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Phase 2 Trial and Open-Label Extension Top-Line Results:

Once-Weekly Canvuparatide in Adults with Hypoparathyroidism

September 22, 2025

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Agenda

Once-Weekly Canvuparatide for the Potential Treatment of Hypoparathyroidism

Top-Line Results Summary Disease Overview and Current Landscape	**Kent Hawryluk**
Avail™ and Open-Label Extension Overview Clinical Results and Safety Data	**Sam Azoulay, MD**
Differentiation and Next Steps	**Kent Hawryluk**
Q&A Session	**All**

Kent Hawryluk
President & CEO

Sam Azoulay, MD
Chief Medical Officer

Rick Bartram, CPA
Chief Financial Officer

Avail™ Once-Weekly Canvuparatide Achieved Primary Endpoint at Week 12; 79% Responder Rate at 6 Months in Open-Label Extension

- 63% of patients receiving once-weekly canvuparatide achieved the primary endpoint at Week 12 vs 31% on placebo ($p<0.05$)
    - All patients completed Avail™ and 94% entered the Open-Label Extension (OLE)
- Responder status increased to 79% at 6 months in the OLE
- At Week 12, urine calcium excretion was reduced in canvuparatide-treated patients with elevated baseline values
- Bone biomarkers increased in canvuparatide-treated patients at Week 12 and continued to improve at 6 months
- Once-weekly canvuparatide was well-tolerated, with no treatment related serious adverse events or discontinuations during the 12-week trial

Results support development for once-weekly dosing and progression into Phase 3

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Hypoparathyroidism: A Chronic, Serious Endocrine Disease

Affects >250,000 patients in the U.S. and E.U., representing a significant unmet need and market opportunity[1,2]

CAUSE

Deficiency in parathyroid hormone (PTH)

Etiology: Inadvertent removal of parathyroid during thyroid surgery and less commonly due to autoimmune disease and genetic disorders

SYMPTOMS[3,4]

Cognition: Cognitive impairment, confusion

Hypocalcemia – low calcium: Tetany, muscle cramping/spasms/twitching, numbness, tingling, seizures

Hypercalcemia – high calcium: Polyuria, nausea, vomiting, constipation, weakness

COMPLICATIONS[3,4]

Depression / Infections

Cardiovascular: Arrythmias, ischemic heart disease

Renal: Kidney stones, chronic kidney disease, nephrocalcinosis

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PTH, parathyroid hormone.

1. Clarke B et al JCEM 2016, 2. Powers J et al JBMR 2013, 3. Khan A et al JBMR 2022, 4. Yao L et al Complications Symptoms JBMR 2022.

Managing Hypoparathyroidism: A Significant Treatment Opportunity

Once-weekly canvuparatide designed to overcome key limitations of current therapies

STANDARD OF CARE

Calcium and active vitamin D[1] supplementation

- Does not address underlying pathophysiology
- Significant pill burden
- Serum calcium fluctuations
- Contributes to renal complications

DAILY INJECTIONS

Daily PTH replacement therapy

Palopegteriparatide

- Approved in U.S. and E.U. for the treatment of hypoparathyroidism in adults

Eneboparatide

- In Phase 3 development

CANVUPARATIDE **WEEKLY** INJECTION

Investigational once-weekly PTH replacement therapy

Designed to:

- ✓ Lower daily peak-to-trough PTH exposures vs. daily injectables
- ✓ Normalize serum and urine calcium
- ✓ Eliminate pill burden
- ✓ Convenient weekly dosing
- ✓ Improve QoL
- ✓ Reduce complications

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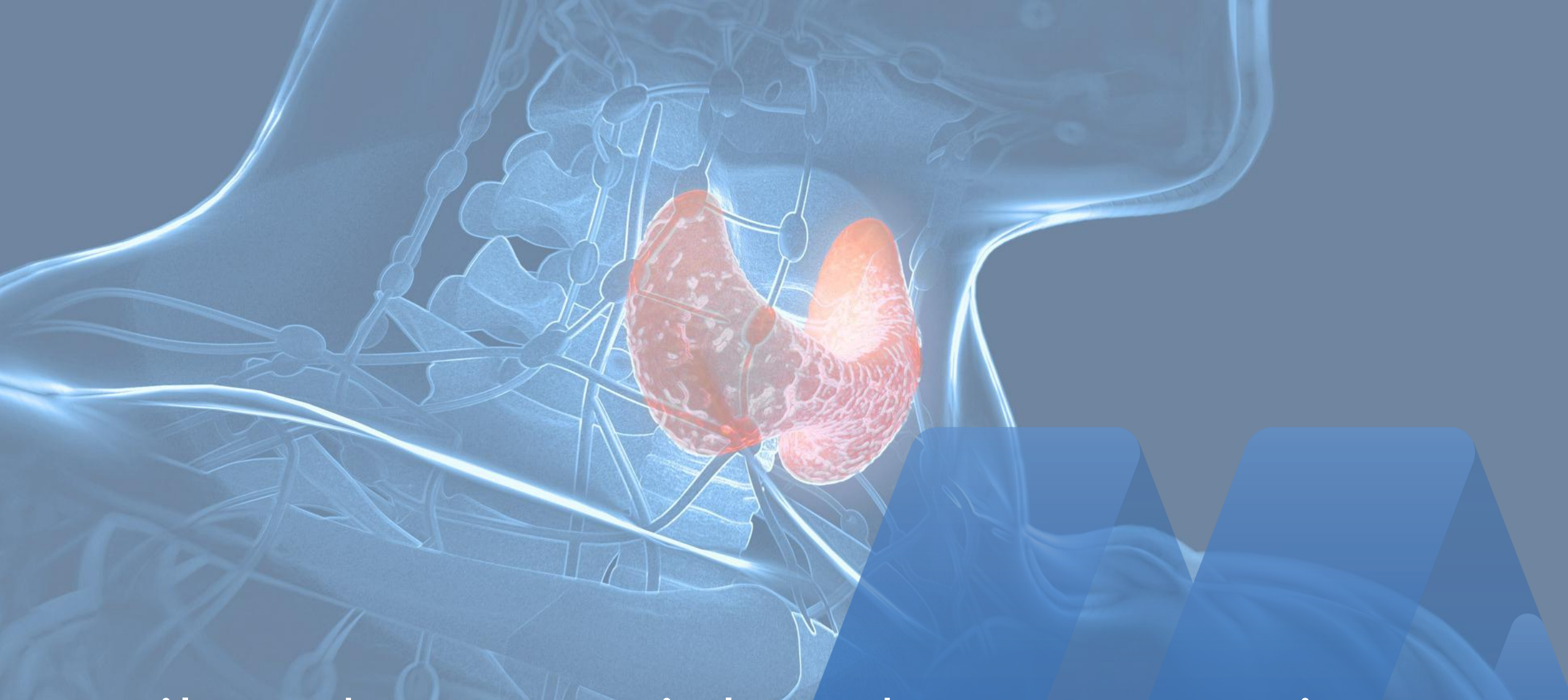
PTH, parathyroid hormone; QoL=quality of life.

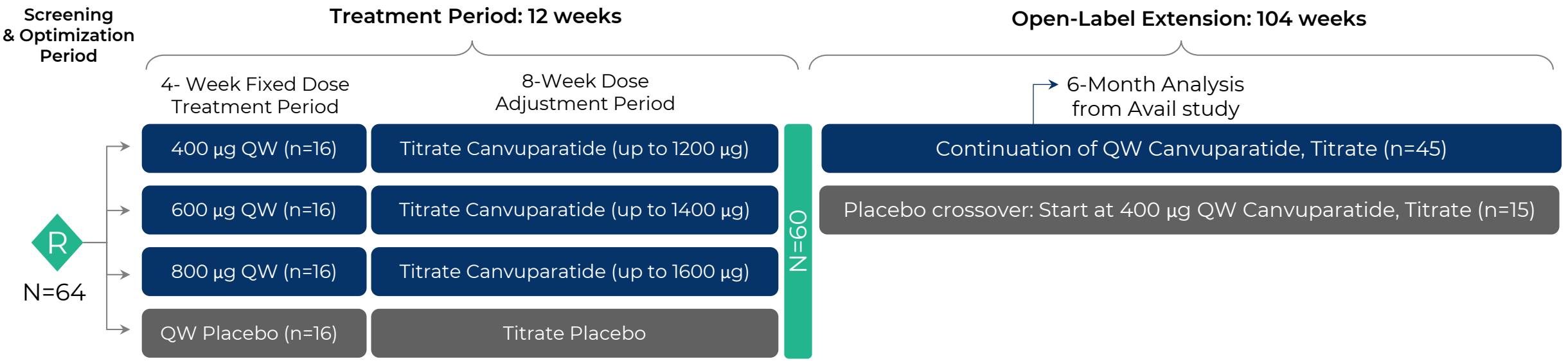
1. Khan A et al. JBMR 2022.



Avail™ Phase 2 Trial and OLE Overview

Avail™ Once-Weekly Canvuparatide Trial Design and Endpoints

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



Key Endpoints from Phase 2 Avail™ and OLE

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
- Calcium supplements (≤600 mg/day)

Select Secondary and Exploratory Endpoints

- % Responders of each starting dose at Week 12
- % Meeting each individual component of composite criteria
- % Responders at 6 months
- Change from baseline in 24h urine calcium excretion
- Change from baseline in bone turnover biomarkers
- Safety and tolerability

QW, once weekly.
ClinicalTrials.gov Identifier: NCT06465108, NCT06531941

Avail™ Baseline Demographic and Clinical Characteristics

Characteristic	Canvuparatide				Placebo (n = 16)	All Patients (N = 64)
	400 µg (n = 16)	600 µg (n = 16)	800 µg (n = 16)	Pooled (n = 48)		
Age, years, median (range)	50.0 (35–68)	45.0 (28–58)	55.5 (23–72)	49.0 (23–72)	44.5 (19–63)	48.5 (19–72)
Female, n (%)	13 (81.3)	15 (93.8)	13 (81.3)	41 (85.4)	15 (93.8)	56 (87.5)
Race, n (%)						
Asian	0	0	0	0	1 (6.3)	1 (1.6)
Black/African American	1 (6.3)	1 (6.3)	2 (12.5)	4 (8.3)	2 (12.5)	6 (9.4)
White	15 (93.8)	15 (93.8)	13 (81.3)	43 (89.6)	13 (81.3)	56 (87.5)
Other	0	0	1 (6.3)	1 (2.1)	0	1 (1.6)
Ethnicity, n (%)						
Hispanic or Latino	11 (68.8)	9 (56.3)	9 (56.3)	29 (60.4)	9 (56.3)	38 (59.4)
Not Hispanic or Latino	5 (31.3)	7 (43.8)	7 (43.8)	19 (39.6)	7 (43.8)	26 (40.6)
BMI, kg/m^2, mean (SD)	30.6 (4.3)	32.9 (7.2)	30.4 (7.0)	31.3 (6.3)	30.2 (5.4)	31.0 (6.1)

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BMI, body mass index.

Avail™ Hypoparathyroidism Baseline Clinical Characteristics

Characteristic	Canvuparatide				Placebo (n = 16)	All Patients (N = 64)
	400 µg (n = 16)	600 µg (n = 16)	800 µg (n = 16)	Pooled (n = 48)		
Duration of hypoparathyroidism, years, mean (SD)	10.5 (7.5)	9.4 (9.9)	11.7 (9.9)	10.5 (9.0)	8.9 (4.8)	10.1 (8.2)
Etiology of hypoparathyroidism, n (%)						
Postsurgical chronic	15 (93.8)	14 (87.5)	14 (87.5)	43 (89.6)	14 (87.5)	57 (89.1)
Idiopathic	1 (6.3)	1 (6.3)	1 (6.3)	3 (6.3)	2 (12.5)	5 (7.8)
Autoimmune	0	1 (6.3)	0	1 (2.1)	0	1 (1.6)
Genetic	0	0	1 (6.3)	1 (2.1)	0	1 (1.6)
Calcium dose, mg/day, median (range)	1900 (1000–12,000)	2400 (800–5400)	2000 (800–13,500)	2000 (800–13,500)	2325 (1300–4000)	2000 (800–13,500)
Vitamin D dose, µg/day, median (range)	0.750 (0.50–2.50)	0.875 (0.50–2.00)	0.875 (0.50–2.00)	0.750 (0.50–2.50)	0.750 (0.50–1.50)	0.750 (0.50–2.50)
Serum AdjCa, mg/dL, mean (SD)	9.3 (0.9)	9.4 (0.7)	9.2 (0.7)	9.3 (0.7)	9.0 (1.0)	9.2 (0.8)
Serum PTH, ng/L, mean (SD)	9.2 (5.8)	10.1 (4.4)	11.2 (7.0)	10.2 (5.7)	12.1 (12.6)	10.6 (7.9)
Urine calcium excretion, n (%)						
< 250 mg/day	9 (56.3)	8 (50.0)	9 (56.3)	26 (54.2)	9 (56.3)	35 (54.7)
≥ 250 mg/day	7 (43.8)	8 (50.0)	7 (43.8)	22 (45.8)	7 (43.8)	29 (45.3)

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AdjCa, albumin-adjusted calcium.

Avail™ Phase 2: Clinical Results

Avail™ 63% of Patients Treated with Once-Weekly Canvuparatide met the Primary Composite Endpoint with Zero PRN use at Week 12

Parameter, n (%)	Canvuparatide (Pooled) (n = 48)	Placebo (n = 16)	*P* Value vs Placebo*
Proportion of Patients Meeting Primary Endpoint Criteria at Week 12 (Responders)	30 (63%)	5 (31%)	0.0427
Proportion of Patients Meeting Each Component of Composite Criteria, (n, %)			
Independence from active vitamin D	47 (98%)	10 (63%)	0.0004
Independence from oral calcium (≤600 mg/day)	36 (75%)	5 (31%)	0.0026
Serum AdjCa within normal range (8.2–10.6 mg/dL)	39 (81%)	7 (44%)	0.0062

*Strata-adjusted differences in proportions and p-value are obtained from Cochran-Mantel-Haenszel test after adjusting for randomization strata (history of surgically-induced hypoparathyroidsim (yes/no) and urine calcium excretion of <250 mg/day or ≥250 mg/day.

AdjCa, albumin-adjusted calcium.

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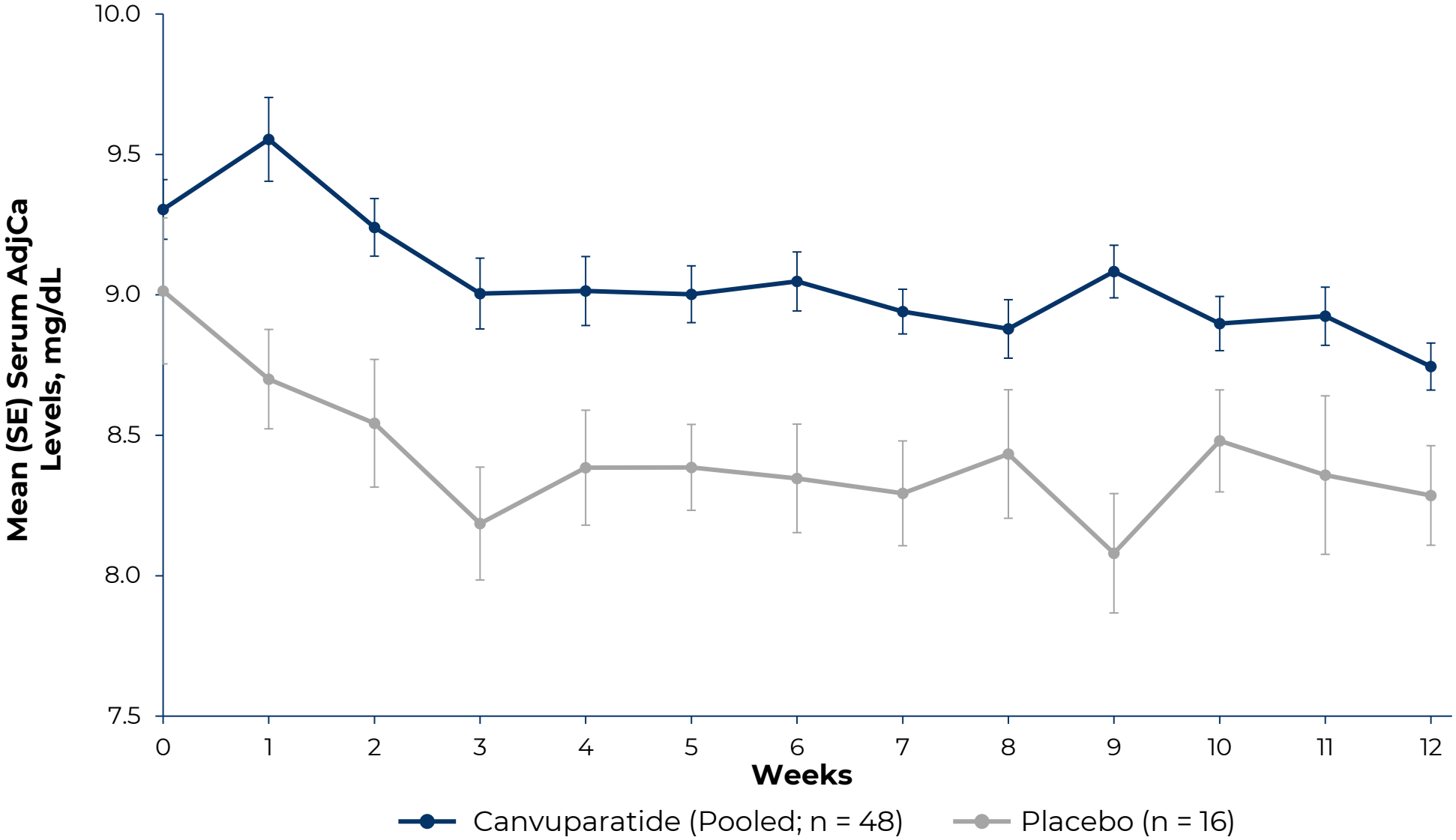
Evidence of Dose Response and Wide Therapeutic Range

Parameter, n (%)	Canvuparatide				Placebo (n = 16)
	400 µg (n = 16)	600 µg (n = 16)	800 µg (n = 16)	Pooled (n = 48)	
Proportion of Patients Achieving Responder Status at Week 12	8 (50%)	11 (69%)	11 (69%)	30 (63%)	5 (31%)
Median Dose for Responders at Week 12, µg (range)	600 (400, 600)	800 (600, 1400)	800 (400, 1400)	800 (400, 1400)	600 (600, 1400)
P Value vs Placebo*	0.2384	0.0637	0.0393	0.0427	

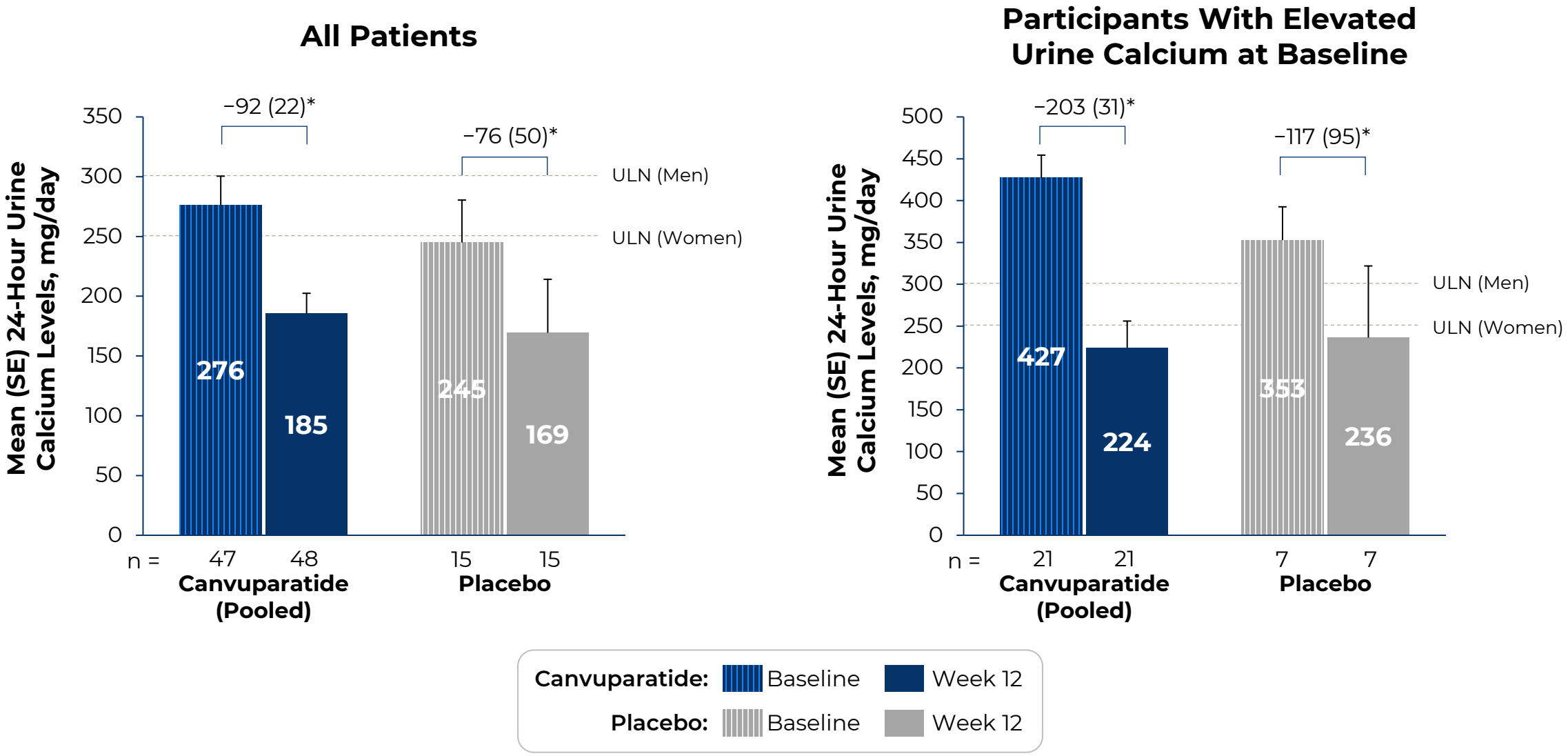
*Strata-adjusted differences in proportions and p-value are obtained from Cochran-Mantel-Haenszel test after adjusting for randomization strata(history of surgically-induced hypoparathyroidsim (yes/no) and urine calcium excretion of <250 mg/day or ≥250 mg/day.

Once-Weekly Canvuparatide Treated Patients Maintained Mean Serum AdjCa Levels Within Normal Range Over 12 Weeks

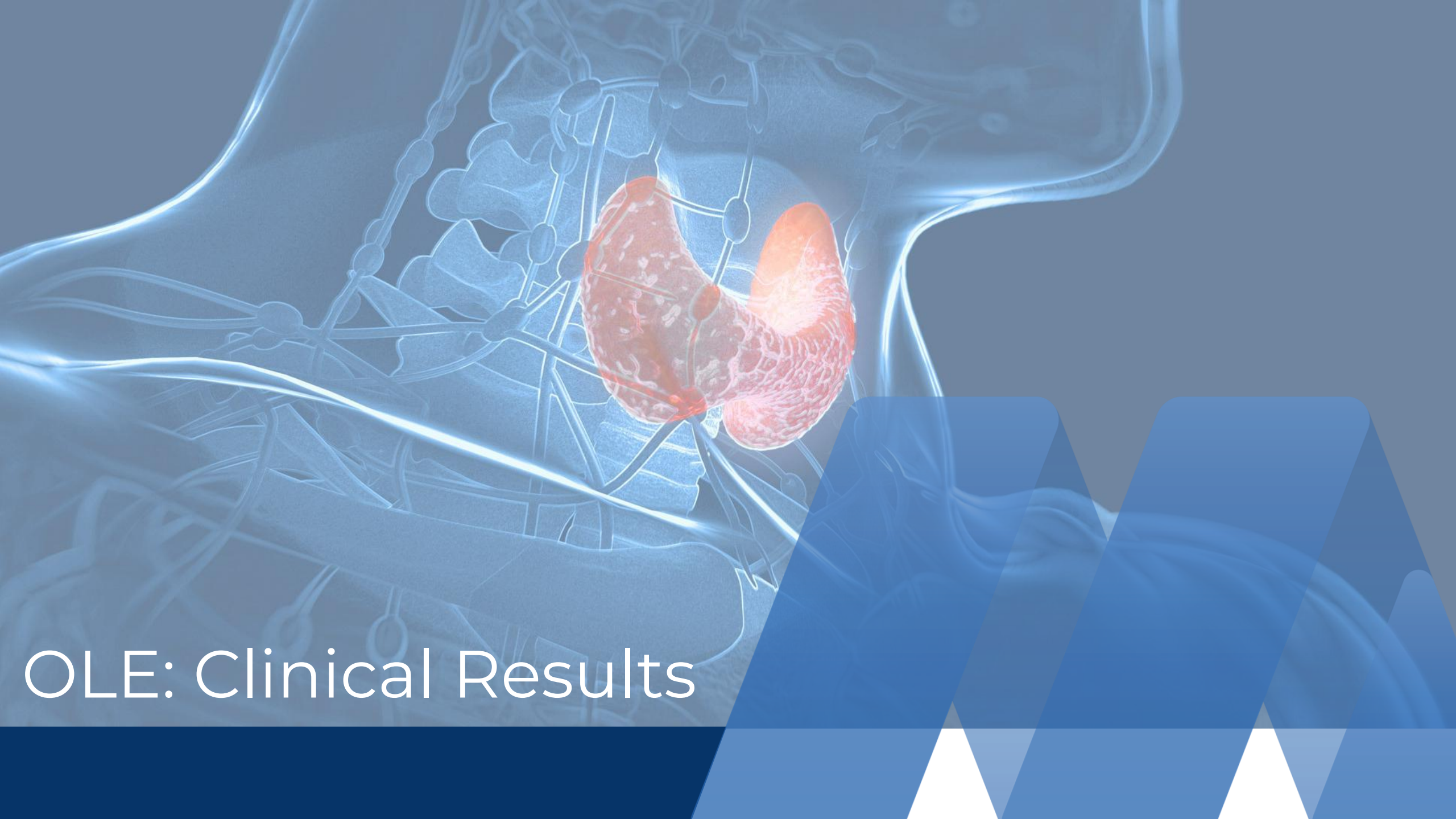


AdjCa, albumin-adjusted calcium.

Once-Weekly Canvuparatide Demonstrated Meaningful Reduction in 24h Urine Calcium



*Mean (SE) difference
ULN, upper limit of normal.



OLE: Clinical Results

Responder Rates Increased to 79% at 6 Months in OLE

96% of responders at Week 12 remained responders at 6 months*

Parameter, n (%)	Week 12	6 Months
	Canvuparatide (Pooled) (n = 48)	All Treated (n = 56)[a]
Proportion of Patients Achieving Responder Status	30 (63%)	44 (**79%**)
Proportion of Patients Meeting Each Component of Responder Criteria, (n, %)		
Independence from active vitamin D	47 (98%)	52 (**90%**)[b]
Independence from oral calcium (≤600 mg/day)	36 (75%)	47 (**81%**)[b]
Serum AdjCa within normal range (8.2–10.6 mg/dL)	39 (81%)	53 (**95%**)

*Based on patients with available data (23 out of 24)

[a]Analysis based on patients with available data for each component of the composite criteria at 6 months. Canvuparatide (pooled) cohort at month 6 includes patients initially randomized to canvuparatide (n=41) and placebo (n=15) for 12 weeks in the Avail study.

[b]Percentages based on 58 patients

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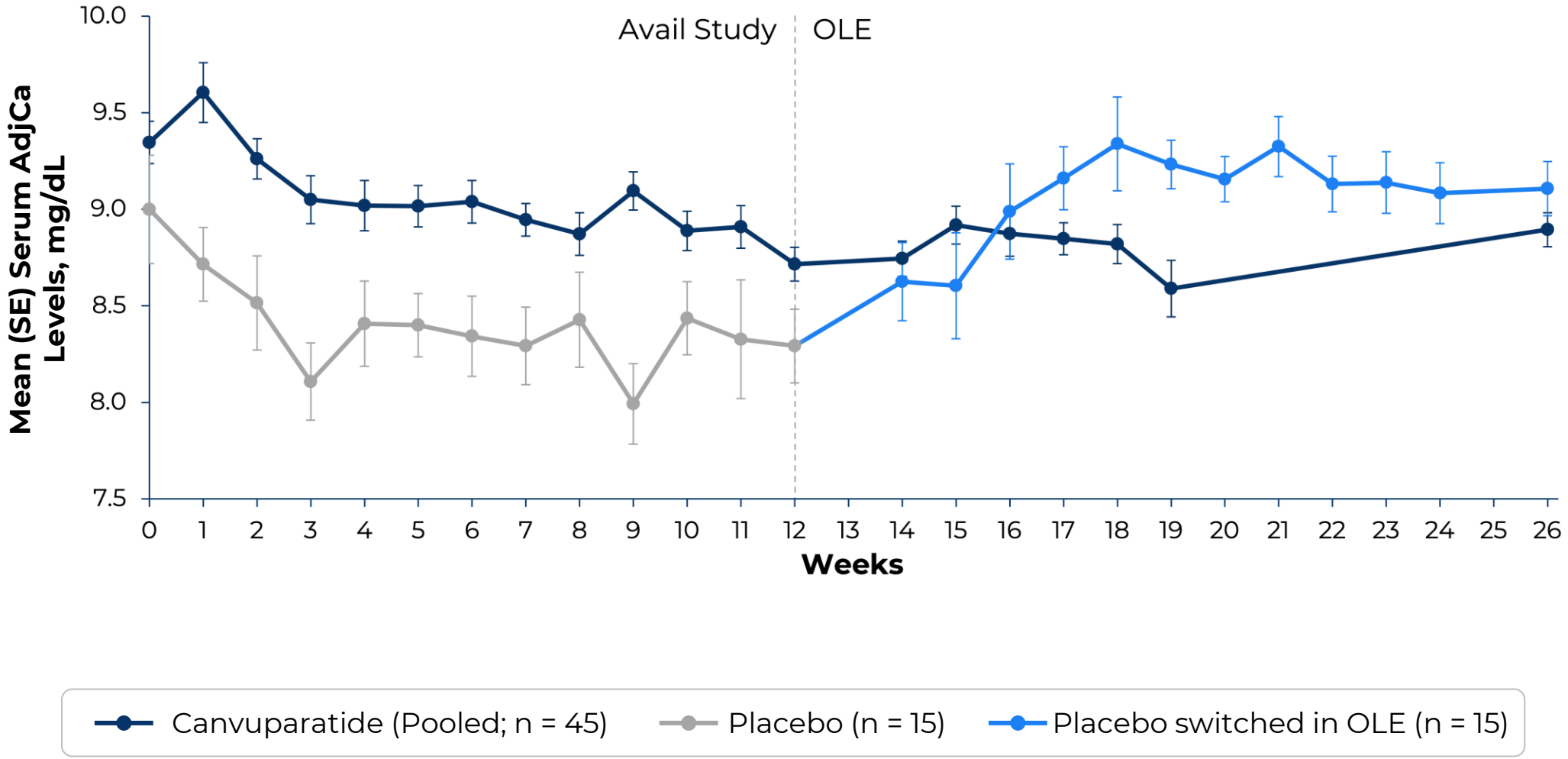
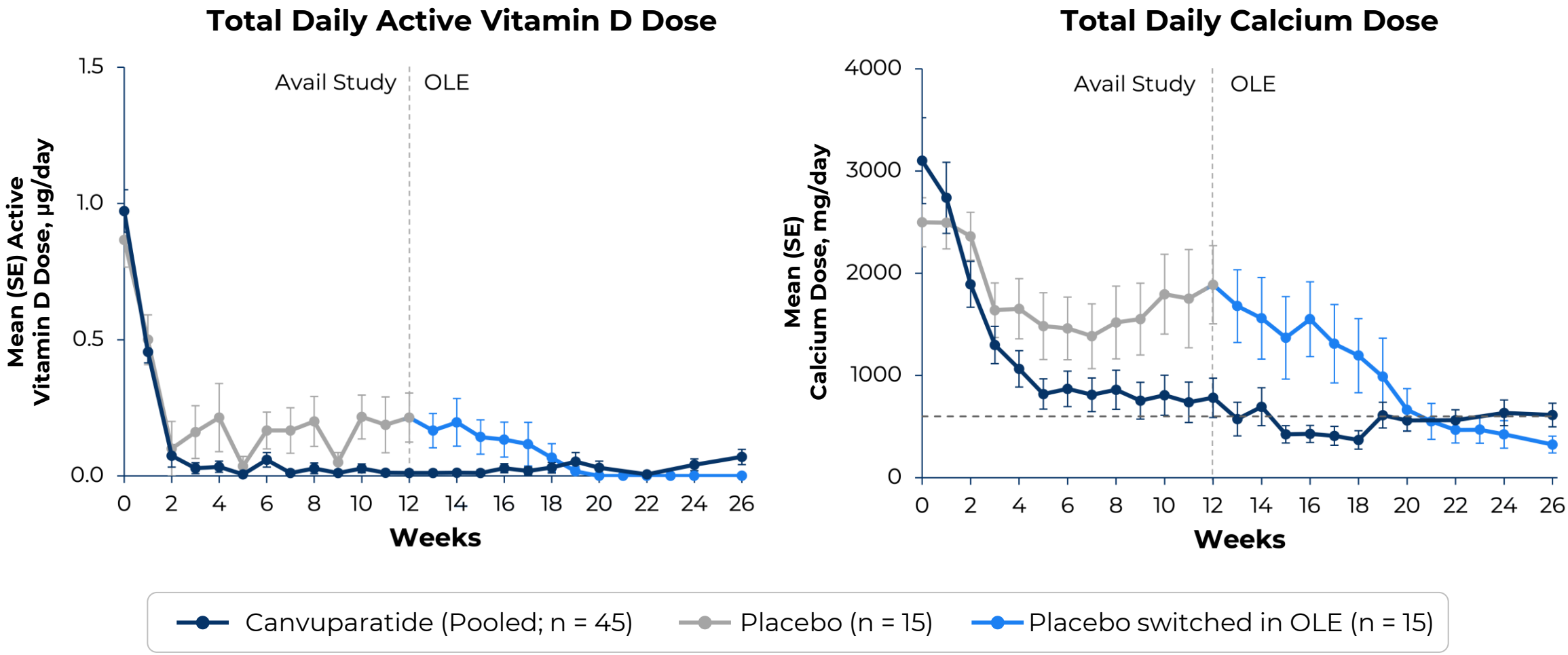
AdjCa,

Once-Weekly Canvuparatide Treated Patients Maintained Mean Serum AdjCa Levels Within Normal Range Over 6 Months



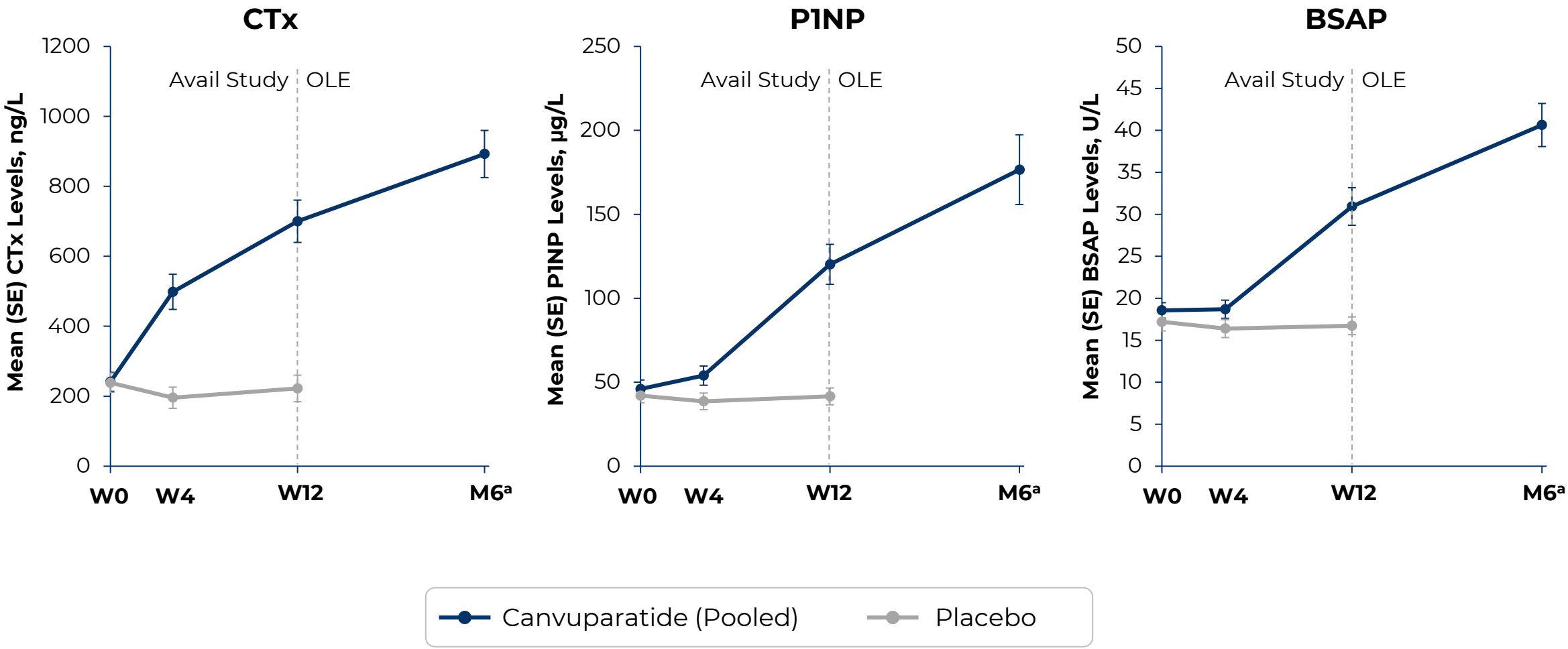
AdjCa, albumin-adjusted calcium; OLE, open-label extension.

Once-Weekly Canvuparatide Lowered Daily Supplement Requirements Over 6 Months



Dashed line indicates target calcium dose (600 mg/day).
OLE, open-label extension.

Bone Turnover Markers Increased Over 12 Weeks and Continued Over 6 Months



[a]The canvuparatide (pooled) cohort at M6 includes patients initially randomized to canvuparatide or placebo for W12 in the Avail study.
BSAP, bone-specific alkaline phosphatase; CTx, C-terminal telopeptide of type I collagen; M, month; OLE, open-label extension; P1NP, procollagen 1 intact N-terminal propeptide; W, week.

Avail™ Phase 2: Safety Results

Avail™ Phase 2 TEAE Summary

TEAE, n (%)	Canvuparatide				Placebo (n = 16)
	400 µg (n = 16)	600 µg (n = 16)	800 µg (n = 16)	Pooled (n = 48)	
TEAE	12 (75.0)	10 (62.5)	13 (81.3)	35 (72.9)	10 (62.5)
Mild	10 (62.5)	5 (31.3)	7 (43.8)	22 (45.8)	9 (56.3)
Moderate	2 (12.5)	3 (18.8)	6 (37.5)	11 (22.9)	1 (6.3)
Severe	0	2[a,b] (12.5)	0	2 (4.2)	0
Treatment-related TEAE	7 (43.8)	8 (50.0)	10 (62.5)	25 (52.1)	6 (37.5)
SAE	0	1[a] (6.3)	0	1 (2.1)	0
Treatment-related SAEs	0	0	0	0	0
TEAE leading to discontinuation					
Of study drug	0	0	0	0	0
Of study	0	0	0	0	0
Deaths	0	0	0	0	0

[a]One patient with Bell's palsy was reported as not treatment related, and resolved without sequelae.
[b]One patient with abdominal pain was reported as possibly treatment related.
SAE, serious treatment-emergent adverse events; TEAE, treatment-emergent adverse event.

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Avail™ Phase 2 Most Common TEAEs (≥ 5% of Any Treatment Group[a])

TEAE, n (%)	Canvuparatide				Placebo (n = 16)
	400 µg (n = 16)	600 µg (n = 16)	800 µg (n = 16)	Pooled (n = 48)	
Headache	5 (31.3)	1 (6.3)	4 (25.0)	10 (20.8)	1 (6.3)
Hypercalcemia	2 (12.5)	2 (12.5)	5 (31.3)	9 (18.8)	1 (6.3)
Arthralgia	1 (6.3)	4 (25.0)	2 (12.5)	7 (14.6)	0
Nausea	1 (6.3)	0	5 (31.3)	6 (12.5)	1 (6.3)
Injection site reaction	2 (12.5)	0	3 (18.8)	5 (10.4)	1 (6.3)
Diarrhea	1 (6.3)	1 (6.3)	2 (12.5)	4 (8.3)	1 (6.3)
Fatigue	0	3 (18.8)	1 (6.3)	4 (8.3)	0
Abdominal pain	0	1 (6.3)	2 (12.5)	3 (6.3)	0
Asthenia	0	0	2 (12.5)	2 (4.2)	1 (6.3)
Injection site erythema	0	2 (12.5)	1 (6.3)	3 (6.3)	0
Muscle spasms	0	2 (12.5)	0	2 (4.2)	1 (6.3)
Vomiting	0	0	3 (18.8)	3 (6.3)	0
Muscle twitching	2 (12.5)	0	0	2 (4.2)	0

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[a]Most common TEAEs defined as ≥ 5% of any treatment group and occurring at a ≥2 % incidence higher than placebo.
TEAE, treatment-emergent adverse event.

Avail™ Phase 2 Treatment-Emergent AESIs

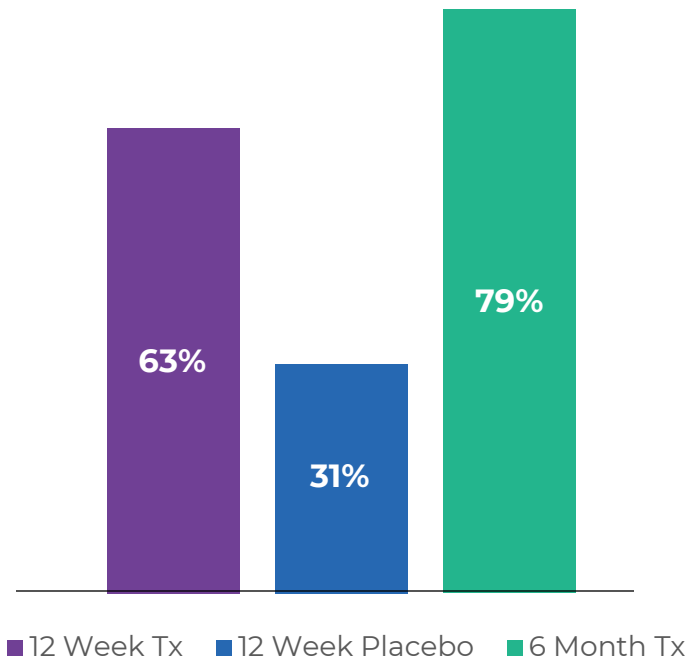
TEAE, n (%)	Canvuparatide				Placebo (n = 16)
	400 µg (n = 16)	600 µg (n = 16)	800 µg (n = 16)	Pooled (n = 48)	
Metabolism and nutrition disorders					
Hypercalcemia	2 (12.5)	2 (12.5)	5 (31.3)	9 (18.8)	1 (6.3)
Urgent care visit	0	0	1 (6.3)	1 (2.1)	0
Required hospitalization	0	0	0	0	0
Hypocalcemia	1 (6.3)	1 (6.3)	2 (12.5)	4 (8.3)	3 (18.8)
Urgent care visit	0	0	0	0	1 (6.3)
Required hospitalization	0	0	0	0	0
General disorders and administration site conditions					
Injection site TEAEs (grouped terms)	3 (18.8)	2 (12.5)	4 (25.0)	9 (18.8)	2 (12.5)

AESI, treatment-emergent of special interest; TEAE, treatment-emergent adverse event.

Summary & Next Steps

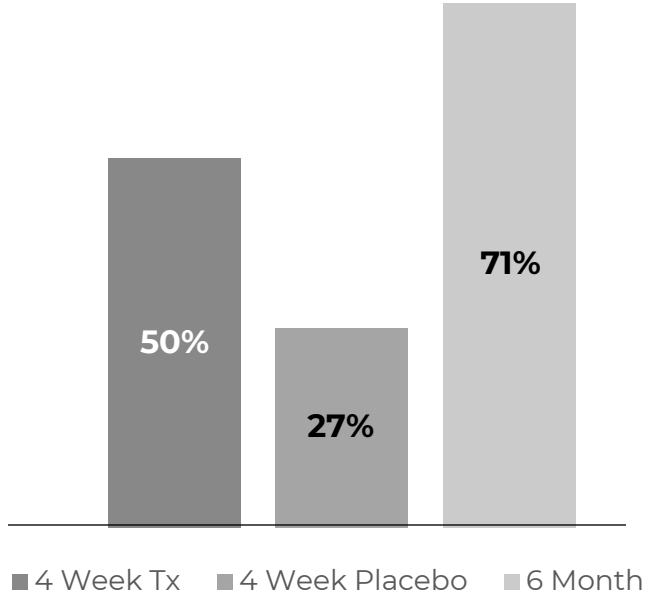
Once-Weekly Canvuparatide Demonstrated a Competitive Responder Rate in the Phase 2 Avail and OLE Studies

Once-Weekly Canvuparatide Phase 2 Responder Rates



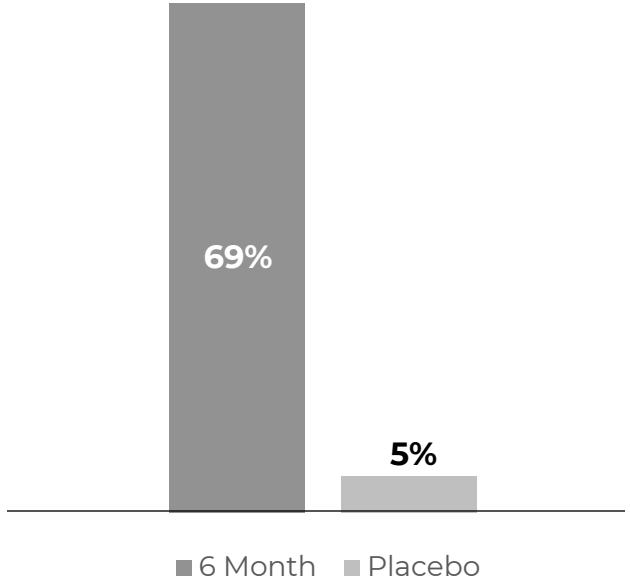
Achieved primary endpoint with statistical significance at Week 12

Once-Daily Injectable Phase 2 Responder Rates[1]



Did **not** achieve primary endpoint with statistical significance at Week 4

Once-Daily Injectable FDA-Approved Label Responder Rates[2]



Achieved primary endpoint with statistical significance at Week 26

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/; (2) Palopegteriparatide prescribing information

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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Once-Weekly Canvuparatide: Potential to Become Preferred Treatment for Hypoparathyroidism

Once-Weekly Canvuparatide

1/week

52/year

Daily Injectable

7/week

365/year

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Plans for Advancing Potential Best-in-Class Canvuparatide Program

- Present Phase 2 topline results at the International HypoPARAthyroidism Conference (Oct 2025)
- Request End-of-Phase 2 meeting with FDA
- Share full Phase 2 results at major medical meeting and in publication
- Report 52-week OLE follow-up data in 2026
- Plan to initiate global Phase 3 in 2026

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We thank the patients and their caregivers, investigators, partners, and the passionate team at MBX who helped to make Avail™ a success

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investors@mbxbio.com

Week 12 Sensitivity Analysis: 60% of Treated Patients with PTH <20 ng/L at Screening met the Primary Composite Endpoint vs 15% on Placebo*

Parameter, n (%)	Canvuparatide (Pooled) (n = 43)	Placebo (n = 13)	*P* Value vs Placebo†
Primary composite endpoint at Week 12: PTH <20 ng/L at screening	26 (60%)	2 (15%)	0.0072
Proportion of Patients Meeting Each Component of Composite Criteria, (n, %)			
Independence from active vitamin D	42 (98%)	7 (54%)	0.0009
Oral Elemental Calcium ≤ 600 mg/day	31 (72%)	2 (15%)	0.0009
Serum AdjCa (8.2–10.6 mg/dL)	35 (81%)	4 (31%)	0.001

*Sensitivity analysis using a screening PTH cutoff of <20 ng/L was conducted based on Brandi ML, et al. Management of Hypoparathyroidism: Summary Statement and Guidelines. J Clin Endocrinol Metab. 2016 Jun;101(6):2273-83.
†Strata-adjusted differences in proportions and p-value are obtained from Cochran-Mantel-Haenszel test after adjusting for randomization strata(history of surgically-induced hypoparathyroidsim (yes/no) and urine calcium excretion of <250 mg/day or ≥250 mg/day.
AdjCa, albumin-adjusted calcium; PTH, parathyroid hormone.