3 trial in SHTG and the NASH Phase 3 trial, and anticipated work with regulatory authorities. 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 initiation of the Phase 3 trial in NASH; 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 NASH 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, 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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