Efficacy and Safety of Once-Weekly Canvuparatide in Patients With Hypoparathyroidism: Results From Avail, a Phase 2, Double-Blind, Placebo-Controlled, Randomized Clinical Trial

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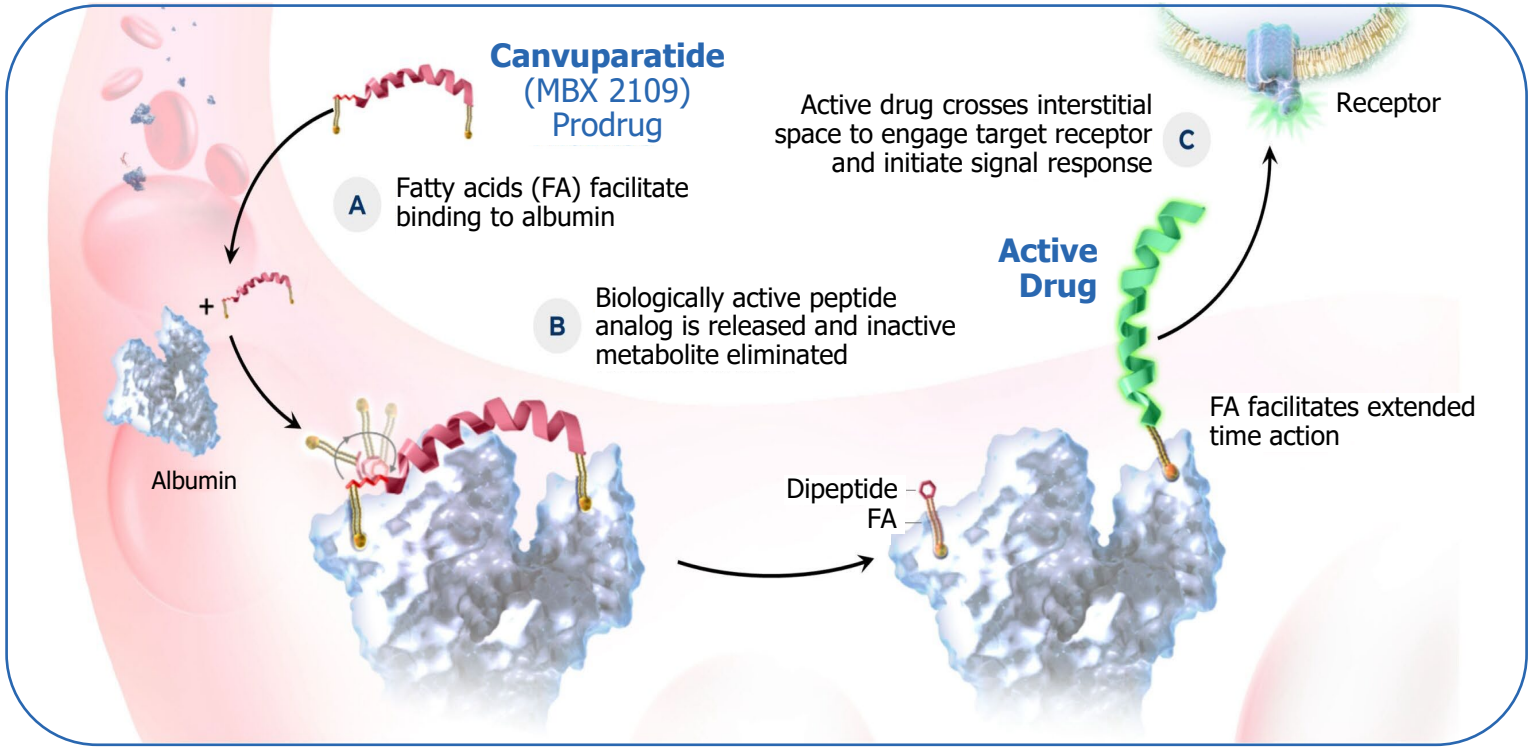
Background

- **Current treatment options** for hypoPT are **limited by** failure to fully alleviate symptoms; complex dosing schedules, high pill burden, and adverse effects (conventional therapy) that may reduce adherence; and short half-lives (PTH analogs) that necessitate multiple daily doses or daily SC injections[1-3]

Canvuparatide (formerly MBX 2109):

- Is an investigational, fatty-acylated, long-acting prodrug of a **PTH analog**[4]
- Is in development as a PTH replacement therapy in **patients with hypoPT**[4]
- Has a T_{max} of 2–3 days and a $T_{1/2}$ of 7.7–8.9 days for the active peptide, supporting **once-weekly dosing**[4]

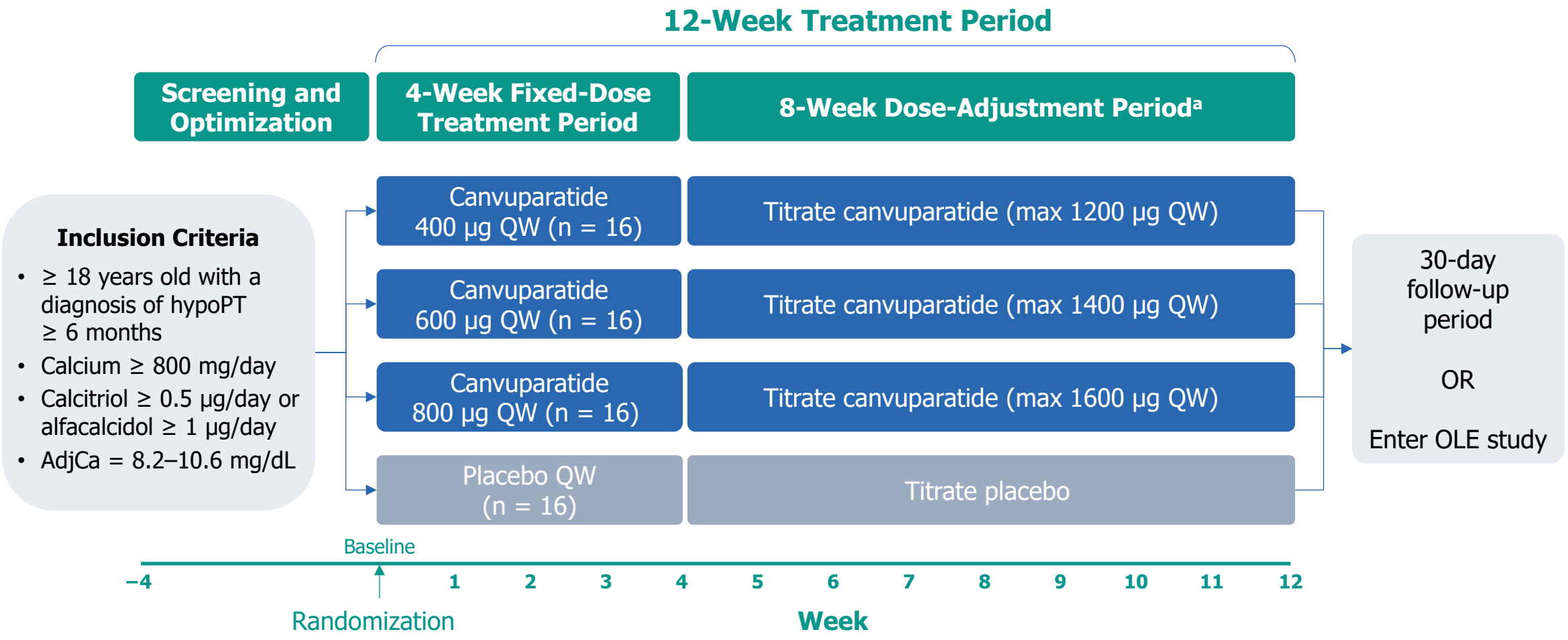


1. Khan AA, et al. *Metabolism*. 2025;171:156335. **2.** Hamny I, et al. *Ann Endocrinol (Paris)*. 2023;84:460–465. **3.** YORVIPATH (palopegteriparatide). Prescribing information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/216490Orig1s005lbl.pdf. **4.** Carney P, et al. *J Clin Endocrinol Metab*. 2025;110:940–950.

hypoPT, hypoparathyroidism; PTH, parathyroid hormone; SC, subcutaneous; $T_{1/2}$, half-life.

Study Design and Key Inclusion Criteria

Avail Is the First Study to Evaluate the Efficacy and Safety of Canvuparatide in Patients With HypoPT



[a]Dose adjustments could be made in 200-µg increments, as needed, every 2 weeks during the dose-adjustment period.

AdjCa, albumin-adjusted calcium; hypoPT, hypoparathyroidism; OLE, open-label extension; QW, once weekly.
ClinicalTrials.gov Identifier: NCT06465108.

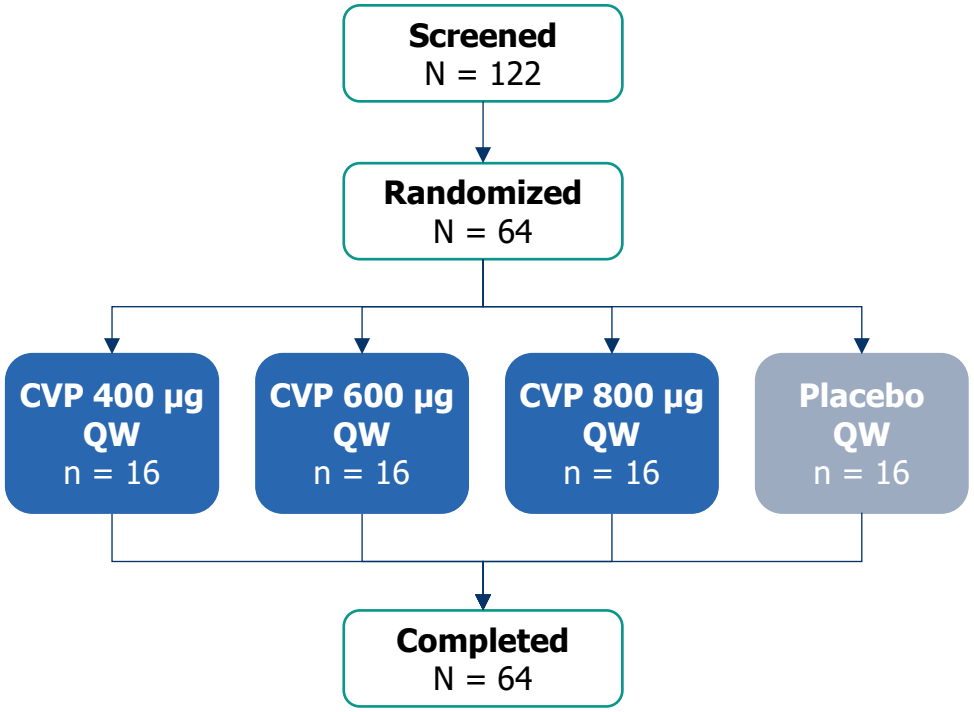
Endpoints and Patient Disposition

Primary Endpoint

- Proportion of patients meeting the following composite criteria at week 12:
  - Independence from active vitamin D supplements
  - Oral elemental calcium supplements ≤ 600 mg/day
  - Serum AdjCa concentration of 8.2–10.6 mg/dL

Secondary and Exploratory Endpoints

- Responders for each individual measure of the primary composite endpoint at week 12
- Change from baseline in 24-hour urine calcium over time
- Change from baseline in bone turnover markers (serum CTx, P1NP, and BSAP) over time
- Safety and tolerability



No discontinuations occurred during the 12-week, double-blind study

AdjCa, albumin-adjusted calcium; BSAP, bone-specific alkaline phosphatase; CTx, C-telopeptide of type 1 collagen; CVP, canvuparatide; P1NP, procollagen type 1 N-terminal propeptide; QW, once weekly.

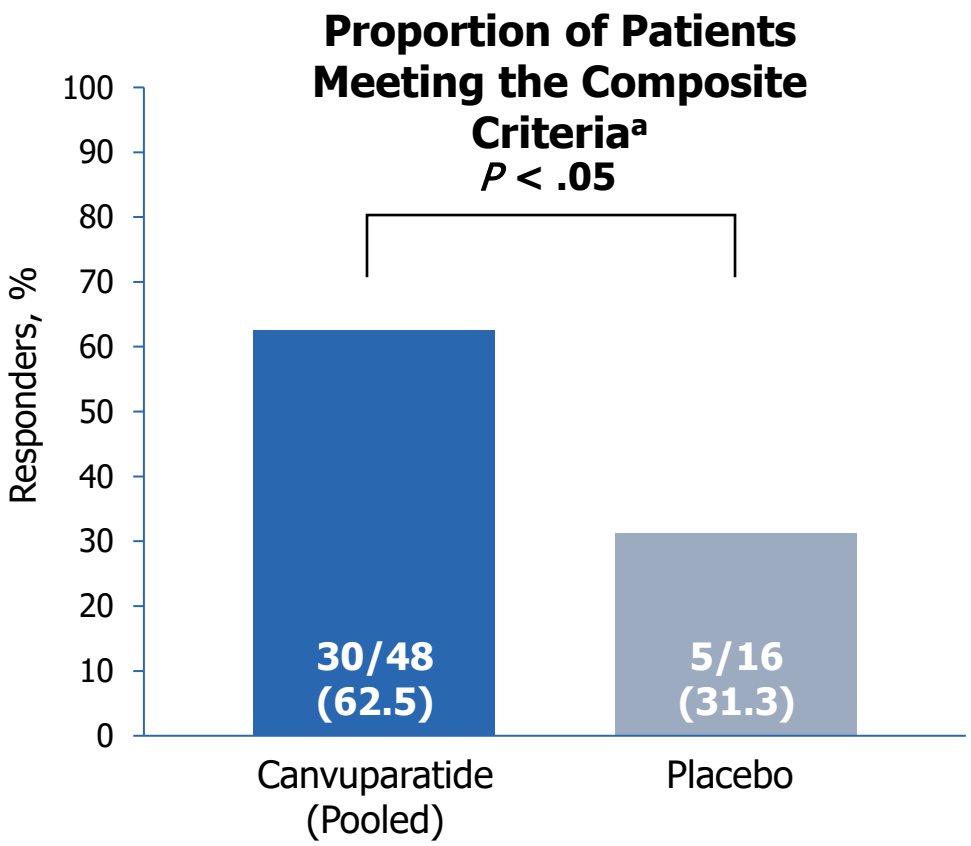
Baseline Demographics and Clinical Characteristics

Characteristic	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 hypoPT, years, mean (SD)	10.5 (9.0)	8.9 (4.8)

Characteristic	Canvuparatide (n = 48)	Placebo (n = 16)
Etiology of hypoPT, 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; hypoPT, 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.

Primary Composite Endpoint at Week 12



Proportion of Patients Meeting Each Component of Composite Criteria

Parameter, n (%)	Canvuparatide (n = 48)	Placebo (n = 16)	*P* value
Independence from active vitamin D	47 (97.9)	10 (62.5)	< .001
Independence from oral calcium (≤ 600 mg/day)	36 (75.0)	5 (31.3)	< .01
Serum AdjCa within normal range (8.2–10.6 mg/dL)	39 (81.3)	7 (43.8)	< .01

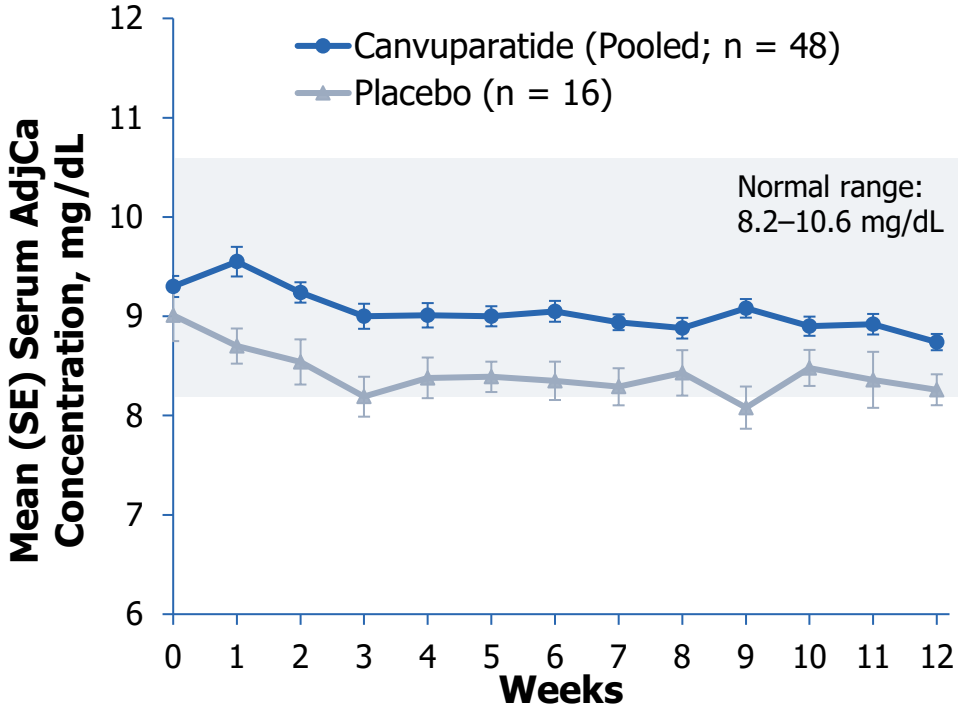
AdjCa, albumin-adjusted calcium; PRN, as needed.
[a]No patients required PRN supplements during the final week of evaluation.

Pharmacokinetics and Serum Calcium Profile

Phase 2 Pharmacokinetics (Drug Exposure)

- PK data from the phase 2 trial continue to support once-weekly dosing
- PK demonstrated consistent concentration of canvuparatide active drug with a T_{max} of 2–3 days, minimum fluctuation and a peak-to-trough ratio of ~1.3

Phase 2 Pharmacodynamics (Serum AdjCa Over Time[a])

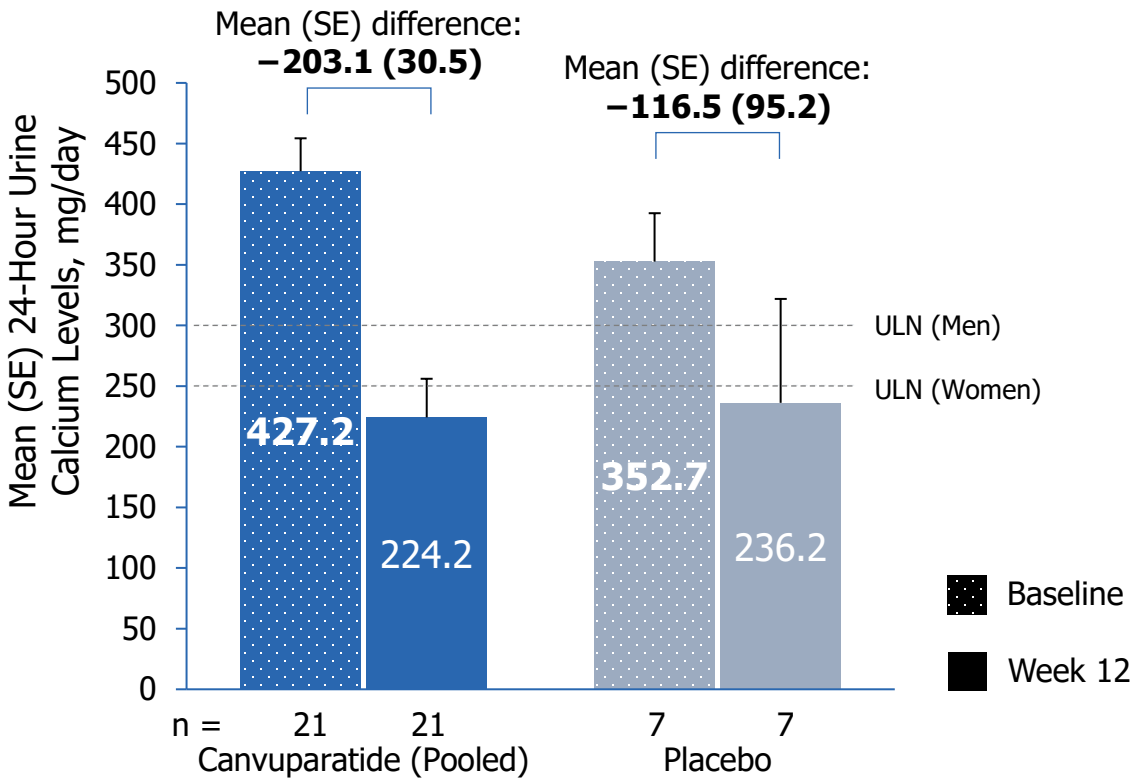


Mean peak-to-trough difference was 0.59 [0.12] mg/dL, consistent with stable calcium control

AdjCa, albumin-adjusted calcium.
[a]As assessed at trough concentration.

Additional Key Parameters

Participants With Elevated Urine Calcium at Baseline



Change in Serum Parameters and Bone Turnover Markers at Week 12

Parameter	Canvuparatide (n = 48)	Placebo (n = 16)
Phosphate, mg/dL	−0.23 (−0.39, −0.06)	0.10 (−0.21, 0.42)
Calcium-phosphorous product, mg^2/dL^2	−3.7 (−5.3, −2.0)	−1.4 (−3.8, 1.0)
Creatinine clearance, mL/min/1.73 m^2	5.3 (1.6, 8.9)	0.6 (−4.4, 5.6)
BSAP, U/L	12.2 (9.0, 15.5)[a]	−0.5 (−1.9, 0.9)
CTx, ng/L	459.1 (363.6, 554.6)	−16.3 (−90.8, 58.3)
P1NP, µg/L	74.2 (52.8, 95.7)[b]	−1.1 (−6.0, 3.7)[c]

Data are presented as mean (95% CI).

AdjCa, albumin-adjusted calcium; BSAP, bone-specific alkaline phosphatase; CTx, C-telopeptide of type 1 collagen; P1NP, procollagen type 1 N-terminal propeptide; ULN, upper limit of normal.
[a]n = 46. [b]n = 45. [c]n = 15.

Safety and Tolerability

TEAE, n (%)	Canvuparatide (n = 48)	Placebo (n = 16)
TEAE	35 (72.9)	10 (62.5)
Mild	22 (45.8)	9 (56.3)
Moderate	11 (22.9)	1 (6.3)
Severe	2 (4.2)	0
Treatment-related TEAE	25 (52.1)	6 (37.5)
SAE	1 (2.1)	0
Treatment-related SAEs	0	0
TEAE leading to discontinuation		
Of study drug	0	0
Of study	0	0
Deaths	0	0

- Most TEAEs were mild or moderate in intensity
- Treatment-emergent AESIs included (canvuparatide vs placebo)
  - Hypercalcemia (18.8% vs 6.3%)
  - Hypocalcemia (8.3% vs 18.8%)
  - All injection site reactions (18.8% vs 12.5%)
- The single SAE, Bell's palsy, was not deemed to be treatment related by the investigator and resolved without sequelae
- No treatment-induced ADAs occurred

ADA, antidrug antibody; AESI, adverse events of special interest; SAE, serious treatment-emergent adverse events; TEAE, treatment-emergent adverse event.

Summary

- After 12 weeks of treatment in the phase 2, Avail study, canvuparatide demonstrated a statistically significant improvement over placebo in the composite primary endpoint and each of its individual components
- Among patients with hypercalciuria, urinary calcium excretion decreased with canvuparatide treatment while maintaining serum calcium in the normal range
- Once-weekly canvuparatide also restored bone metabolism as demonstrated by an increase in bone turnover markers
- Canvuparatide was generally well tolerated at all doses, and no patients discontinued treatment
- These results support further evaluation of canvuparatide as a once-weekly PTH replacement therapy in a phase 3 randomized, placebo-controlled, clinical trial

HypoPT, hypoparathyroidism; PTH, parathyroid hormone.