MBX Biosciences Announces Once-Weekly Canvuparatide Achieved Primary Endpoint in Phase 2 Trial with 63% Responder Rate at 12 Weeks; 79% Responder Rate at 6 Months in Open-Label Extension

September 22, 2025

Statistically significant responder rate achieved at 12 weeks with zero contribution from rescue therapy (PRN) and further improvement sustained in open-label extension (OLE)

Positive findings in bone and kidney biomarkers

All patients completed the 12-week Avail™ trial and 94% entered the OLE

Once-weekly canvuparatide was generally well tolerated, with no treatment-related serious adverse events or discontinuations during the 12-week trial

Preparation underway to initiate Phase 3 trial in 2026

Company to host conference call at 8:00 am ET today

CARMEL, Ind., Sept. 22, 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 once-weekly canvuparatide achieved the primary endpoint with statistical significance at Week 12 in its Phase 2 Avail™ trial, and demonstrated positive 6-month results from the OLE, in adult patients with chronic hypoparathyroidism (HP). All patients (n=64) completed the 12-week study, and 94% of patients elected to enroll in the OLE.

In the 12-week randomized portion of the trial, 63% of canvuparatide-treated patients met the prespecified primary composite endpoint with zero contribution from PRN rescue therapy. In the OLE, 79% of patients receiving once-weekly canvuparatide achieved responder status at 6 months. Responders were defined as patients who maintained serum calcium levels in the normal range (8.2–10.6 mg/dL) and independence from conventional therapy (active vitamin D and >600 mg/day of calcium supplements).

Based on these positive results, MBX is preparing to initiate a Phase 3 clinical trial of once-weekly canvuparatide in 2026.

“The results from the Avail trial are encouraging. A once-weekly therapy could simplify administration and help address important unmet medical needs of patients with hypoparathyroidism,” said Mishaela Rubin, MD, MS, Professor of Medicine at Columbia University Vagelos College of Physicians and Surgeons and an investigator in the Avail clinical trial. “Hypoparathyroidism poses a substantial burden to patients, who often face complex treatment regimens and unpredictable swings in calcium levels that can lead to serious complications. The 12-week and 6-month data provide promising early evidence that this investigational therapy may offer a potential option for long-term management, pending further study.”

“We are very pleased with the clinically meaningful and statistically significant topline results from our once-weekly canvuparatide Phase 2 trial. These data reinforce our conviction that canvuparatide could become a potential best-in-class treatment for hypoparathyroidism and demonstrate the value of our novel Precision Endocrine Peptide platform technology,” said Kent Hawryluk, President and Chief Executive Officer of MBX Biosciences. “We believe the totality of the data support a once-weekly product profile with continuous infusion-like PTH exposure. These 12-week and 6-month results represent the potential for a meaningful improvement over current treatment options for HP patients and provide a strong foundation for further development. We look forward to sharing additional once-weekly canvuparatide clinical data at an upcoming medical meeting as we prepare for initiation of our Phase 3 trial.”

Phase 2 Avail Topline Results

12-week and 6-month Responder Rates:

- **At 12 Weeks:** The primary composite endpoint (maintaining albumin-adjusted serum calcium levels in the normal range (8.2–10.6 mg/dL) and independence from conventional therapy (active vitamin D and >600 mg/day of calcium supplements)) was achieved in 63% of canvuparatide-treated patients (30/48) compared with 31% in placebo-treated patients (5/16) (p=0.042) at Week 12
- **At 6 Months:** In the OLE, 79% of patients (44/56 evaluable) who received treatment achieved responder status at 6 months, including patients initially randomized to placebo

Select Secondary and Exploratory Endpoints

- **Pharmacokinetics:** Pharmacokinetic (PK) findings were consistent with the Phase 1 results, supporting a once-weekly dosing schedule
- **Bone Activity:** Bone turnover and formation markers (BSAP, CTx and P1NP) increased over 12 weeks compared to placebo, consistent with enhanced bone remodeling
- **Kidney Activity:** In patients with elevated urine calcium at screening that normalized at Week 12, mean urine calcium was reduced by 48% in patients treated with once-weekly canvuparatide compared with 33% on placebo

Safety Summary

- All doses of canvuparatide were generally well-tolerated with no discontinuations related to canvuparatide
- Most treatment emergent adverse events were categorized as mild or moderate

- No SAEs related to canvuparatide were reported
- Injection site reactions (ISRs): 19% in the pooled treatment group versus 13% in placebo
- No deaths were reported

“We are thrilled with these trial results,” said Patty Keating, Executive Director of the HypoPARAthyroidism Association. “For so many in our community, life with hypoparathyroidism means living with constant symptoms and the limitations of daily supplements. A once-weekly treatment option that maintains stable calcium control while reducing the day-to-day burden would be a major step forward.”

The Company will present additional data from the Phase 2 trial and OLE at an upcoming major medical meeting.

Conference Call

The Company will host a conference call and webcast today at 8 am ET to discuss the results from the Avail™ Phase 2 trial. Those who would like to participate may access the live webcast here or dial 1-877-407-0779 (US) or 1-201-389-0914 (international). The live and archived webcast of the call and slide presentation will be available in the Investors section of the Company’s website at https://investors.mbxbio.com/news-events/events.

About the Avail ™Trial

The Avail™ Phase 2 trial (NCT06465108) is a multicenter, randomized, double-blind, placebo-controlled study to evaluate the safety, pharmacokinetics, and efficacy of canvuparatide in patients with hypoparathyroidism. The study randomized 64 patients into four treatment arms: canvuparatide 400ug, 600ug, 800ug administered by subcutaneous once-weekly injection, and a placebo arm. The 12-week treatment period includes a four-week fixed dose period followed by an 8-week titration period during which canvuparatide dosing may be adjusted every two weeks in 200ug increments. The primary endpoint for efficacy is normalization of albumin adjusted serum calcium while independent from active vitamin D and calcium supplements (<600 mg/day) at Week 12. Secondary endpoints include safety and tolerability; pharmacokinetic profile; urine calcium, serum phosphorus, 1,25 dihydroxyvitamin D, and bone biomarkers. Following the 12-week treatment period, 60 patients (94%) elected to receive once-weekly canvuparatide in the two-year open-label extension study.

About Hypoparathyroidism (HP)
HP is a rare endocrine disease caused by a deficiency of parathyroid hormone (PTH) released by the parathyroid glands that results in decreased calcium levels in the blood, leading to hypocalcemia. Hypocalcemia can cause a variety of 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 arrhythmia. HP can interfere with daily activities, negatively impacting the quality of life for patients. We estimate that HP affects more than 250,000 individuals in the U.S. and Europe. The current standard of care for HP does not address the underlying cause of the disease, PTH deficiency, and consists primarily of high doses of oral calcium and active vitamin D supplements.

About Canvuparatide (MBX 2109)
Canvuparatide 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, canvuparatide 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. Canvuparatide 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 canvuparatide (MBX 2109) for the treatment of chronic hypoparathyroidism (HP) in Phase 2 development; imapextide (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: trial results from MBX’s Phase 2 trial of canvuparatide, including topline results; statements related to the potential for canvuparatide to be a once-weekly PTH replacement therapy; expectations regarding future clinical evaluation of canvuparatide; and statements relating to canvuparatide having a favorable safety profile.

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 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 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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