MBX Biosciences Announces MBX 2109 Phase 1 Study Results Published in The Journal of Clinical Endocrinology and Metabolism

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Peer-reviewed publication features positive results from multiple ascending dose (MAD) portion of Phase 1 MBX 2109 study in healthy participants

CARMEL, Ind., Dec. 02, 2024 (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 the publication of a peer-reviewed article highlighting results from the Phase 1 study of MBX 2109, the Company's parathyroid hormone (PTH) peptide prodrug in development for the treatment of hypoparathyroidism (HP). The publication, titled "MBX 2109, a Once-Weekly Parathyroid Hormone Replacement Therapy Prodrug: Phase 1, First-in-Human, Randomized Trial", was published in *The Journal of Clinical Endocrinology and Metabolism (JCEM)* and can be accessed here.

"We are pleased to have published results from our Phase 1 MAD study of MBX 2109 in *JCEM*, a leading peer-reviewed journal of endocrine and metabolic research," said Kent Hawryluk, President and Chief Executive Officer of MBX Biosciences. "MBX 2109's long half-life and flat exposure profile demonstrated in the Phase 1 study may lead to a more consistent therapeutic effect and minimize symptoms from large fluctuations in calcium compared to PTH agonists with a shorter half-life. These results, combined with its safety profile to date and pharmacodynamic activity, support the continued development of MBX 2109 as a potential once-weekly PTH prodrug for the treatment of HP. We look forward to completing enrollment in our Phase 2 Avail™ trial of MBX 2109 in patients with HP in the first quarter of 2025 and reporting topline results in the third quarter of 2025."

The publication features results from the multiple ascending dose portion of the Phase 1 study of MBX 2109, a peptide prodrug yielding a biologically active PTH agonist. The Phase 1 study was a randomized, double-blind, placebo-controlled trial designed to evaluate safety, pharmacokinetics (PK), and pharmacodynamics (PD) of MBX 2109 in healthy adults. Forty participants were randomized 4:1 to receive four once-weekly subcutaneous doses of either placebo or MBX 2109 at 200, 400, 600, or 900 µg.

Key highlights from the publication:

- The observed half-lives of the prodrug (79-95 hours) and the active drug (184-213 hours) reflected the prodrug design and were supportive of once-weekly administration.
- Peak-to-trough exposures to the active drug with weekly dosing were relatively flat, with ratios ranging from 1.47 and 1.79 across dose levels.
- With weekly injections, dose-proportional increases in albumin-adjusted serum calcium and concomitant suppression of endogenous PTH(1-84) were observed, consistent with the expected PTH pharmacology in healthy participants.
- Repeat doses of MBX 2109 were generally well-tolerated at all doses tested.
- Most treatment emergent adverse events (TEAEs) were mild in severity. Injection-site reaction was the most common TEAE.
- No MBX 2109 dose-related serious or severe adverse events or deaths were reported.

About Hypoparathyroidism
HP is a rare endocrine disease caused by a deficiency of PTH released by the parathyroid glands that results in decreased calcium levels in the blood leading to hypocalcemia. Hypocalcemia can result in a variety of acute symptoms, such as muscle cramping or spasm, tingling, and neurological symptoms such as depression, confusion and cognitive impairment. More serious complications can occur, including seizures and cardiac arrhythmias. As a result, HP can interfere with daily activities, negatively impacting the quality of life for patients and we estimate that HP affects approximately 120,000 people in the United States and more than 250,000 in the United States and Europe. The most common cause for HP, in approximately 75% of cases, is the inadvertent removal or damage to the parathyroid glands during neck surgery. It can also be caused by certain autoimmune processes and genetic conditions. The current standard of care for HP does not address the PTH deficiency, which is the underlying cause of the disease. To avoid hypocalcemia and its symptoms due to PTH deficiency, the current standard of care consists primarily of high doses of oral calcium supplements and active vitamin D.

About MBX 2109
MBX 2109 is a parathyroid hormone peptide prodrug that is designed as a potential long-acting hormone replacement therapy for the treatment of HP. Leveraging the company's proprietary Precision Endocrine Peptide™ (PEP™) platform technology, MBX 2109 was designed to provide convenient, once-weekly administration and a continuous, infusion-like PTH exposure with lower daily peak-to-trough ratios than observed with daily PTH dosing regimens. MBX 2109 received orphan drug designation from the U.S. Food and Drug Administration for the treatment of HP.

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: MBX Biosciences’ expectations regarding the Phase 2 Avail™ trial of MBX 2109, including the timing of enrollment of patients and topline results; and statements relating to MBX 2109’s clinical profile, including the potential to be a once-weekly PTH prodrug for the treatment of HP.

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; 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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