MBX Biosciences Announces Positive Phase 1 Topline Results for MBX 1416 for the Treatment of Post-bariatric Hypoglycemia

January 7, 2025

Phase 1 results support proceeding to Phase 2 in patients with post-bariatric hypoglycemia (PBH), which is expected to begin in 2H 2025

Phase 1 trial in healthy volunteers showed MBX 1416 was generally well-tolerated with a favorable safety profile

Pharmacokinetic results demonstrated sustained dose-dependent exposure and support once-weekly dosing

Company to host conference call to discuss results today at 8:30 am ET

CARMEL, Ind., Jan. 07, 2025 (GLOBE NEWSWIRE) -- MBX Biosciences, Inc. (Nasdaq: MBX), a clinical-stage biopharmaceutical company focused on the discovery and development of novel precision peptide therapies for the treatment of endocrine and metabolic disorders, today announced positive results from its Phase 1 single ascending dose (SAD) and multiple ascending dose (MAD) clinical trial of MBX 1416 in healthy adult volunteers. MBX 1416 is the Company's investigational long-acting glucagon-like peptide 1 (GLP-1) receptor antagonist, being developed for the treatment of PBH.

"We are encouraged by the positive topline Phase 1 results in healthy volunteers that showed MBX 1416 was generally well-tolerated with a favorable safety profile and a promising pharmacokinetic profile supportive of once-weekly dosing," said Kent Hawryluk, President and Chief Executive Officer of MBX Biosciences. "We also observed an apparent increase in GLP-1 peak during the first hour after a mixed meal tolerance test, which is an encouraging signal that we believe may translate into a therapeutic benefit in patients with PBH. Based on these results, we intend to initiate a Phase 2 study in patients with PBH in the second half of 2025 to further optimize dosing, pending alignment with the FDA on our proposed study design."

Phase 1 Trial Topline Results
Key results from the study are as follows:

- MBX 1416 was generally well-tolerated with a favorable safety profile.
- No MBX 1416 dose-related serious adverse events were observed and the majority of treatment-emergent adverse events were mild or moderate in severity.
- Injection site reactions (ISR), predominantly characterized by erythema, were commonly observed in both single and multiple ascending dose cohorts. These reactions were mild or moderate in 88% of the subjects with ISRs and resolved within approximately seven days in the MAD cohort.
- MBX 1416 concentrations increased dose-proportionally in both the SAD and MAD cohorts.
- In the MAD cohort, MBX 1416 median half-life was approximately 90 hours, supporting once-weekly administration, and at steady state the median T_{max} was between 36 and 48 hours.
- In the MAD cohort, MBX 1416 appeared to increase GLP-1 within 60 minutes of a mixed meal tolerance test, suggesting a pharmacodynamic (PD) effect in healthy volunteers that may translate into a therapeutic benefit in PBH patients.
- Consistent with known GLP-1 antagonism effect on gastric motility, a slight acceleration of gastric emptying was observed with MBX 1416 based on acetaminophen exposure.
- In the drug-drug interaction (DDI) portion of the trial, MBX 1416 was observed to have no meaningful effect on rosuvastatin exposure, a commonly prescribed statin.

Phase 1 Trial Design
The Phase 1 clinical trial was a randomized, double-blind, placebo-controlled study designed to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of MBX 1416 in healthy adult volunteers. The trial was conducted in the United States and enrolled a total of 69 subjects. The single ascending dose (SAD) portion of this Phase 1 trial evaluated 32 healthy adults randomized to receive placebo (n=8) or subcutaneous MBX 1416 doses of 10 mg (n=6), 30 mg (n=6), 100 mg (n=6) and 200 mg (n=6). The multiple ascending dose (MAD) portion of the trial evaluated 23 healthy adults randomized to receive placebo (n=5) or subcutaneous MBX 1416 doses of 10 mg (n=6), 30 mg (as two injections; n=6) and 30 mg (as one injection; n=6). An additional cohort evaluated rosuvastatin and acetaminophen pharmacokinetics in the presence and absence of MBX 1416 (n=14).

MBX Biosciences intends to discuss these results with the U.S. Food and Drug Administration (FDA) in an End-of-Phase 1 meeting in mid-2025. Pending alignment with the FDA, a Phase 2 study of MBX 1416 in patients with PBH is anticipated to initiate in the second half of 2025.

MBX Biosciences will host a conference call and webcast today, January 7, 2025, at 8:30 am Eastern Time to discuss the results from the MBX 1416 Phase 1 trial. Participants can register here to access the live webcast of the conference call. Those who prefer to join the call via phone can register using this link receive a dial-in number and unique PIN. Following the live event, a replay will be available on the Investors section of the Company's website.

About MBX 1416
MBX 1416 is an investigational long-acting glucagon-like peptide-1 (GLP-1) receptor antagonist in development as a potential treatment for PBH. It was designed using the Company's novel, proprietary PEP™ platform to prevent the occurrence of severe hypoglycemia in individuals with PBH so they can lead healthier and more independent lives.

About Post-bariatric Hypoglycemia
Post-bariatric hypoglycemia (PBH) is a rare and serious complication of bariatric surgery. PBH is characterized by repeated episodes of symptomatic hypoglycemia, triggered by exaggerated secretion of GLP-1 levels following a meal, and can present as early as six months after Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy. Hypoglycemic episodes can occur multiple times per day and can periodically manifest with severe symptoms, such as dizziness, confusion, loss of consciousness or seizure. The unpredictability of hypoglycemic episodes and their associated risks may meaningfully hinder daily activities. As a result, the patient burden can be substantial, and many individuals cannot drive, work or live alone. To date,

there are no approved pharmacotherapies to treat PBH. As the use of surgery to address metabolic conditions continues to rise, the incidence of PBH is expected to increase, reinforcing the need for safe and effective therapies.

About MBX Biosciences
MBX Biosciences is a biopharmaceutical company focused on the discovery and development of novel precision peptide therapies based on its proprietary PEP™ platform, for the treatment of endocrine and metabolic disorders. The Company is advancing a pipeline of novel candidates for endocrine and metabolic disorders with clinically validated targets, established endpoints for regulatory approval, significant unmet medical needs and large potential market opportunities. The Company's pipeline includes its lead product candidate MBX 2109, in Phase 2 development for the treatment of chronic hypoparathyroidism (HP); MBX 1416, in Phase 1 development for the treatment of post-bariatric hypoglycemia (PBH); and an obesity portfolio that includes MBX 4291, as well as multiple discovery and pre-clinical candidates in development for the treatment of obesity. The Company is based in Carmel, Indiana. To learn more, please visit the Company website at www.mbxbio.com and follow it on LinkedIn.

About MBX's Proprietary Precision Endocrine Peptide (PEP™) Platform
MBX was founded by global leaders with a transformative approach to peptide drug design and development. Leveraging this expertise, the Company designed its proprietary Precision Endocrine Peptide™ (PEP™) platform to overcome the key limitations of unmodified and modified peptide therapies and to improve clinical outcomes and simplify disease management for patients. PEPs are selectively engineered to have optimized pharmaceutical properties, including extended time-action profiles and consistent drug concentrations with low peak-to-trough concentration ratios, consistent exposure to target tissues, and less frequent dosing.

Forward-looking Statements
This press release contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, each as amended. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, but are not limited to, express or implied statements regarding: trial results from MBX's Phase 1 trial of MBX 1416, including topline results, statements relating to the ability of MBX 1416 to treat patients with PBH, expectations regarding future clinical evaluation of MBX 1416 in PBH, statements relating to MBX 1416 having a favorable safety profile, and statements relating to a potential meeting with the FDA and the intention to initiate a Phase 2 study in patients with PBH in the second half of 2025.

Forward-looking statements are based on management's current expectations and are subject to risks and uncertainties that could negatively affect MBX Biosciences' business, operating results, financial condition and stock value. Factors that could cause actual results to differ materially from those currently anticipated include: risks relating to the Company's research and development activities; uncertainties relating to preclinical and clinical development activities; the risk that preliminary results may not be indicative of later results and that early-stage trials may not be predictive of later-stage trials; the Company's dependence on third parties to conduct clinical trials; MBX Biosciences' ability to attract, integrate and retain key personnel; risks related to regulatory developments and approval processes of the U.S. Food and Drug Administration and comparable foreign regulatory authorities; as well as other risks described in "Risk Factors," in MBX Biosciences' Registration Statement on Form S-1 filed with the Securities and Exchange Commission (SEC), most recent Quarterly Report on Form 10-Q, as well as subsequent filings with the SEC. MBX Biosciences expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in its expectations or any changes in events, conditions or circumstances on which any such statement is based, except as required by law, and claims the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

MBX uses and intends to continue to use its Investor Relations website as a means of disclosing material nonpublic information and for complying with its disclosure obligations under Regulation FD. Accordingly, investors should monitor the Company's Investor Relations website, in addition to following the Company's press releases, SEC filings, public conference calls, presentations, and webcasts.

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