MBX Biosciences Doses First Participant in Phase 1 Trial of MBX 4291 for the Treatment of Obesity

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Preclinical data support the potential for improved weight loss and tolerability with once-monthly administration of MBX 4291

CARMEL, Ind., Sept. 04, 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 dosing of the first participant in its Phase 1 trial of MBX 4291, the Company's Precision Endocrine Peptide™ (PEP™) glucagon-like peptide-1 (GLP-1)/ glucose-dependent insulinotropic polypeptide (GIP) co-agonist prodrug candidate for the treatment of obesity.

"Initiation of our first clinical trial in obesity is a significant milestone for the Company and an important step in addressing this global public health issue," said Kent Hawryluk, President and Chief Executive Officer of MBX Biosciences. "MBX 4291 has demonstrated positive preclinical results and is designed to be a best-in-class weight loss prodrug, with the potential for convenient once-monthly administration, improved weight loss, and better gastrointestinal tolerability compared to currently available treatment options. We look forward to topline results anticipated in 2027."

The Phase 1 trial is a randomized, double-blind, placebo-controlled first-in-human study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of single and multiple ascending doses of MBX 4291 in adult participants with obesity. The Phase 1 trial will include:

Part A Single Ascending Dose (SAD): single ascending doses of MBX 4291 or matching placebo will be administered in 5 cohorts consisting of 8 participants each. Participants will be randomized on Study Day 1 to receive MBX 4291 or matching placebo in a 3:1 ratio. Participants in each cohort will be followed for 63 days after the single study intervention administration.

Part B Multiple Ascending Dose (MAD) (4 weeks): multiple ascending doses of MBX 4291 or matching placebo will be administered in 3 cohorts consisting of 8 participants each. Participants will be randomized on Study Day 1 to receive MBX 4291 or matching placebo in a 3:1 ratio. Participants in each cohort will receive a total of 4 study intervention administrations one week apart and will be followed for 71 days after the first study intervention administration.

Following completion of Parts A and B, the Company plans to evaluate multiple ascending doses of MBX 4291, or matching placebo, administered over 12 weeks in up to two cohorts consisting of 30 participants each in a 2:1 randomization ratio. Participants are expected to receive up to a total of 12 study intervention administrations one week or one week and one month apart with increasing doses of MBX 4291 and will be followed for 120 days after the first dose.

More information on the trial can be found at www.clinicaltrials.gov, identifier NCT07142707.

About MBX 4291
MBX 4291 is an investigational long-acting GLP-1/GIP receptor co-agonist prodrug candidate in development as a potential treatment for obesity. It was designed using the Company's novel, proprietary PEP™ platform as a long-acting dual agonist designed to address the unmet need with existing obesity therapies. MBX 4291 is designed to provide improved tolerability, increased adherence to treatment at maximum efficacious doses, and to achieve greater long-term weight loss and greater improvement in weight-related comorbidities.

In preclinical studies, the active component of MBX 4291 demonstrated a similar activity profile and body weight loss as tirzepatide, an approved weekly GLP-1/GIP co-agonist. Extended duration of action of the active component of MBX 4291 was observed in additional preclinical studies compared to tirzepatide, supporting the potential for once-monthly administration

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 canvuparatide (MBX 2109) for the treatment of chronic hypoparathyroidism (HP) in Phase 2 development; imapextide (MBX 1416) for the treatment of post-bariatric hypoglycemia (PBH) in Phase 2 development; and an obesity portfolio that includes MBX 4291 in Phase 1 development, as well as multiple discovery and pre-clinical obesity candidates. The Company is based in Carmel, Indiana. To learn more, please visit the Company website at https://mbxbio.com/ and follow it on LinkedIn.

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: MBX Biosciences' expectations regarding the Phase 1 trial of MBX 4291, including the timing of topline results; and the potential for MBX 4291 to be a best-in-class weight loss prodrug, with convenient once-monthly administration, improved weight loss, and better gastrointestinal tolerability compared to currently available treatment options.

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; MBX Biosciences' ability to execute on its strategy including obtaining the requisite regulatory approvals on the expected timeline, if at all; uncertainties relating to preclinical and clinical development activities; the Company's dependence on third parties to conduct clinical trials, manufacture its product candidates and develop and commercialize its product candidates, if approved; MBX Biosciences' ability to attract, integrate and retain key personnel; risks related to the Company's financial condition and need for substantial additional funds in order to complete development activities and commercialize a product candidate, if approved; risks related to regulatory developments and approval processes of the U.S. Food and Drug Administration and comparable foreign regulatory authorities; risks related to establishing and maintaining MBX Biosciences' intellectual property protections; and risks related to the competitive landscape for MBX Biosciences' product candidates; as well as other risks described in "Risk Factors," in MBX Biosciences' Annual

Report on Form 10-K for the year ended December 31, 2024 filed with the Securities and Exchange Commission (SEC), its Quarterly Report on Form 10-Q for the quarter ended June 30, 2025 filed with the SEC, 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 Biosciences 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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