# 89bio Announces Positive Topline Results from its Phase 1b/2a Trial of BIO89-100 in NASH

September 14, 2020

*All dose groups achieved statistically significant reductions in liver fat, with relative reductions of up to 60% versus baseline and up to 70% versus placebo*

*Favorable safety and tolerability profile*

*Strong efficacy profile with every two-week dosing*

*Statistically significant improvements in markers of liver injury and key lipid parameters*

*Conference call and webcast scheduled for 8:30 am ET (5:30 am PT) today*

SAN FRANCISCO, Sept. 14, 2020 (GLOBE NEWSWIRE) -- 89bio, Inc. (Nasdaq: ETNB) today announced positive topline results from its Phase 1b/2a trial with BIO89-100, an investigational FGF21 analog, in patients with nonalcoholic steatohepatitis (NASH). All dose groups demonstrated significant reductions in liver fat at week 13, with relative reductions up to 60% versus baseline and up to 70% versus placebo, as measured by magnetic resonance imaging – proton density fat factor (MRI-PDFF). A significant proportion of subjects responded to therapy with up to 88% and 71% of subjects achieving a ≥30% or a ≥50% reduction in liver fat versus baseline, respectively. Treatment with BIO89-100 also resulted in significant improvements in liver transaminases, with a 35 U/L decrease in ALT from baseline in subjects with elevated baseline levels, and reductions in ProC3, a marker of fibrosis. Importantly, BIO89-100 is the first FGF21 analog to show benefit in subjects with NASH with every two-week dosing. BIO89-100 was well tolerated at all doses with low incidence of adverse events that occurred in ≥10% of subjects and very low frequency of gastrointestinal (GI) events relative to placebo.

The MRI-PDFF results are summarized in the table below:

| | | BIO89-100 (once-weekly) | | | | BIO89-100 (once every two weeks) | |
|---|---|---|---|---|---|---|---|
| Measure | Placebo (n= 19) | 3mg (n= 6) | 9mg (n= 12) | 18mg (n= 11) | 27mg (n= 10) | 18 mg (n= 14) | 36 mg (n= 9) |
| Relative reduction/increase in liver fat vs. baseline | +10% | -37%** | -50%** | -36%** | -60%** | -43%** | -50%** |
| Relative reduction in liver fat vs. placebo | | -47%** | -59%** | -46%** | -70%** | -53%** | -60%** |
| Proportion of subjects with ≥30% relative reduction in liver fat | 0% | 60%* | 82%** | 60%** | 86%** | 69%** | 88%** |
| Absolute change in liver fat vs. baseline | +1.4 | -7.5%* | -10%** | -7.5%** | -13.5%** | -9.0%** | -9.7%** |

**p<0.01; **p<0.001 vs. placebo. n based on subjects randomized. Least square mean based on MRI analysis set (N=75) and responder analysis based on subjects with MRI at Week 13. Levels of liver fat in the BIO89-100 and placebo groups at baseline were 21.2% (on a pooled basis) and 21.8%, respectively. Baseline liver fat levels and changes in liver fat were similar in biopsy-confirmed NASH and phenotypical NASH subjects.*

“The robust reductions in liver fat and key liver markers add to a growing body of evidence demonstrating the promise of BIO89-100 for the treatment of NASH and cardio-metabolic diseases,” said Rohit Loomba, MD, MHSc, Director of the UC San Diego NAFLD Research Center and Director of Hepatology at UC San Diego School of Medicine. “The magnitude of ≥30% relative reduction in liver fat has been shown in the literature to translate into higher odds of histologic response and potential to deliver clinically meaningful benefit to patients with NASH.”

BIO89-100 had a favorable safety and tolerability profile with no deaths or serious adverse events related to treatment. The frequency of GI events compared favorably to placebo with diarrhea (BIO89-100 12.7% vs. placebo 22.2%) and nausea (BIO89-100 7.9% vs. placebo 16.7%) being the only GI events occurring in ≥5% of BIO89-100-treated subjects. The only treatment-related adverse event that occurred in ≥10% of all BIO89-100-treated subjects was mild, increased appetite (15.9%) consistent with other investigational FGF21 analogs. No adverse effects on heart rate or blood pressure were observed.

Treatment with BIO89-100 resulted in significant reductions in triglycerides (up to 28%; p <0.05), non-HDL (up to 16%; p<0.01) and LDL-C (up to 16%; p<0.05). Triglycerides were reduced to a greater extent in subjects with elevated triglycerides at baseline (TG≥200 mg/mL), and 53% of the BIO89-100 subjects in this group normalized triglyceride levels versus 0% in the placebo group. BIO89-100 also demonstrated significant increases in the insulin-sensitizing hormone adiponectin (up to 61%; p<0.001).

This study was a randomized, double-blind, placebo-controlled, multiple ascending dose-ranging trial in biopsy-proven NASH or phenotypical NASH (PNASH) subjects. A total of 81 subjects were randomized to receive weekly or every two-week dosing of BIO89-100 or placebo for up to 12 weeks. Key endpoints assessed were safety, tolerability, and PK of BIO89-100 as well as change in liver fat measured by MRI-PDFF and other metabolic markers.

“The favorable safety and tolerability profile of BIO89-100 together with potential best-in-class dosing regimen could be important considerations for a NASH therapeutic given the chronic and generally asymptomatic nature of the disease,” said Hank Mansbach, MD, Chief Medical Officer, 89bio. “These factors, combined with improvements in liver fat and metabolic markers, unequivocally support advancing the clinical development of

BIO89-100 in NASH and reinforce our confidence in the severe hypertriglyceridemia program. We plan to initiate our next trial in NASH in the first half of 2021."

"We are pleased with this data that highlight BIO89-100's promising clinical profile and its potential to be a leading FGF21 analog in a class with the potential to become a backbone treatment approach for NASH," said Rohan Palekar, Chief Executive Officer, 89bio. "I would like to sincerely thank all of our investigators, clinical sites, subjects, and employees who supported the trial, especially amid a pandemic that has severely impacted the global healthcare system in an unprecedented manner."

**Conference Call/Webcast Details**
89bio will host a conference call and webcast with slides at 8:30am ET (5:30am PT) this morning, September 14. Details for the live conference call are as follows: Domestic – (833) 570-1145; International – (914) 987-7092; and Passcode - 5064866. To access the live webcast and slides, please visit "Events and Presentations" under the "Investors" section of 89bio's website at https://ir.89bio.com/events-and-presentations. Following the live audio webcast, a replay will be available on the company's website for 90 days.

**About NASH**
NASH is the most advanced stage of nonalcoholic fatty liver disease (NAFLD). It is a complex metabolic disorder that causes fat buildup in the liver, as well as inflammation and eventually fibrosis, and it can worsen to cirrhosis and liver failure. NASH affects more than 16 million adults in the United States, and by 2030 its prevalence is predicted to increase by 63 percent. The exact cause of NASH is unknown, but it is commonly found in people with obesity and type 2 diabetes. While there are currently no approved treatments, the biopharmaceutical industry is actively involved in addressing this unmet medical need.

**About the Phase 1b/2a Study**
This clinical study was a multicenter, randomized, double-blind, placebo-controlled, multiple ascending dose-ranging trial. It was designed to assess the safety, tolerability, and PK properties of BIO89-100 as well as change in liver fat measured by MRI-PDFF and key biomarker assessments in subjects with biopsy-proven NASH with fibrosis or patients with phenotypical NASH (PNASH). PNASH was defined as patients with steatosis greater than 10% who have central obesity and Type 2 diabetes or central obesity and evidence of liver injury. Both populations that were enrolled had similar disease characteristics at baseline. A total of 81 subjects were randomized to receive weekly or every two weeks subcutaneous dosing of BIO89-100 or placebo for up to 12 weeks.

**About BIO89-100**
BIO89-100 is a glycoPEGylated analog of FGF21 being developed for the treatment of NASH. 89bio has optimally engineered BIO89-100 using a proprietary glycoPEGylation technology to balance efficacy and longer dosing interval. Recent Phase 1b/2a data show BIO89-100 demonstrated a favorable safety and tolerability profile and robust reductions in liver fat and key lipid markers when dosed weekly or once every two weeks. BIO89-100 is also being developed for the treatment of severe hypertriglyceridemia (SHTG) and is currently in a Phase 2 trial.

**About 89bio**
89bio is a clinical-stage biopharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of liver and cardio-metabolic diseases. The company's lead product candidate is BIO89-100, is a specifically engineered glycoPEGylated analog of FGF21. BIO89-100 is being developed for the treatment of NASH and severe hypertriglyceridemia (SHTG). 89bio is headquartered in San Francisco with operations in Herzliya, Israel. For more information, visit www.89bio.com.

**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, 89bio's expectations and guidance regarding its business plans and objectives for BIO89-100, including the therapeutic potential and clinical benefits thereof, as well as the safety and tolerability of BIO89-100 and future clinical development plans; 89bio's statements regarding the Phase 1b/2a Trial of BIO89-100; and the potential impact of COVID-19 on patient retention, strategy, future operations and clinical trials, including the anticipated timing of the next 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: expectations regarding the timing and outcome of 89bio's initiation of the next trial in NASH; 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; regulatory developments in the United States; 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; and other risks and uncertainties identified in 89bio's Annual Report on Form 10-K for the year ended December 31, 2019 and its Quarterly Report on Form 10-Q for the quarter ended June 30, 2020 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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