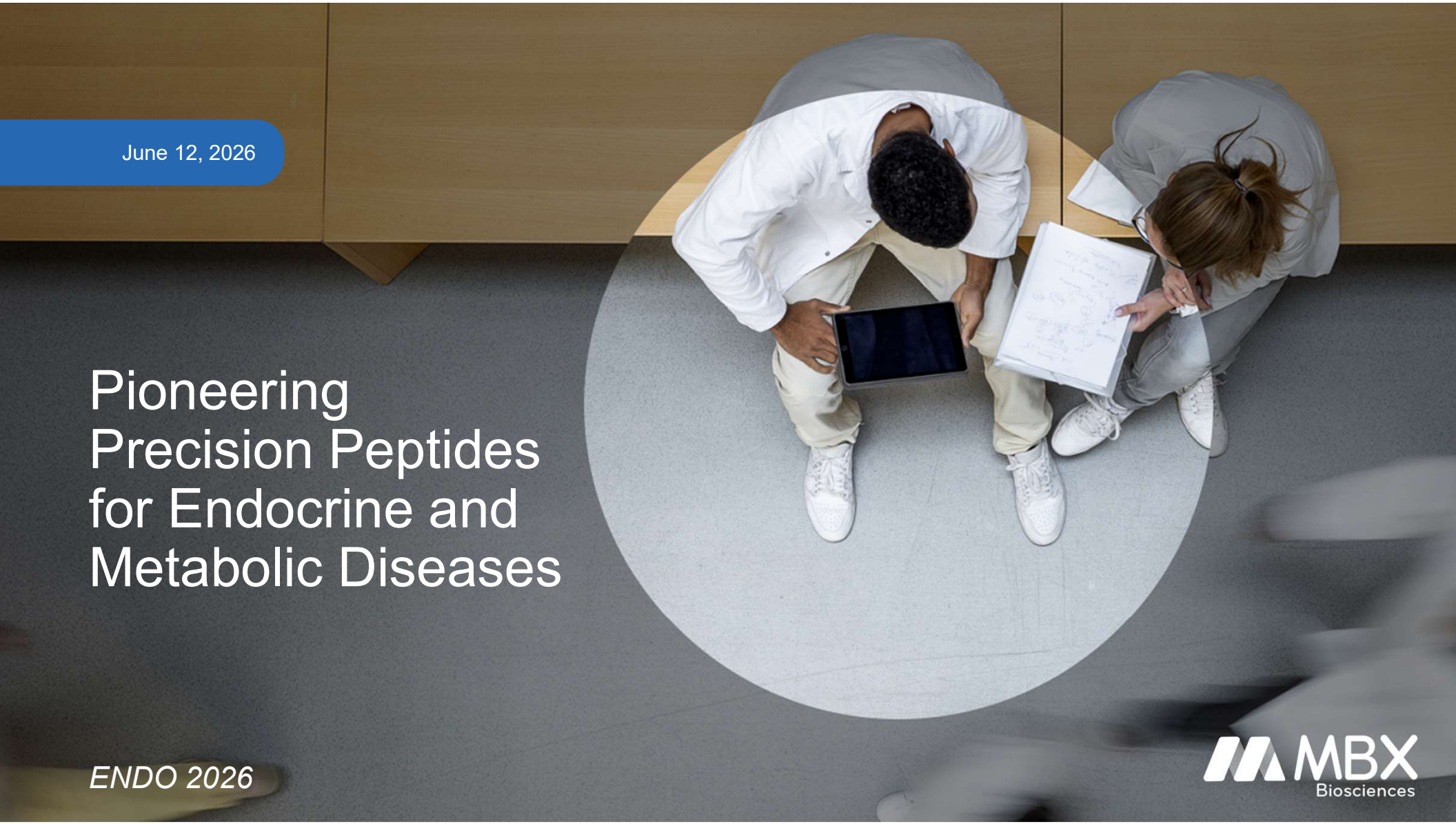
June 12, 2026

# Pioneering Precision Peptides for Endocrine and Metabolic Diseases



*ENDO 2026*

MBX Biosciences

# Introduction

**Kent Hawryluk**

MBX President & CEO

# Disclaimer

This presentation includes forward looking statements. All statements other than statements of historical facts contained in this presentation, including statements regarding our product candidates, preclinical study and/or clinical trial timelines, including projected data announcements, future results of operations and financial position, strategy and plans, industry environment, potential growth opportunities, and our expectations for future operations, are forward looking statements The words " believe," " may," "will," " estimate," " continue," " anticipate," " design," " " expect," " could," " plan," " potential," " predict," " seek," " should," "would," or the negative version of these words and similar expressions are intended to identify forward looking statements.

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# Our Mission

Transforming the Lives of People Impacted by Endocrine and Metabolic Diseases through Precision Peptides

# MBX ENDO 2026 Canvuparatide 12-week Avail™ & OLE Update

1

**Welcome/Introductions**

Kent Hawryluk, MBX
President & CEO

2

**MBX Canvuparatide Overview**

Richard DiMarchi, Ph.D.,
Distinguished Professor of Chemistry at Indiana University, MBX Co-founder

3

**Market Landscape & Opportunity**

Michael T. Collins, M.D.
Endocrinologist
Special Volunteer and Senior Clinical Advisor, National Institutes of Health

4

**Canvuparatide 1-year OLE Results**

Sam Azoulay, M.D.,
MBX Chief Medical Officer

5

**Conclusion/Q&A**

Kent Hawryluk

# MBX Proprietary PEP™ Platform

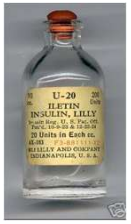
**Richard DiMarchi, PhD**

MBX Scientific Co-Founder

Distinguished Professor of Chemistry and Gill Chair in Biomolecular Sciences at Indiana University

# MBX: Building on a Century of Progress in Peptide-Based Drugs

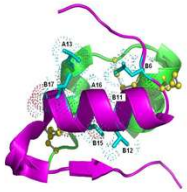
**1923** — Eli Lilly produces the first insulin




**1982** — **Commercial Synthesis**: first rDNA hormone introduced[1]


**1985** — First cancer-focused peptide therapeutics approved


**1996** — **Commercial Optimization**: first rDNA chemically optimized therapeutic (Humalog)[1]



**2001** — First rDNA-derived human parathyroid hormone for treatment of osteoporosis[1]

FORTEO®
teriparatide injection
20-mcg daily dose in a 2.24-mL prefilled delivery device
helps build new bone
A Lilly Medicine

**2014** — First once-weekly GLP-1 agonist[1]


**2019** — First oral GLP-1 treatment for type 2 diabetes


**The Next Frontier**

[1]Contributions made by MBX scientific founder, Dr. Richard DiMarchi

rDNA, recombinant DNA.



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# Clinically Validated Precision Endocrine Peptide (PEP™) Platform

## Created by MBX and Scientific Co-Founder Richard DiMarchi, PhD

### INNOVATIVE PEPTIDE DESIGN

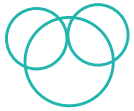
With a goal to optimize:

- Multiple mechanisms of action within a single peptide
- Increased potency
- Enhanced physical properties, including stability and solubility

### PROGRAMMABLE PRODRUG

Designed to provide:

- Gradual, controlled release of active drug
- Slow rise to maximum exposure
- Flattened exposure



### FATTY ACYLATION

With a goal to optimize:

- Longer time action
- More convenient dosing

Combining PEP technologies to deliver differentiated and best-in-class medicines for patients



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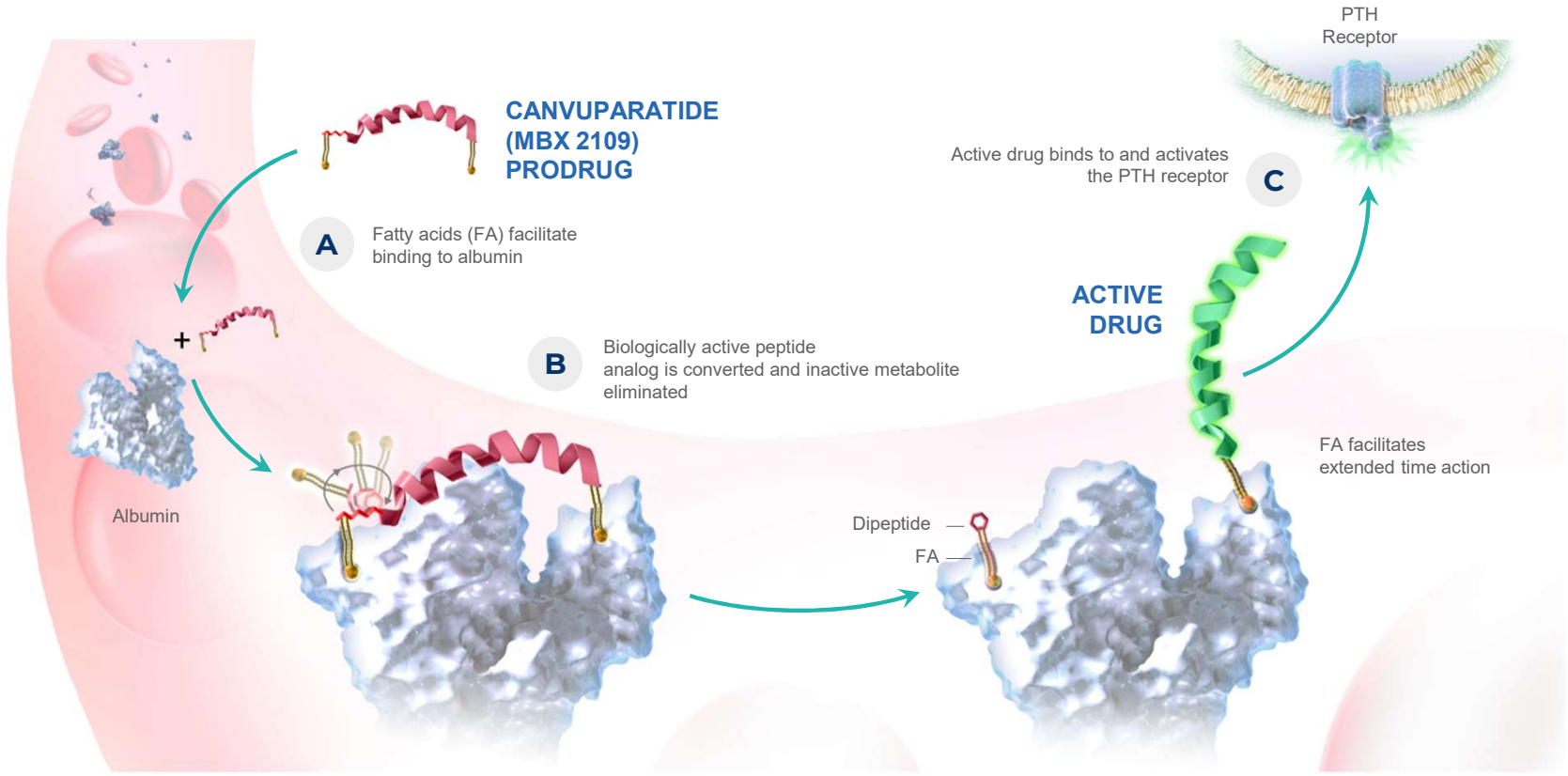
# Canvuparatide: Prodrug Chemically Converts to Active Drug at a Precisely Controlled Rate Under Physiologic Conditions




PTH, parathyroid hormone.

# Hypoparathyroidism Market Landscape

**Michael T. Collins, M.D.**

Endocrinologist

Special Volunteer and Senior Clinical Advisor at the National Institutes of Health



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# Hypoparathyroidism (HP) is a Serious Chronic Condition

*Hypoparathyroidism occurs when the **parathyroid glands produce too little parathyroid hormone (PTH),** resulting in a spectrum of findings*

| | | | |
|---|---|---|---|
| Symptoms and Presentation | **Hypocalcemia,** cramping, paresthesia, tetany, seizures, arrhythmias, kidney disease, neurocognitive deficits ("brain fog"), depression, increase in major adverse cardiac events | | |
| Onset and Etiology | **Typical Onset**<br>40-65 years old | **Main cause**<br>Post-surgical complications of neck procedures (75%)[1] | **Other causes**<br>Genetic disorders, autoimmune disease, radiation therapy, idiopathic |
| | Chronic HP defined as symptoms persisting ≥12 months | | |
| Prognosis | **Impaired QoL**<br>Due to persistence of mild symptoms (e.g., hypocalcemia, brain fog, fatigue) | **Impaired Renal Function**<br>Due to hypercalciuria, nephrocalcinosis, nephrolithiasis | |

[1]Powers. J Bone Miner Res. 2013 found 73% post-surgical and Clarke. J Clin Endocrinol Metab. 2016 found 78%. Sources: Abate. Front Endocrinol (Lausanne). 2017; Bilezikian. JCEM. 2020; Brandi. JCEM. 2016; Cipriani. J Endocr. Soc. 2021; Clarke. J Clin Endocrinol Metab. 2016; Khan. J Bone Miner Res. 2022; Mannstadt. Nat Rev Dis Primers. 2017; Powers. J Bone Miner Res. 2013; Ahn SH et al, Long-Term Morbidity after Postoperative Hypoparathyroidism in Thyroid Cancer Patients: A Nationwide Population-Based Cohort Study; Thyroid 2026;36(3):320-329; UpToDate; Advocacy Groups; Clearview Analysis.



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# Chronic HP Affects Thousands of Patients Worldwide

**Prevalence** + **Annual Incidence**

>250K in US and EU[1]

>7K in US and EU[2,3]

Majority (~75%) of patients are **post-surgical**

Majority post-surgical patients **diagnosed within months** of surgery

**Large population with increased healthcare utilization in need of effective treatments[4]**

Source: [1]Mannstadt et al, Nat Rev Dis Primers, 2017; Powers et al, *JBMR.,* 2013; Vadiveloo et al, *JBMR* 2017; Cianferotti et al, *Calcif Tissue Int,* 2018; Swartling et al, *J Clin Endocrinol Metab,* 2022; Underbjerg et al, *JBMR.* 2013; Soibelman et al, Clin Otolaryngol, 2025; ClearView Analysis. [2]Powers et al, JBMR, 2013. [3]Internal estimates [4]Chen K, Krasner A, Li S, et al. Clinical burden and healthcare resource utilization among patients with chronic hypoparathyroidism, a retrospective cohort study. Journal of Medical Economics. 2019;22(11):1145-1153. PMID: 31124721



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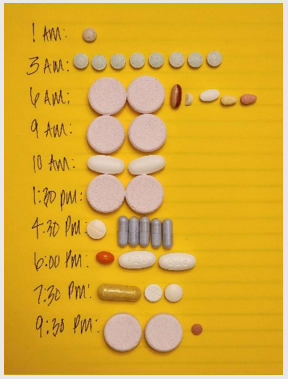
# Patients with Chronic HP have a Significant Disease Burden

**Symptoms Can Be Debilitating**





**Taking Daily Supplements Is Highly Disruptive**




*From Chronic HP patient*

**Pill Burden**
(conventional therapy)

- 10-30+ pills a day
- Every few hours
- Missed dose anxiety

***"If I go without my meds, I will be dead in days. If I skip/miss calcium, I will be in the ED in 12 hours."*** *- Chronic HP Patient*

***"I no longer have the luxury of sleeping through the night."*** *– Chronic HP Patient*

**Supplements Do Not Restore Physiologic Stability**

Treatment frequently causes hypercalciuria leading to renal calcification nephrocalcinosis, nephrolithiasis and chronic kidney disease



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# Yorvipath® Uptake Validates Need and Acceptance of Injectable PTH Replacement Therapy; But Significant Gaps Remain

## Daily Injection Fatigue

Daily injections lead to injection fatigue and the risk of not staying on therapy

## Anxiety About Missing Daily Dose

Patients worry about disruptions leading to missed injections

## Continued Symptoms

Many patients continue to experience symptoms while on treatment

Source: MBX market research May 2026

# Canvuparatide Demonstrated Positive Results in Phase 2
# Phase 3 Initiating in Q3'26

## Phase 2

Avail

Demonstrated **compelling efficacy** across comorbidities related to PTH deficiency

Confirmed **tolerability** profile

Determined **starting dose** for Ph3 study

## Phase 3

Kickoff Q3'26

Clear registrational path with endpoints that matter to **physicians** and **payers**

**Normalization** of serum calcium, and **independence** from active vitamin D and therapeutic doses of calcium

Normalization of **urine calcium**

Patient reported outcomes

Source: Canvuparatide AVAIL Ph2 study results



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# Once-Weekly Canvuparatide has the Potential to be the New Standard of Care for Patients with Chronic HP

**Canvuparatide Potential**
(to be proven in Ph3 study)

- **First once-weekly** PTH replacement therapy
- **Restore** normal serum calcium and phosphate
- **Protect** kidneys from long-term damage
- **Restore** bone turnover
- **Free** patients from daily disease management

***In market research…***

**HCPs**

PTH-***Naïve*** Patients

HCPs would make canvuparatide the **preferred** choice

PTH-***Treated*** Patients

HCPs would **switch** large **majority** over time

**Patients**

**Most patients** would choose once-weekly canvuparatide

**If week-over-week consistency** is born out: eliminate the **rollercoaster** of crashes and **debilitating** symptoms

Source: MBX market research May 2026



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# In Summary….

1. Chronic HP is a damaging disease affecting **>250K** patients across US and EU
2. Yorvipath® uptake **validates** need/acceptance of PTH replacement; **significant gaps** remain
3. **Once-weekly** canvuparatide has the potential to set a **new standard** for treating chronic HP
4. The **majority** of HCPs and patients would **choose once-weekly first**



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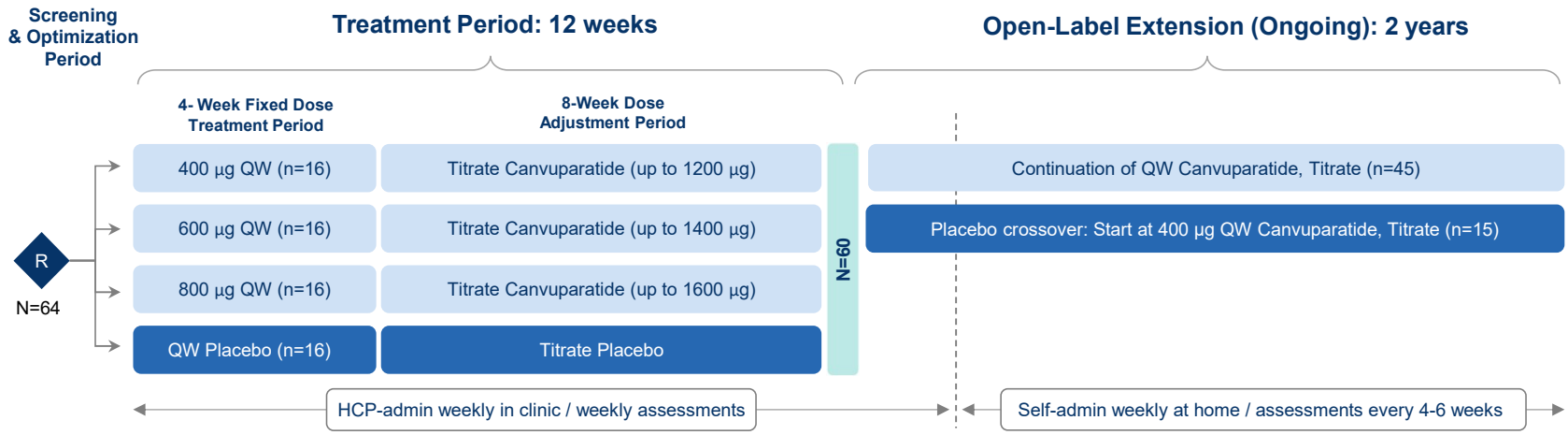
# Canvuparatide One-Year OLE Results

**Sam Azoulay, M.D.**

MBX Chief Medical Officer

# Phase 2 and OLE Study: Trial Design and Endpoints

## 12-Week Trial and 2-Year Open-Label Extension Study Design




### Phase 2 Key Endpoints

**Primary Composite Endpoint (Week 12)**

Proportion of patients (% responders) meeting all three criteria:

- Normal albumin-adjusted serum calcium (8.2 mg/dL to 10.6 mg/dL)
- Independence from active vitamin D supplements
- Oral calcium supplements (≤600 mg/day)

### OLE Key Endpoints

**Primary Endpoints**

- Safety and tolerability

**Select Secondary and Exploratory Endpoints**

- Responders at one year
- Responders for each individual component of composite criteria
- 24h urine calcium excretion, bone biomarkers, bone mineral density over time
- Immunogenicity (ADA)

ADA, anti-drug antibodies; OLE, open-label extension; QW, once weekly.
ClinicalTrials.gov Identifier: NCT06465108, NCT06531941



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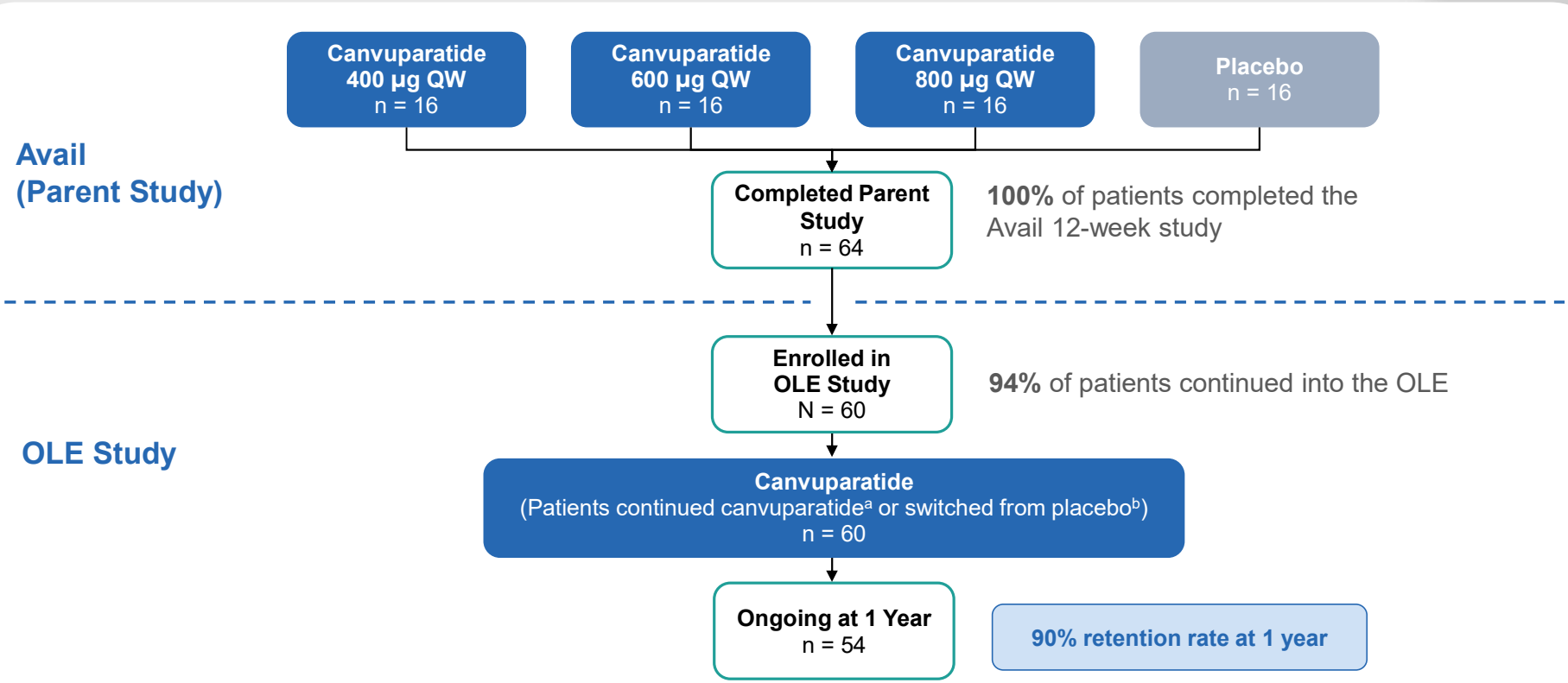
# Baseline Characteristics: Representative of HP Population and Well Balanced

| Characteristics | Canvuparatide (n = 48) | Placebo (n = 16) |
|---|---|---|
| Age, years, median (range) | 49.0 (23–72) | 44.5 (19–63) |
| Female, n (%) | 41 (85.4) | 15 (93.8) |
| Race, n (%) | | |
| White | 43 (89.6) | 13 (81.3) |
| Black or African American | 4 (8.3) | 2 (12.5) |
| Other | 1 (2.1) | 1 (6.3) |
| Hispanic or Latino, n (%) | 29 (60.4) | 9 (56.3) |
| BMI, kg/m$^2$, mean (SD) | 31.3 (6.3) | 30.2 (5.4) |
| Duration of HP, years, mean (SD) | 10.5 (9.0) | 8.9 (4.8) |

| Characteristics | Canvuparatide (n = 48) | Placebo (n = 16) |
|---|---|---|
| Etiology of HP, n (%) | | |
| Postsurgical chronic | 43 (89.6) | 14 (87.5) |
| Nonsurgical[a] | 5 (10.4) | 2 (12.5) |
| Calcium dose, mg/day, mean (SD) | 3208.0 (2872.3) | 2455.3 (918.1) |
| Vitamin D dose, µg/day, mean (SD) | 0.94 (0.52) | 0.84 (0.39) |
| Serum PTH, ng/L, mean (SD) | 10.2 (5.7) | 12.1 (12.6) |
| Serum AdjCa, mg/dL, mean (SD) | 9.3 (0.7) | 9.0 (1.0)[b] |
| Serum phosphorus, mg/dL, mean (SD) | 4.6 (0.8) | 4.6 (0.8) |
| Urine calcium, ≥ 250 mg/day, n (%) | 22 (45.8) | 7 (43.8) |

AdjCa, albumin-adjusted calcium; BMI, body mass index; HP, hypoparathyroidism; PTH, parathyroid hormone.
[a]Nonsurgical etiologies included idiopathic (canvuparatide, 6.3%; placebo, 12.5%), autoimmune (canvuparatide, 2.1%; placebo, 0%), and genetic (canvuparatide, 2.1%; placebo, 0%); [b]n = 14.

# Patient Disposition




[a]Patients randomized to canvuparatide in the parent study continued on the last dose they received in the parent study if they were able to be withdrawn from active vitamin D and calcium; if not, their dose was adjusted in accordance with the titration algorithm. [b]Patients randomized to placebo in the parent study were switched to canvuparatide 400 µg QW in the OLE, with dose adjustments made to maintain serum calcium 8.2–10.6 mg/dL following the titration algorithm.

# Primary Composite Endpoint and Components at 1 Year (OLE)

| Parameter, n (%) | 12-Week Study | 1 Year (OLE) |
|---|---|---|
| | Canvuparatide (n = 48) | Canvuparatide[1] (n = 54) |
| Proportion of Patients Meeting Response Criteria (Responders) | 30 (63%)[2,3] | 31 (57%)[3] (CI: 44-71%) |
| Proportion of patients meeting each component of responder criteria, n (%) | | |
| Independence from active vitamin D | 47 (98%) | 46 (85%) |
| Independence from oral calcium (≤600 mg/day) | 36 (75%) | 39 (72%) |
| Serum AdjCa within normal range (8.2−10.6 mg/dL) | 39 (81%) | 41 (75%) |

1. The canvuparatide cohort at 1 year includes patients initially randomized to canvuparatide (n = 39) or placebo (n = 15) for 12 weeks in the parent study.
2. P < .05 vs placebo
3. Zero contribution from rescue therapy (PRN) in the last week of the treatment period



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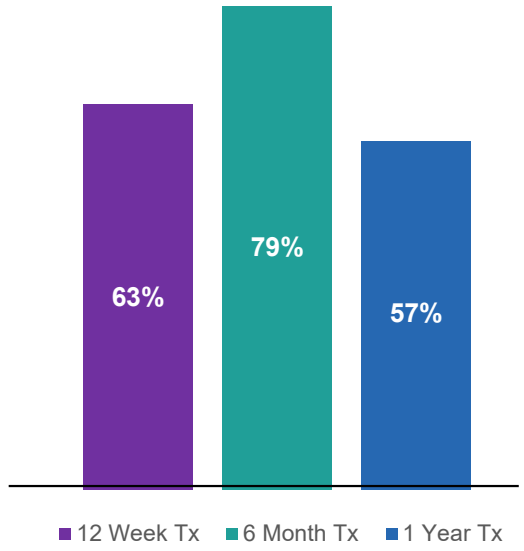
# Once-Weekly Canvuparatide Demonstrated Competitive Responder Rates in the Phase 2 Avail Trial and OLE

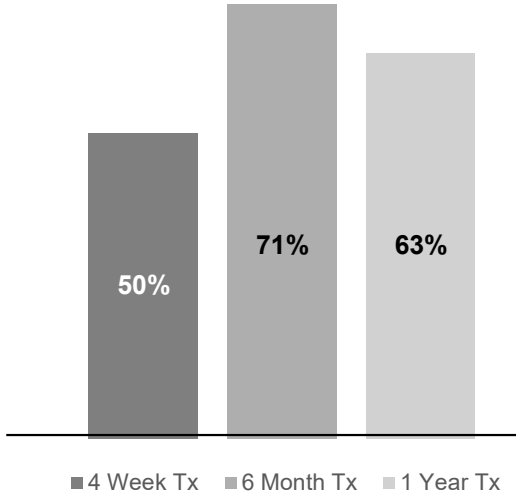
1/week

## Once-Weekly Canvuparatide Phase 2 Responder Rates



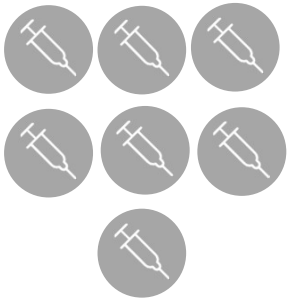

Achieved primary endpoint at Week 12

## Once-Daily Yorvipath® Phase 2 Responder Rates[1, 2]




Did **not** achieve primary at Week 4

7/week



Tx, treatment; Data sourced from (1)"PaTH Forward: A Randomized, Double-Blind, Placebo-Controlled Phase 2 Trial of TransCon PTH in Adult Hypoparathyroidism", https://pmc.ncbi.nlm.nih.gov/articles/PMC8684498/ and (2) Center for Drug Evaluation and Research, NDA/BLA Multi-disciplinary Review and Evaluation NDA 216490, Yorvipath (Palopegteriparatide), p73. Note: These data are derived from different clinical trials at different points in time, with differences in trial design, including endpoints, and patient populations. As a result, cross-trial comparisons cannot be made, it is only provided for illustrative purposes, and no head-to-head clinical trials have been conducted.



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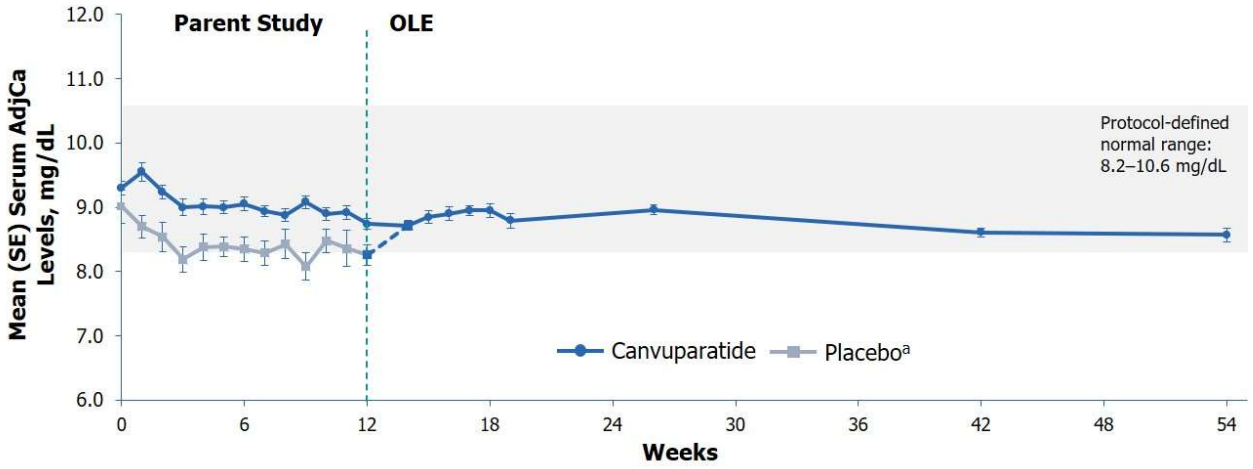
# Pharmacokinetics and Serum Calcium Profile Continue to Support Once-Weekly Dosing

## Phase 2 Pharmacokinetics (Drug Exposure)

PK in chronic HP patients demonstrated consistent concentration of canvuparatide active drug with a $T_{max}$ of 2-3 days, minimal fluctuation and a **peak-to-trough ratio of ~1.3 over a week**

## Phase 2 Pharmacodynamics (Serum AdjCa Over Time*)




Mean peak-to-trough serum calcium difference was 0.59 [0.12] mg/dL, consistent with stable calcium control

*As assessed at trough concentration.
[a]Starting after the baseline of the OLE (at week 12 overall), patients in the placebo group were switched to canvuparatide.



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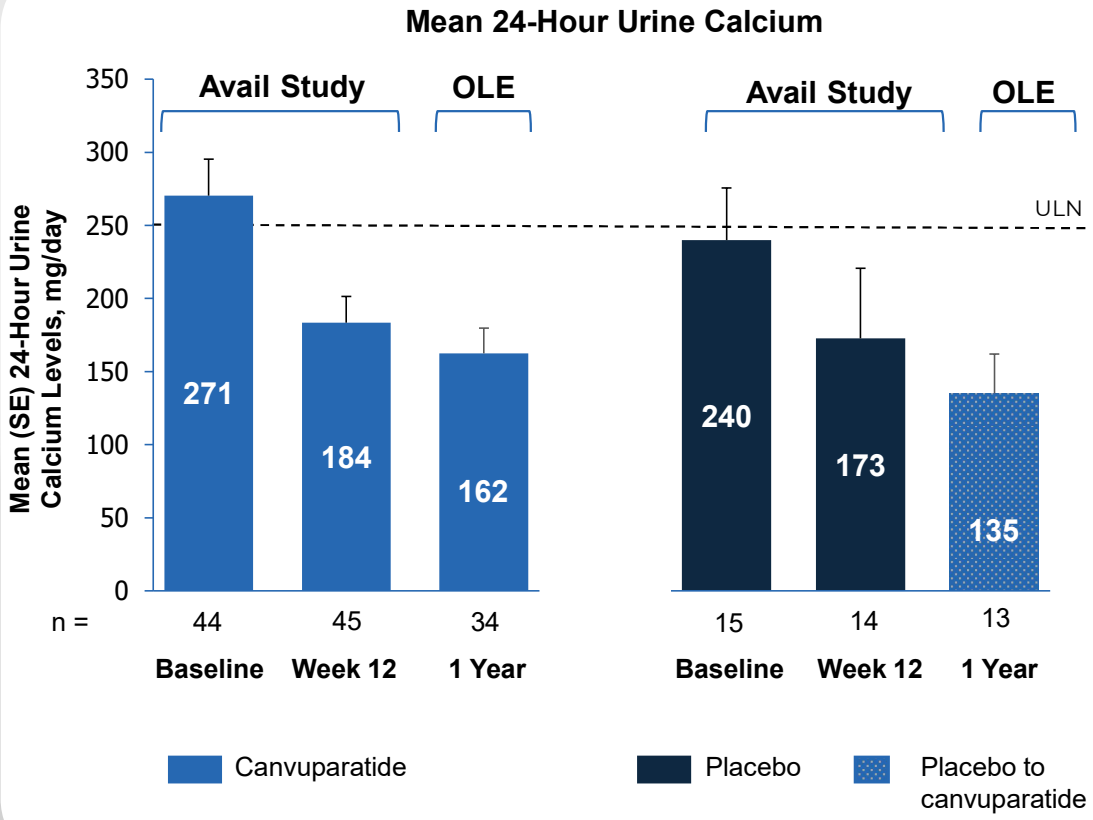
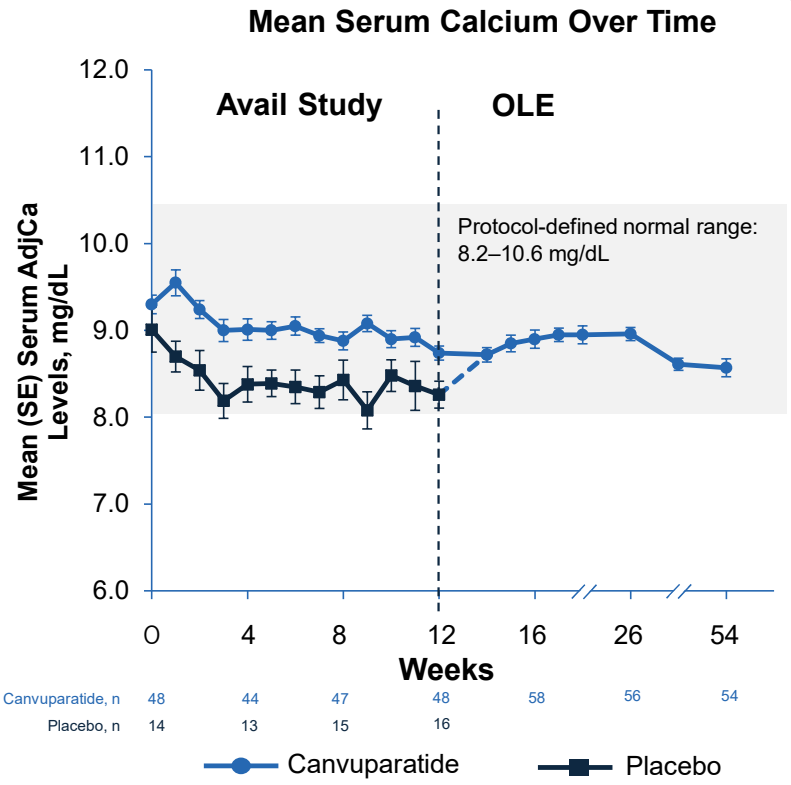
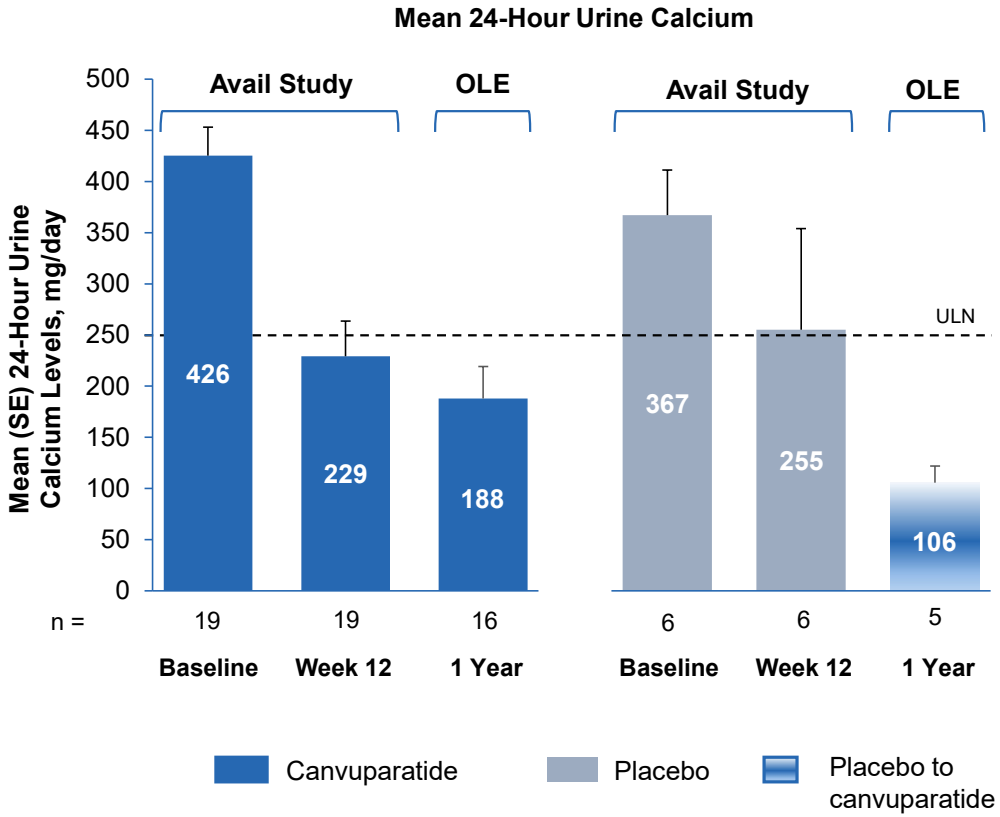
# Once-Weekly Canvuparatide Reduced 24h Urine Calcium While Maintaining Stable Serum Calcium Through 1 Year




N = patient data available at 1 year.

# In Patients With Elevated Baseline Urine Calcium, Urine Calcium Continued to Decrease Through 1 Year




N = patient data available at 1 year.

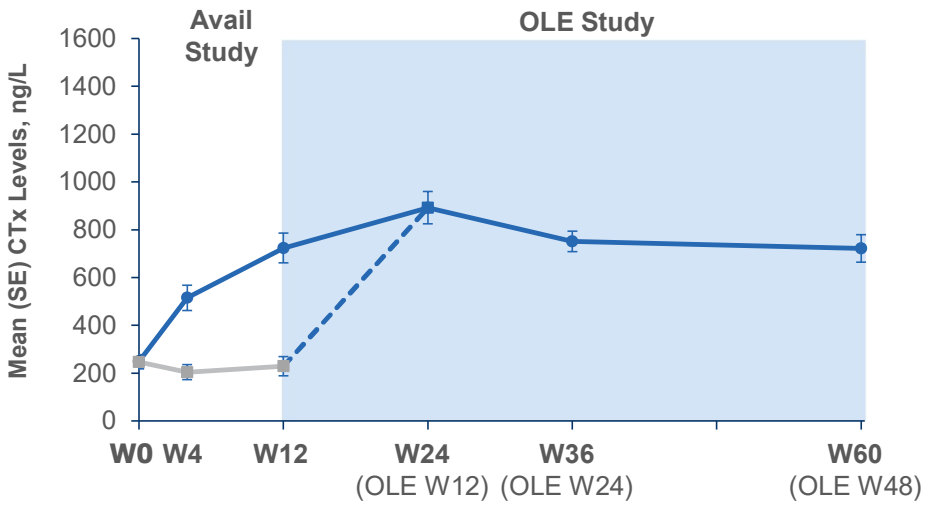
# Once-Weekly Canvuparatide Demonstrated Expected Effects of PTH in the Kidney

| Parameter, Mean (SE) | Change from Baseline at 1 Year (OLE)[a] |
|---|---|
| | Canvuparatide (n = 54) |
| Phosphate, mg/dL | –0.4 (0.1) |
| Calcium-phosphate product, $mg^2/dL^2$ | –5.9 (0.8)[b] |
| 1,25-Dihydroxyvitamin D3, ng/L | 3.5 (3.6) |
| Estimated glomerular filtration rate, $mL/min/1.73m^2$ | 5.3 (2.1) |

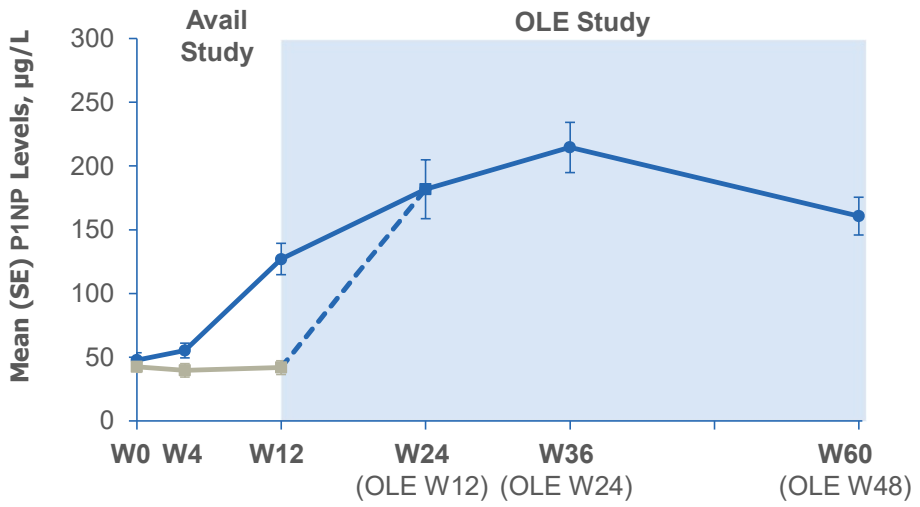
eGFR, estimated glomerular filtration rate.
[a]1 year includes 12 weeks of the parent study and corresponds to week 48 of the OLE study..
[b]n = 53.

# Canvuparatide Restored Bone Metabolism

## C-Terminal Telopeptide of Type 1 Collagen (CTx)



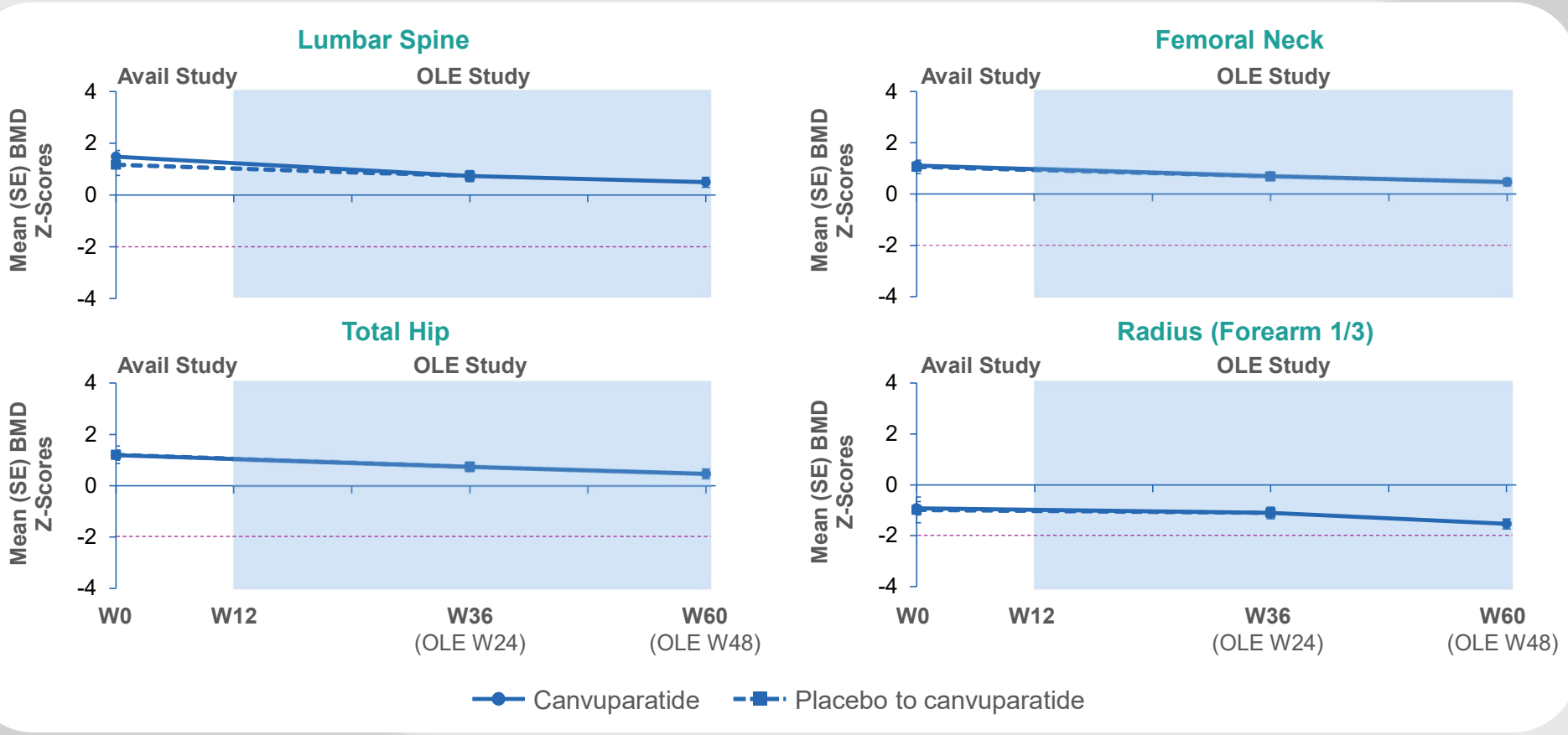

## Procollagen Type 1 N-Terminal Propeptide (P1NP)




Canvuparatide | Placebo | Placebo to canvuparatide[a]

Reference ranges are: CTx (female high, 1008 ng/L; male high, 854 ng/L), and P1NP (female, 14.3–97.0 µg/mL; male, 13.3–79.7 U/L).
[a]During the OLE (starting after Week 12), patients in the placebo group received canvuparatide.

# BMD Changes Were Consistent with Restored Bone Metabolism and Remained Within the Normal Range






Z-score normal range: ≥ -2.0 (up to 2 standard deviations below the mean)
BMD, bone mineral density; W, week.

# Immunogenicity to Canvuparatide Was Minimal

| Patients With Treatment-Induced ADAs, n (%) | Canvuparatide | |
|---|---|---|
| | ADA to Canvuparatide | ADA to Active Peptide |
| Week 12 (Avail parent trial) | 0 | 0 |
| Week 60 (OLE week 48) | 1/59 (1.7)* | 0 |

ADA: anti-drug antibodies
* Low titer.

# OLE: Treatment Emergent Adverse Events and Adverse Events of Special Interest

| TEAE, n (%) | Canvuparatide (n = 60) |
|---|---|
| TEAE | 48 (80.0) |
| Mild | 22 (36.7) |
| Moderate | 23 (38.3) |
| Severe | 3 (5.0) |
| Treatment-related TEAE | 23 (38.3) |
| SAE | 5 (8.3) |
| Treatment-related SAEs | 0 |
| TEAE leading to discontinuation | 3 (5.0) |
| Deaths | 0 |
| **AESI (>5% patients), n (%)** | **Canvuparatide (n = 60)** |
| Hypocalcemia[a] | 12 (20.0) |
| Hypercalcemia[b] | 7 (11.7) |
| All injection site reactions | 6 (10.0) |

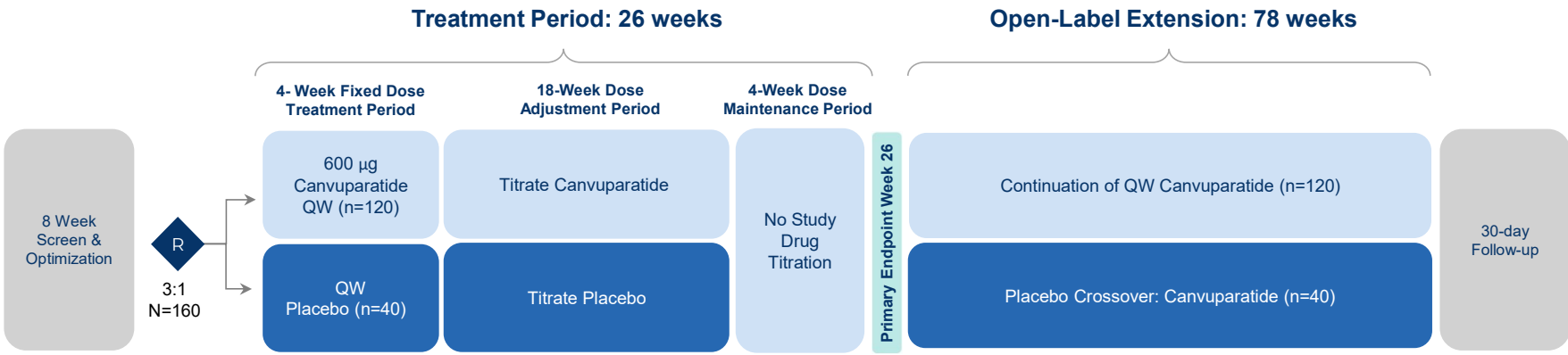
SAE, serious treatment-emergent adverse events; TEAE, treatment-emergent adverse event.
[a]Symptomatic of greater intensity or duration then expected
[b]Symptomatic or serum calcium level >11.0 mg/dL

# One-Year Data Demonstrate Sustained Benefit of Once-Weekly Canvuparatide as a Potential PTH Replacement Therapy in Chronic HP

- Results consistent with restoration of systemic PTH activity through serum calcium normalization, reduction of urine calcium excretion, restoration of bone metabolism and increase of eGFR
- Responder rate of 57% at one year in OLE comparable to Phase 2 Avail™ rate of 63% at 12 weeks
- High retention rate with 90% of patients entering the OLE remaining in the study at one year
- Generally well tolerated with no new safety signals during the OLE
- Pharmacokinetics support once-weekly dosing, with low peak-to-trough ratio and stable exposure
- Phase 3 pivotal trial remains on track to initiate in Q3 2026

# Phase 3 Trial Design and Endpoints for Once-Weekly Canvuparatide

**26-Week Double-blind Placebo-Controlled Trial followed by a 78-Week Open-Label Extension**




## Phase 3 Trial Endpoints

**Primary Composite Endpoint (Week 26)**

Proportion of patients (% responders) meeting all four criteria:

- Normal albumin-adjusted serum calcium (8.3 mg/dL to 10.6 mg/dL)
- Independence from active vitamin D
- Calcium supplements (≤600 mg/day)
- Stable with no increase in canvuparatide dose during last 4 weeks

**Key Secondary Endpoints**

- Proportion of patients (% responders) with elevated 24-hour urine calcium who normalize urine calcium excretion while maintaining normal albumin-adjusted serum calcium
- Patient-reported outcomes (PROs)

QW: once weekly



MBX Biosciences

# Conclusion

**Kent Hawryluk**

MBX President & CEO

# Once-Weekly Canvuparatide: Paving the Way for a Potential New Standard of Care in Chronic HP

- One-year OLE data support canvuparatide as a once-weekly PTH replacement therapy
- Market research indicates majority of HCPs and patients would choose once weekly first
- Phase 3 trial preparations underway, initiation anticipated in Q3 2026

# MBX: Catalyst-Rich Year

| Program | Milestone | Anticipated Timing |
|---|---|---|
| Canvuparatide (MBX 2109) | End-of-Phase 2 FDA Meeting | ☑ |
| | Avail™ Phase 2 presentation and one-year OLE data | ENDO 2026 |
| | Phase 3: Initiation | Q3 2026 |
| MBX 4291 (GLP-1/GIP) | Phase 1: 12-week MAD results | Q4 2026 |
| MBX 5765 (amycretin) | Nominate development candidate | ☑ |
| MBX 6XXX (GLP-1/GIP/GCGR) | Nominate development candidate | Q3 2026 |

**$440 million in cash expected to provide runway into 2029[1]**



[1] Unaudited cash, cash equivalents and marketable securities as of March 31, 2026

# Our Mission

Transforming the Lives of People Impacted by Endocrine and Metabolic Diseases through Precision Peptides