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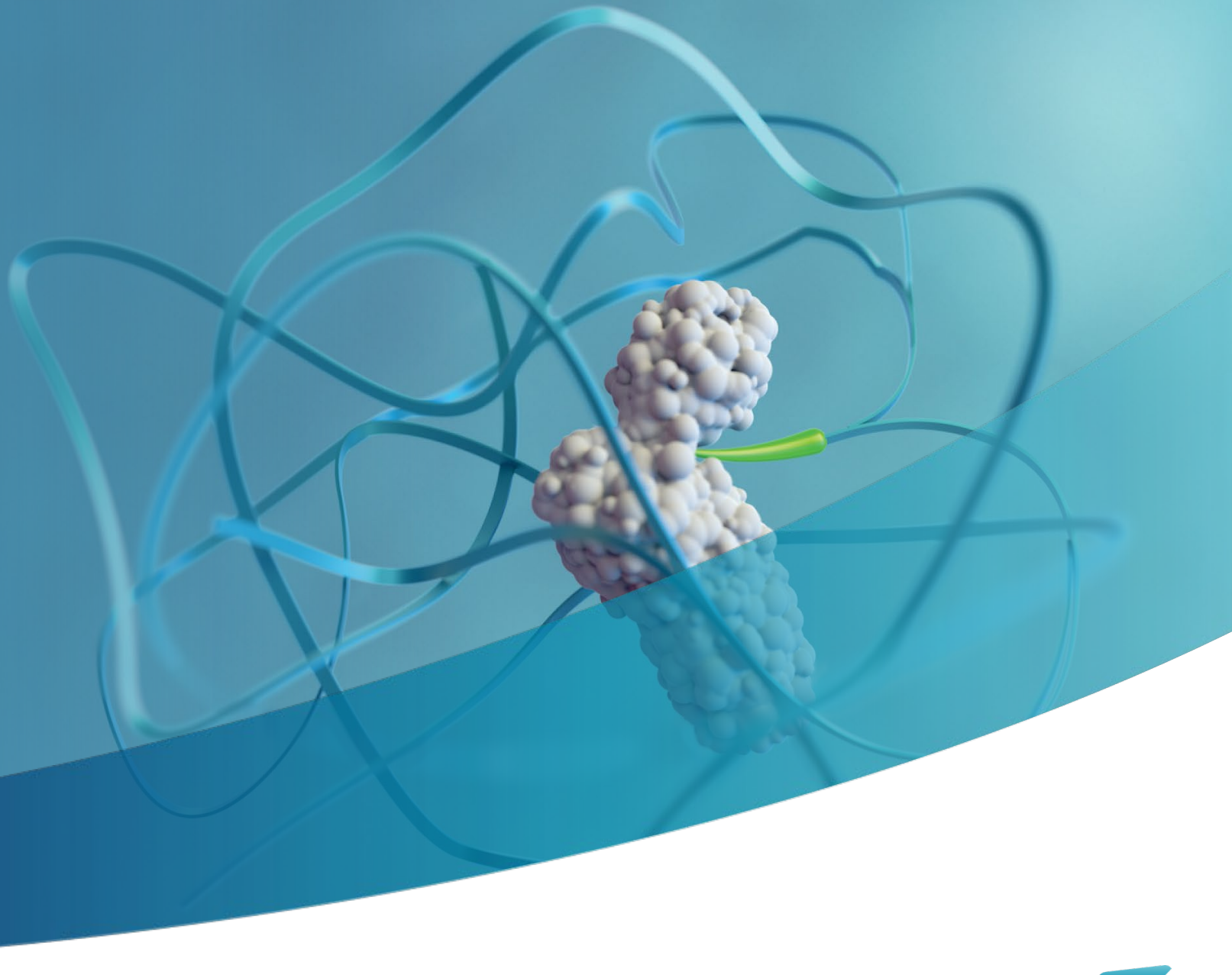

TransCon PTH (Palopegteriparatide)

Four Year Results
Phase 2 PaTH Forward Trial

May 2025

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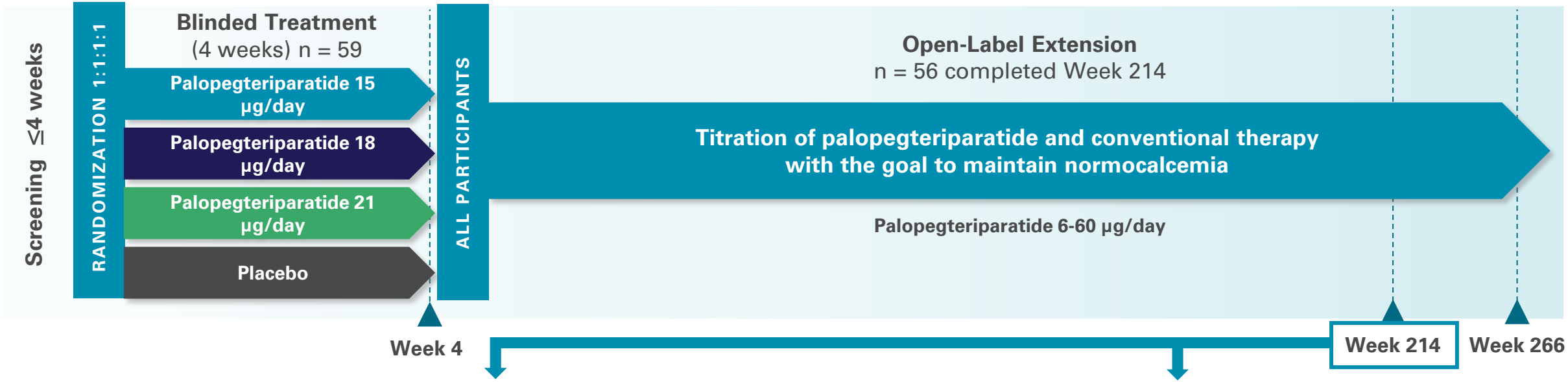
PaTH Forward Trial of Palopegteriparatide in Adults with Chronic Hypoparathyroidism

Phase 2 trial with a 4-week randomized, double-blind, placebo-controlled period followed by an open-label extension period through Week 266



Select Open-Label Extension Endpoints

- Levels of serum calcium (normocalcemia)
- Independence from conventional therapy (defined as taking no active vitamin D and ≤ 600 mg/day elemental calcium)
- Levels of 24-hour urinary calcium
- Incidence of AEs, SAEs, TEAEs

Skeletal Remodeling and Renal Endpoints

- Bone turnover markers (P1NP and CTx)
- Bone mineral density by DXA of the lumbar spine L1-L4, femoral neck, total hip, and distal 1/3 radius
- Renal function as assessed by eGFR

AE, adverse event; SAE, serious adverse event; TEAE, treatment-emergent adverse event; P1NP, procollagen type 1 N-terminal propeptide; CTx, C-terminal telopeptide of type 1 collagen; DXA, dual X-ray absorptiometry; eGFR, estimated glomerular filtration rate.

Baseline Demographics and Disease Characteristics

	All participants (N = 59)
Mean age, years (SD)	50 (12)
Sex, n (%) female	48 (81)
Menopausal status, n (%) postmenopausal	17 (35)
Race, n (%) White	54 (92)
Geographic region, n (%)	
North America	38 (64)
Europe	21 (36)
Cause of hypoparathyroidism, n (%)	
Acquired from neck surgery	47 (80)
Autoimmune disease	1 (2)
Idiopathic disease	11 (19)
Median duration of hypoparathyroidism, years (range)	9 (1-39)
Conventional therapy, mean TDD	
Calcium (mg)	1909
Calcitriol (µg)[a]	0.79
Alfacalcidol (µg)[b]	2.38

SD, standard deviation; TDD, total daily dose. Numbers may not add to 100% due to rounding.
[a]n = 46 (78%) participants used calcitriol at baseline. [b]n = 13 (22%) participants used alfacalcidol at baseline.

High Proportion of Participants Achieved Independence From Conventional Therapy

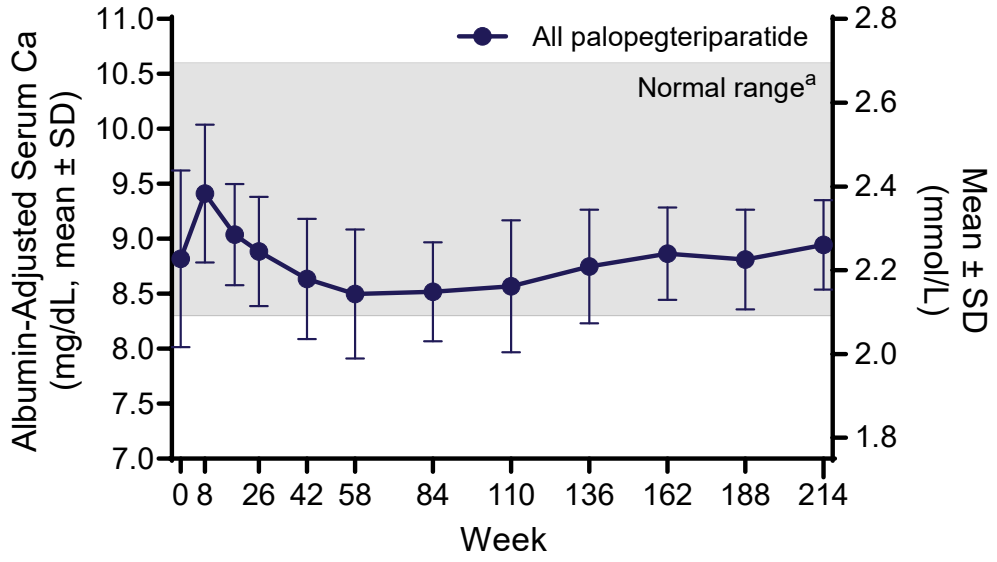
	All palopegteriparatide
Number of participants continuing through Week 214	56
Active vitamin D = 0 µg/day, n (%)	53 (95%)
Calcium ≤ 600 mg/day, n (%)	53 (95%)
Active vitamin D = 0 µg/day ***and*** calcium ≤ 600 mg/day, n (%)	52 (93%)

93% were independent from conventional therapy at week 214[a]

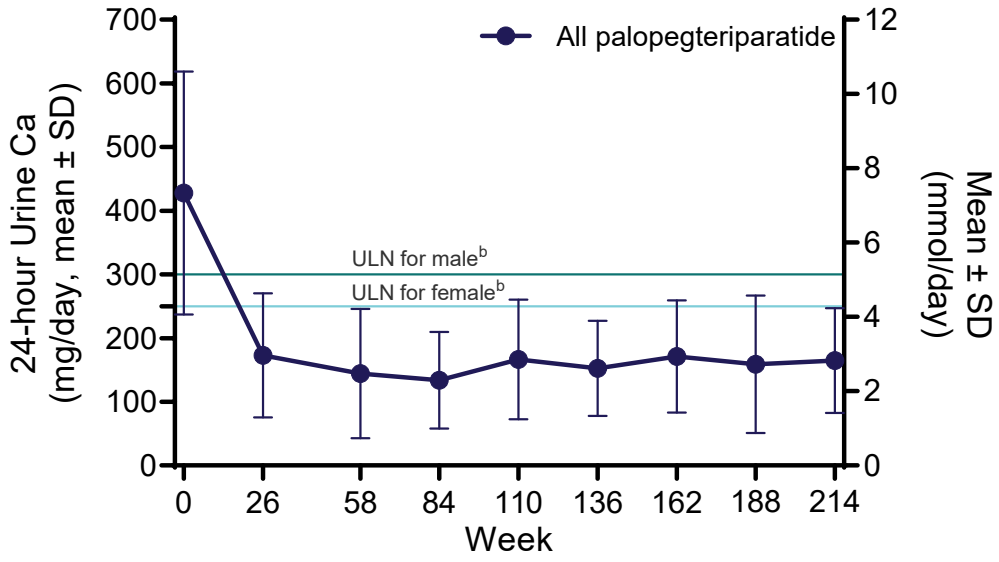
[a]Not taking active vitamin D and taking ≤ 600 mg/day of elemental calcium.

Serum and 24-Hour Urine Calcium Remained in the Normal Range Through Week 214

Mean Serum Calcium



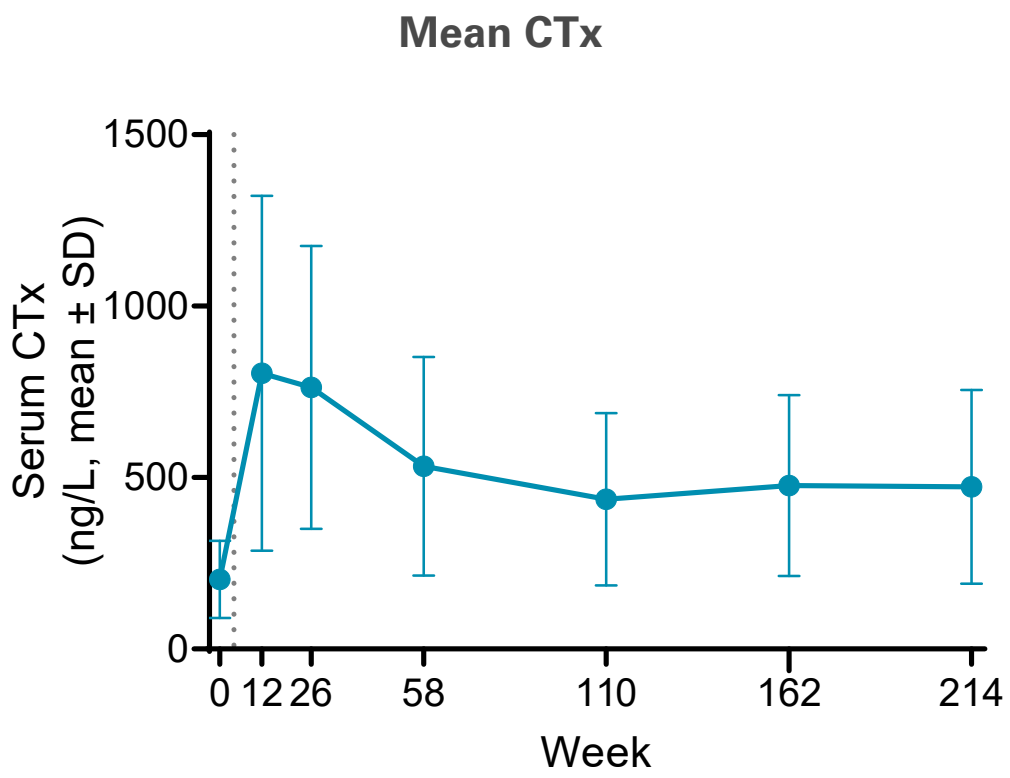
Mean 24-Hour Urine Calcium

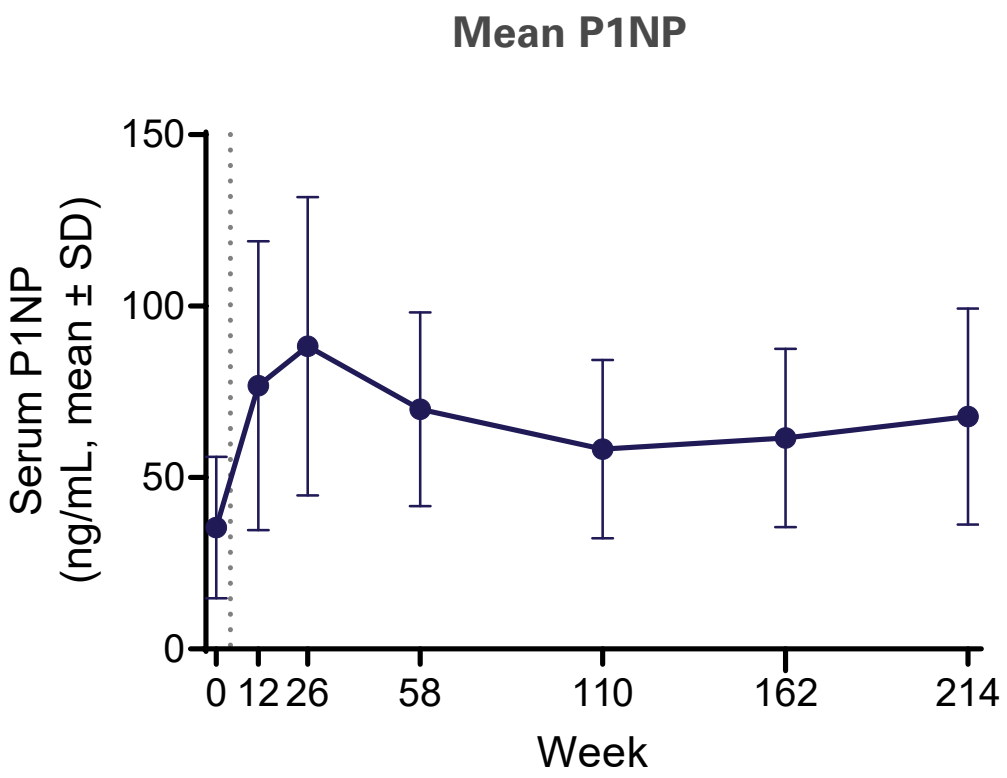


98% had normal serum calcium at week 214; mean 24-hour urine calcium normalized within 26 weeks

Serum calcium: n=59 at week 0; n=58 at week 58; n=57 at week 42 and 188; n=56 at weeks 26, 162, and 214; n=55 at week 136; n=54 at weeks 8 and 110; n=52 at week 18
24-hour urine calcium: n=55 at week 58; n=54 at weeks 84, 110, and 214; n=53 at week 188; n=50 at week 0; n=51 at weeks 136 and 162; n=49 at week 26
Ca, calcium; SD, standard deviation; ULN, upper limit of normal.
[a]The shaded area represents the normal serum calcium range of 8.3-10.6 mg/dL. [b]The ULN for males and females are depicted by teal and light blue lines, respectively.

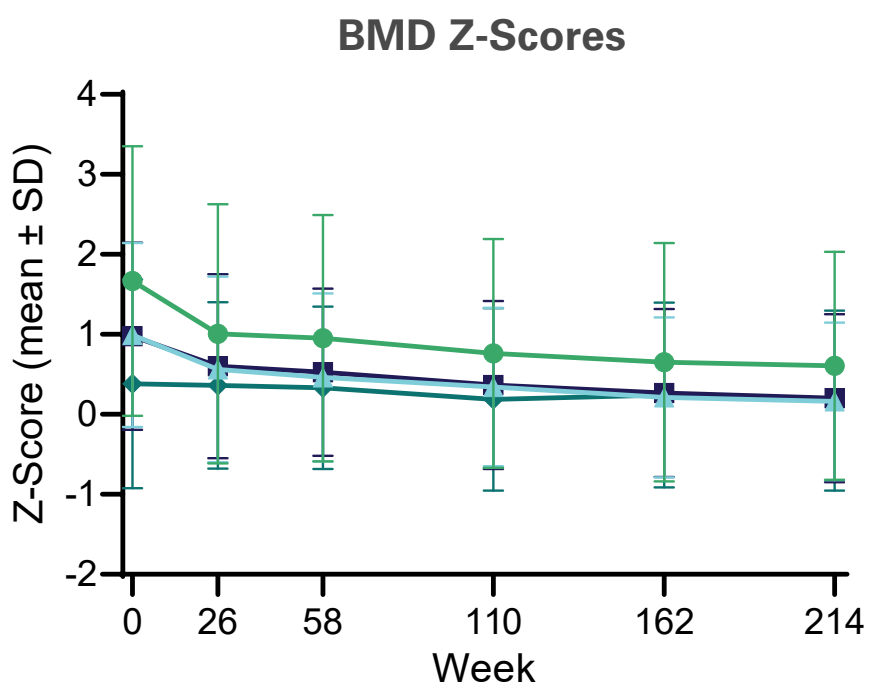
CTx and P1NP Were Consistent From Week 110 Through Week 214

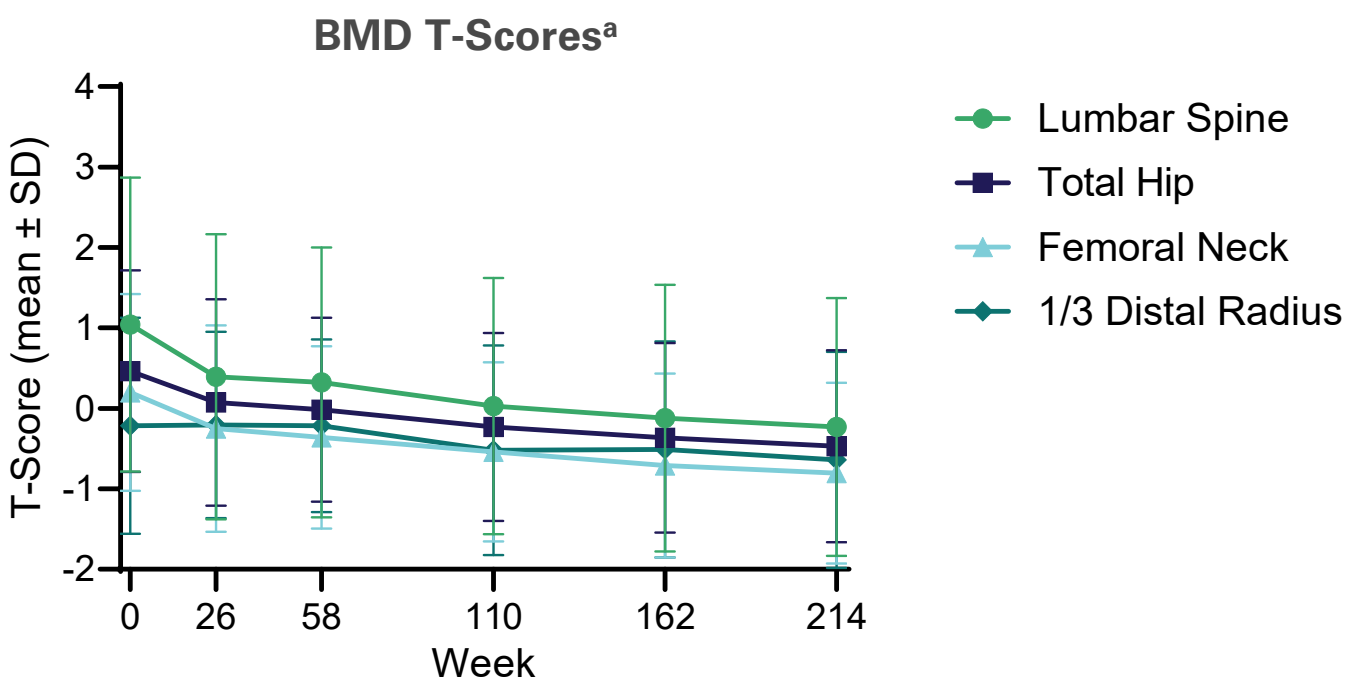




CTx: n=58 at week 0; n=46 at week 12; n=55 at weeks 26 and 110; n=57 at week 58; n=54 at week 162 and 214. P1NP: n=59 at week 0, n=47 at week 12; n=56 at weeks 26, 58, 110, 162, and 214.
CTx, C-terminal telopeptide of type 1 collagen; P1NP, procollagen type 1 N-terminal propeptide; SD, standard deviation.

Bone Mineral Density by DXA: Consistent From Week 26 Through Week 214

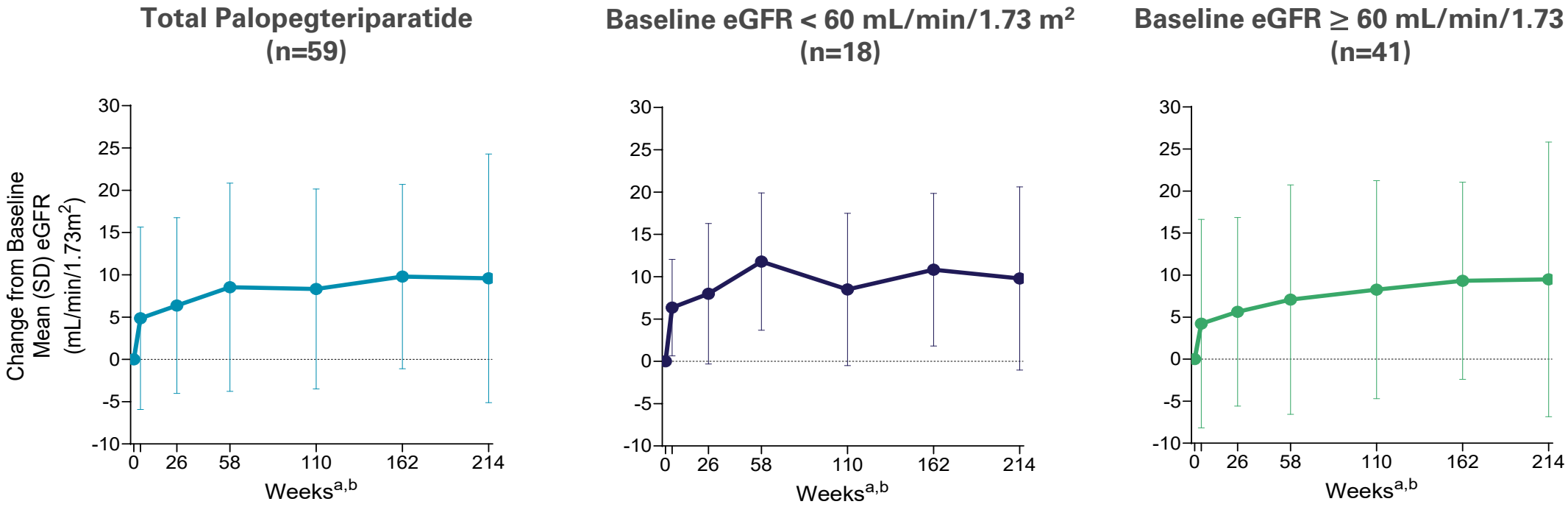




Mean T- and Z-scores were elevated at baseline and remained within the normal range

Lumbar spine, total hip, and femoral neck: n=57 at week 0; n=46 at weeks 26 and 58; n=55 at weeks 110 and 162; n=54 at week 214. 1/3 distal radius: n=55 at week 0; n=43 at weeks 26and 58; n=53 at week 110; n=52 at week 162 and 214.
BMD, bone mineral density; DXA, dual X-ray absorptiometry; SD, standard deviation.
[a] T-score reference point: young (30-year-old) Caucasian adult (Kanis JA. *Lancet*. 2002;359:1929–36).

eGFR Increase With Palopegteriparatide Treatment was Sustained Through Week 214



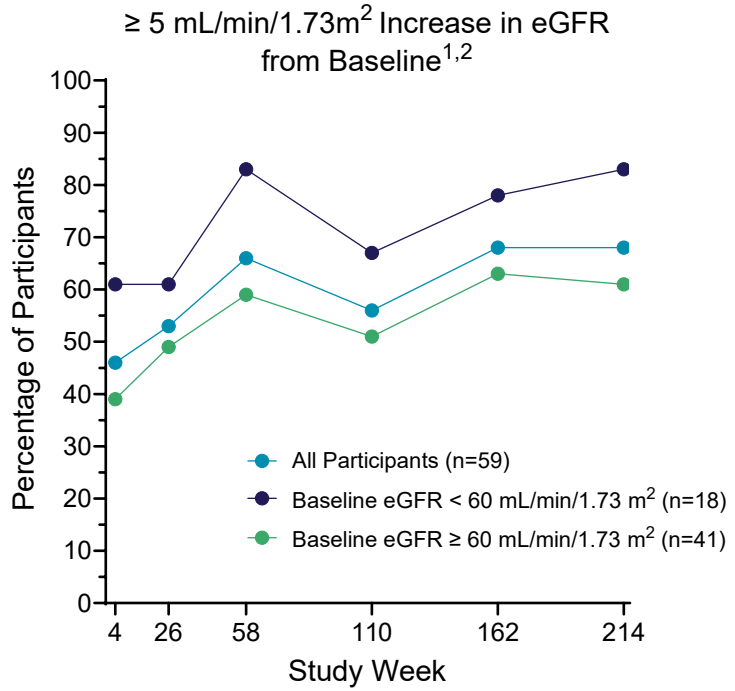
Mean (SD) eGFR for total population increased approximately 9.6 (14.7) mL/min/1.73m^2 from baseline[c]

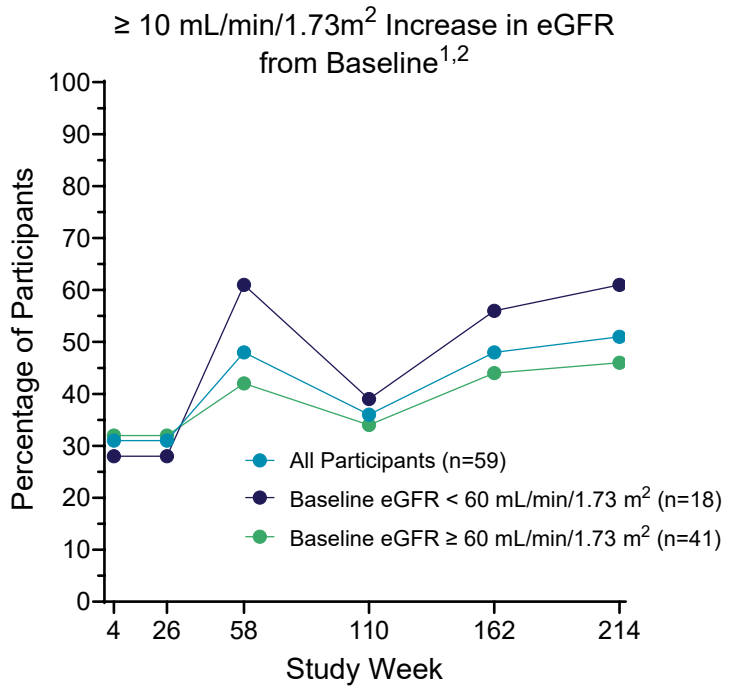
[a]All participants received TransCon PTH during the open-label extension. [b]Second (unlabeled) X-axis tick in each figure denotes 4 weeks [c]Calculated according to the Modified Diet in Renal Disease Equation (MDRD): eGFR (mL/min/1.73 m2) = 175 × (serum creatinine mg/dL)$^{-1.154}$ × (age)$^{-0.203}$ × 0.742 [if female] × 1.212 [if Black].

Total palopegteriparatide: n=59 at week 4; n=58 at week 58; n=56 at week 214; n=55 at weeks 26, 162; n=53 at week 110. Baseline eGFR < 60 mL/min/1.73 m^2: n=18 at weeks 4, 58, 214; n=17 at weeks 26, 162; n=16 at week 110. Baseline eGFR ≥ 60 mL/min/1.73 m2: n=41 at week 4; n=40 at week 58; n=38 at weeks 26, 162, 214; n=37 at week 110.

eGFR, estimated glomerular filtration rate; SD, standard deviation

Proportions of Participants With ≥ 5 and ≥ 10 mL/min/1.73 m^2 Increases in eGFR





Most participants (67.8%)[a] had a clinically meaningful[1,2] ≥ 5 mL/min/1.73 m^2 increase in eGFR at week 214

[a] Percentages calculated based on ITT population.

1. Mayne TJ, et al. *Clin Transplant*. 2021;35(7):e14326.
2. Ku E, et al. *J Am Soc Nephrol*. 2016;27(7):2196-204.

Treatment-Emergent Adverse Events Summary Through Week 214

TEAEs during palopegteriparatide treatment, n (%)	All palopegteriparatide (N = 59)
Any TEAE	58 (98.3)
Serious TEAE	7 (11.9)
Serious treatment-related TEAE	0
Treatment-related TEAE	27 (45.8)
Treatment-related TEAEs occurring in ≥ 5% of participants	
Headache	7 (11.9)
Hypocalcaemia	6 (10.2)
Hypercalcaemia	4 (6.8)
Nausea	4 (6.8)
Paraesthesia	4 (6.8)
TEAE related to hypercalcaemia or hypocalcaemia leading to ED/urgent care visit and/or hospitalization	0
TEAE leading to discontinuation of trial or of study drug	0
TEAE leading to death	0

Most TEAEs were mild or moderate and not related to study drug; no new safety signals were identified

ED, emergency department; PTH, parathyroid hormone; TEAE, treatment-emergent adverse event.

Conclusions

Palopegteriparatide demonstrated sustained efficacy and safety over a 4-year period

- 93% of remaining participants were independent from conventional therapy and 98% had normal albumin-adjusted serum calcium levels at Week 214
- Mean BMD T- and Z-scores declined from elevated baseline levels and stabilized within the normal range through Week 214
- eGFR increased with palopegteriparatide treatment and was sustained through Week 214
- Palopegteriparatide was generally well tolerated, with no treatment discontinuation due to related adverse events