5-Year Data from the Phase 2 PaTH Forward Trial of TransCon PTH in Adults with Hypoparathyroidism

June 2026

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PTH Therapy for Hypoparathyroidism

- An intact PTH axis maintains normal serum and urine calcium and phosphate homeostasis[1,2,3]
- PTH is the primary regulator of calcium/phosphate balance, acting directly on bone and kidney, and indirectly on the intestine[4,5]
- Conventional therapy for hypoparathyroidism (active vitamin D (calcitriol) and oral calcium) aims to alleviate hypocalcemic symptoms but fails to restore normal PTH physiology[6]
- PTH replacement therapy for hypoparathyroidism should provide PTH levels within the physiological range and restore downstream calcitriol, promoting independence from conventional therapy and normalizing:
  - Serum and urine calcium and phosphate
  - Skeletal health
  - Quality of life

PTH = parathyroid hormone

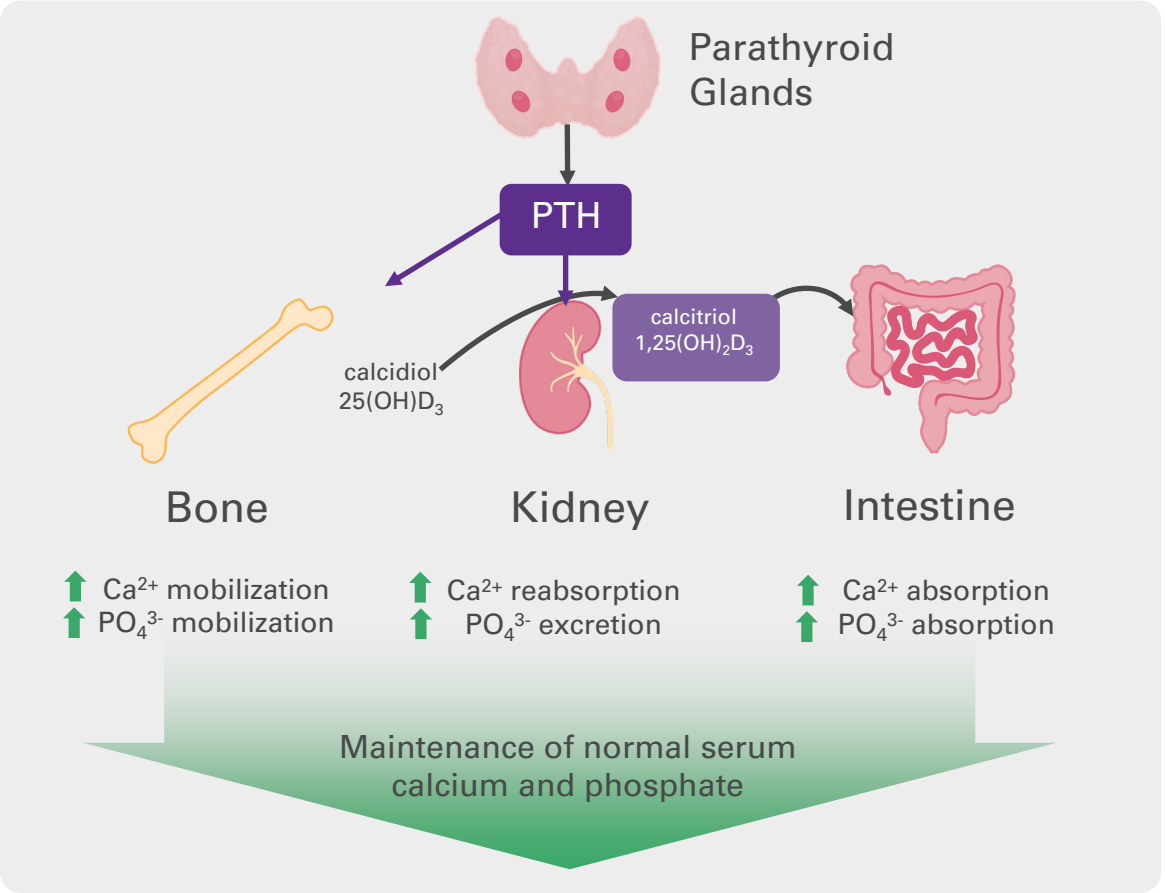
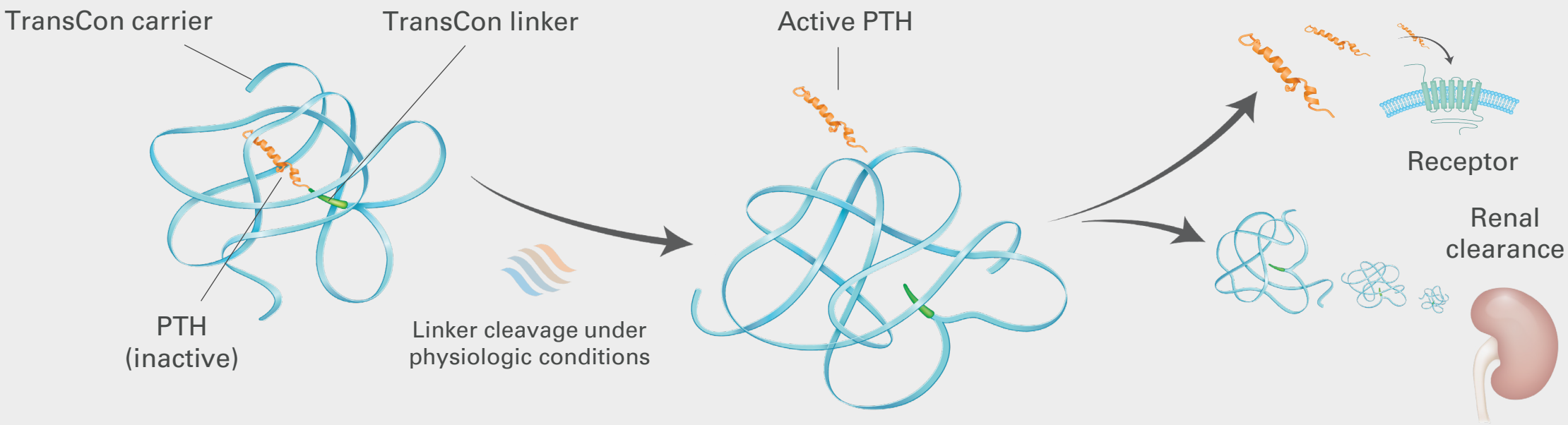


Figure adapted from Shoback D. *N Engl J Med.* 2008;359:391-403.[7]

1. Khan AA, et al. *J Bone Miner Res*. 2022;37:2568-2585. 2. Shoback DM, et al. *J Clin Endocrinol Metab*. 2016;101(6):2300-2312. 3. Bilezikian JP, et al. *J Clin Endocrinol Metab*. 2016;101(6):2313-2324. 4. Mannstadt M, et al. *Nat Rev Dis Primers*. 2017; 3:17055. 5. Brandi ML, et al. *J Clin Endocrinol Metab* 2016;101(6):2273-83. 6. Khan AA, et al. *Eur J Endocrinol*. 2019;180(3):R33-63. 7. Shoback D. *N Engl J Med*. 2008;359:391-403.

TransCon® PTH (Palopegteriparatide) Design

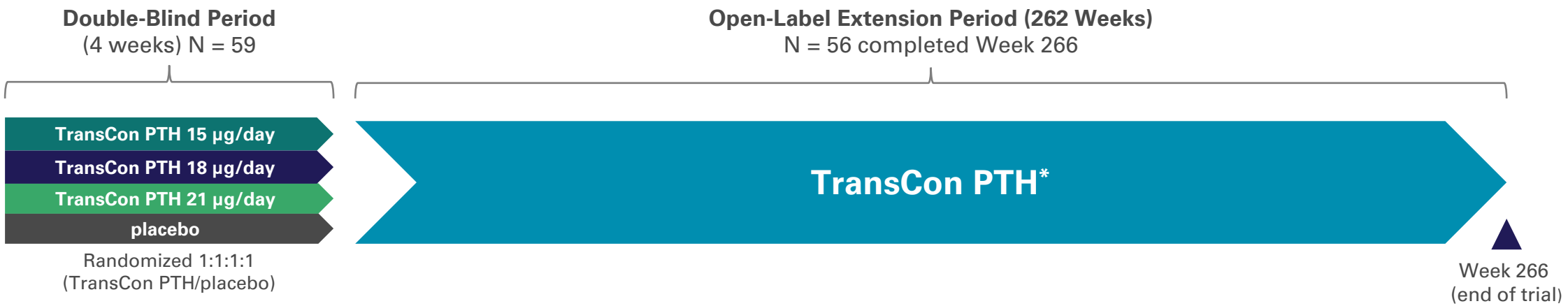


- TransCon PTH is a prodrug of PTH (1-34), administered once daily, that provides active PTH within the physiological range for 24 hours per day[1,2]
- TransCon PTH has received regulatory approval in the US[a], EU[b], and other jurisdictions

PTH = parathyroid hormone; TransCon = transient conjugation.
[a] Indicated for the treatment of hypoparathyroidism in adults. [b] Indicated for the treatment of adults with chronic hypoparathyroidism.
1. Karpf DB, et al. *J Bone Miner Res*. 2020;35(8):1430-1440. 2. Holten-Andersen L, et al. *J Bone Miner Res*. 2019;34(11):2075-2086.

Phase 2 PaTH Forward Trial Design

Randomized, double-blind, placebo-controlled trial followed by an open-label extension period in adults with chronic hypoparathyroidism



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, Renal, and PRO 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
- Hypoparathyroidism Patient Experience Scales (HPES) assessments evaluating symptoms and functional impacts

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; PRO = patient-reported outcomes.* TransCon PTH (palopegteriparatide) 6-60 ug/day and conventional therapy titrated per algorithm to maintain normocalcemia.

Baseline Demographics & Disease Characteristics

	All participants (N = 59)
Age (years), mean (SD)	50 (12)
Sex, n (%) female	48 (81)
Postmenopausal, n (%)	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)
Duration of hypoparathyroidism (years), median (range)	9 (1 to 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.

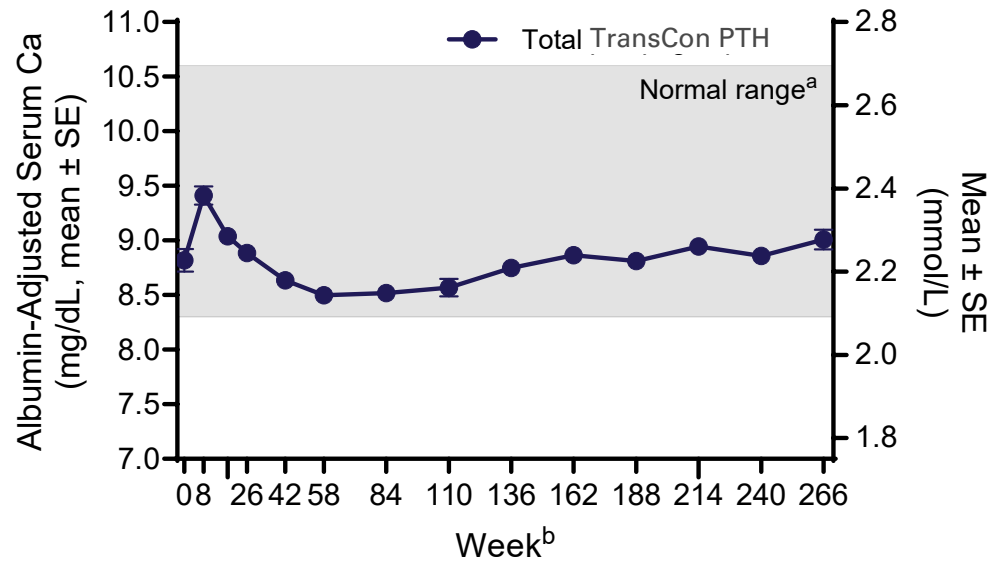
Sustained Independence from Conventional Therapy Observed in High Proportion of Participants

	Total TransCon PTH
Number of participants continuing through Week 266	56
Normal albumin-adjusted serum calcium,[a] n (%)	49 (88%)
Independence from active vitamin D,[b] n (%)	54 (96%)
Independence from therapeutic doses of calcium,[b] n (%)	53 (95%)

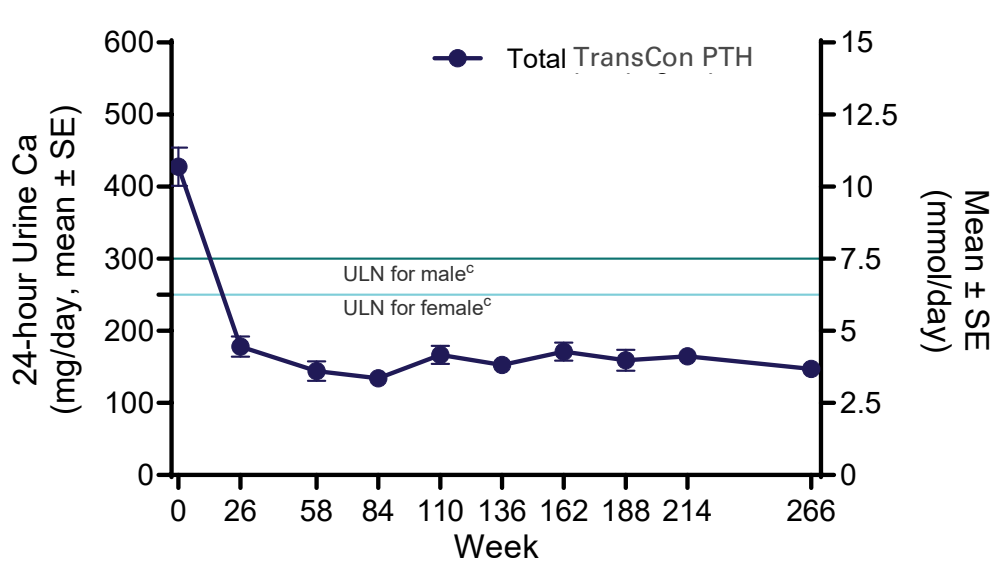
[a]Normal albumin-adjusted serum calcium levels defined as 8.3-10.6 mg/dL. [b]Independence defined as a standing dose of active vitamin D equal to zero and elemental calcium ≤600 mg on the day prior to the Week 266 visit
Percentages are calculated based on participants who had data on all criteria.

Consistency of Mean Serum and Urine Calcium Values Observed Over 5 Years of Treatment

Mean Serum Calcium



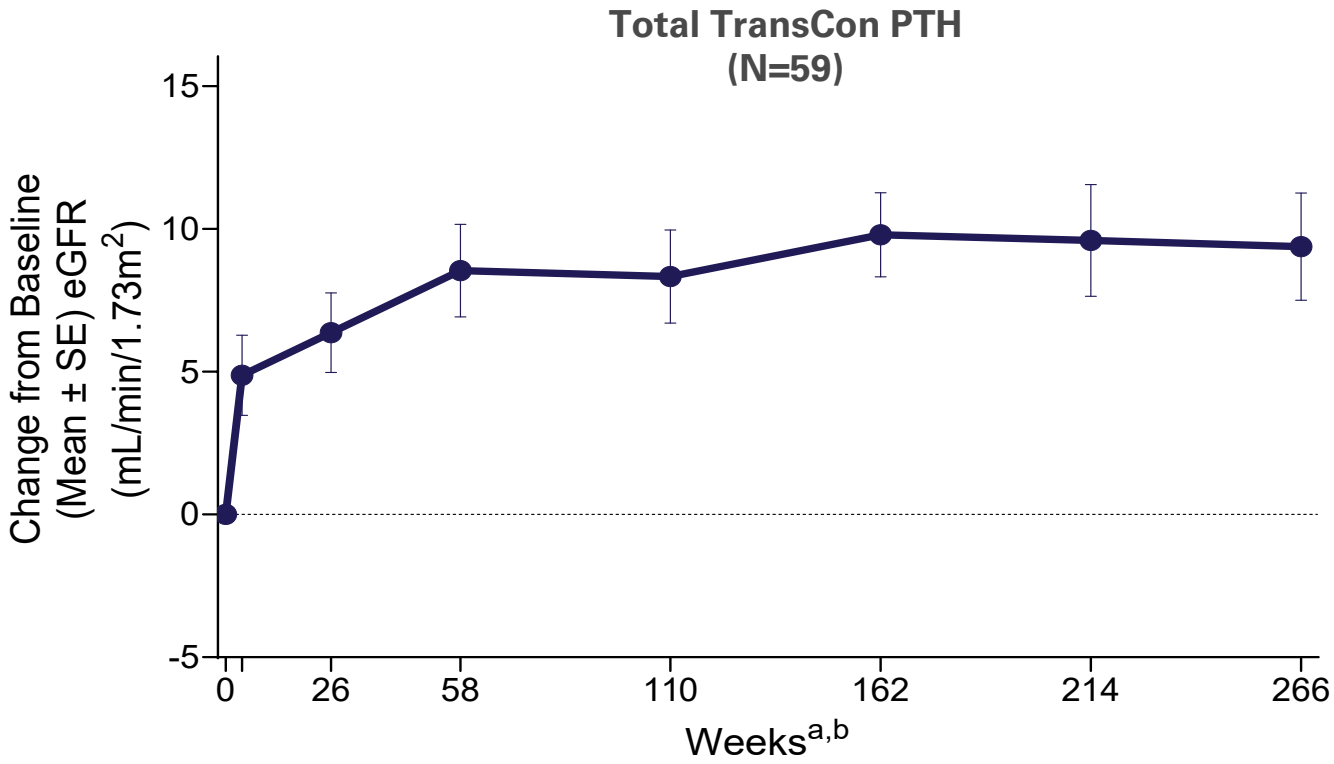
Mean 24-Hour Urine Calcium



Mean serum calcium values remained within the normal range throughout the trial
24-hour urine calcium normalized within 26 weeks and remained normal through Week 266

Ca = calcium; SE = standard error; ULN = upper limit of normal.
[a]The shaded area represents the normal serum calcium range of 8.3-10.6 mg/dL (2.07-2.64 mmol/L). [b]Week 18 is captured by unlabeled x axis tick mark. [c]The ULN for males and females are depicted by teal and light blue lines, respectively.

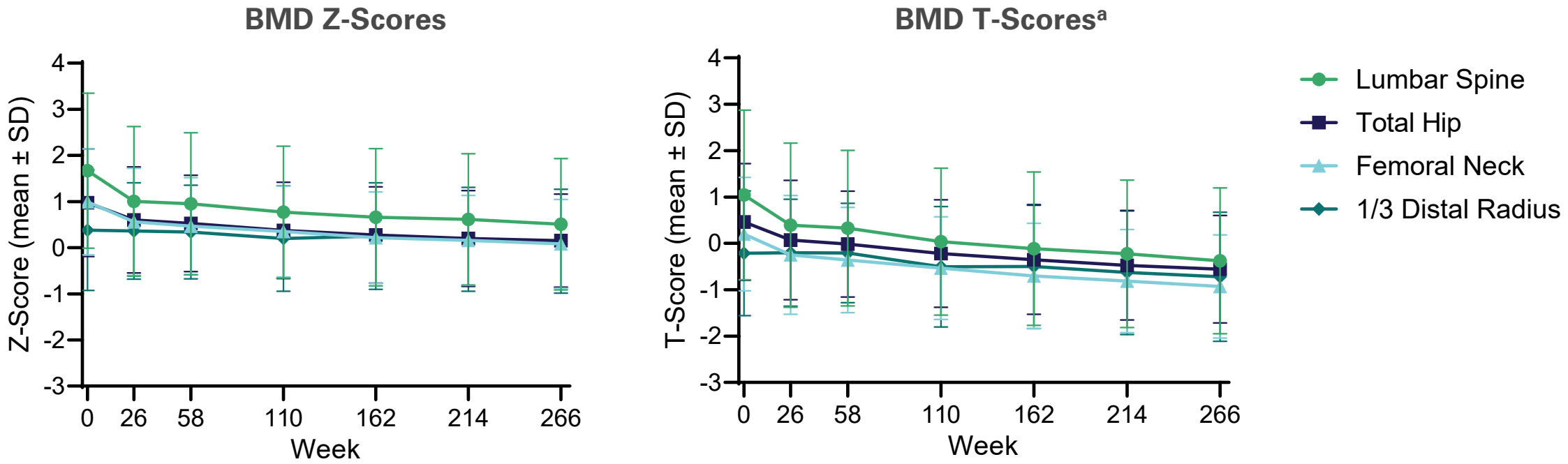
Durable Increase in eGFR Through 5 Years with TransCon PTH Treatment



The increase in eGFR from baseline was sustained through Week 266, with mean (SE) increase in eGFR of 9.4 (1.9) mL/min/1.73m^2 for the total population[c]

[a]All participants received TransCon PTH (palopegteriparatide) during the open-label extension. [b]Second (unlabeled) X-axis tick in each figure denotes 4 weeks [c]Calculated according to the Modification of Diet in Renal Disease Equation (MDRD): eGFR (mL/min/1.73 m^2) = 175 × (serum creatinine mg/dL)$^{-1.154}$ × (age)$^{-0.203}$ × 0.742 [if female] × 1.212 [if Black].
eGFR = estimated glomerular filtration rate; SE = standard error

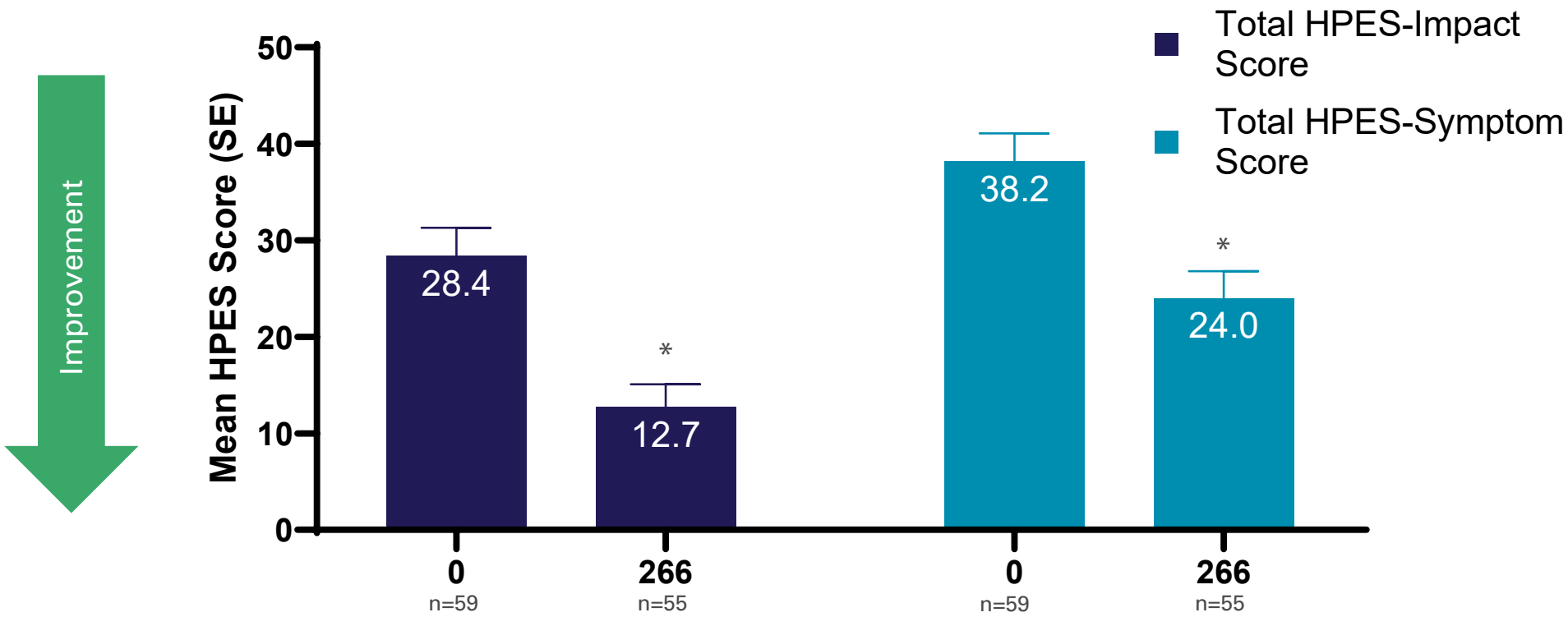
Mean Bone Mineral Density Scores Trended Towards Age- and Sex-Matched Norms



Mean BMD T- and Z-scores declined from elevated baseline levels and stayed within normal limits through Week 266

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).

Improvement in PROs with TransCon PTH Treatment Sustained Through Week 266



Hypoparathyroidism-related physical and cognitive symptoms and impacts on physical functioning and daily life improved with TransCon PTH treatment and were maintained through Week 266

* P value < 0.0001 when compared versus baseline
PRO = patient-reported outcome; HPES = Hypoparathyroidism Patient Experience Scales.

Safety Profile Over 5 Years of TransCon PTH Treatment

TEAEs during TransCon PTH treatment, n (%)	Total TransCon PTH (N = 59)
Serious TEAE	8 (13.6)
Serious treatment-related TEAE	2 (3.4)
Treatment-related TEAE	28 (47.5)
TEAE related to hypercalcemia or hypocalcemia leading to ED/urgent care visit and/or hospitalization	3 (5.1)

Treatment-related TEAEs occurring at a rate of ≥ 5% among all participants (N=59) included:

- Hypocalcemia (13.6%)
- Headache (11.9%)
- Hypercalcemia (10.2%)
- Nausea (6.8%)
- Paresthesia (6.8%)

Most TEAEs were mild or moderate and not related to study drug;
no TEAEs led to discontinuation of trial of study drug

ED = emergency department; TEAE = treatment-emergent adverse event.

PaTH Forward: Conclusions

- 82% of patients were responders for the multi-component endpoint of (1) serum calcium in the normal range, (2) taking no active vitamin D, and (3) taking ≤600 mg/day of calcium
  - Nearly all patients achieved independence[a] from conventional therapy
- Sustained normalization of 24-hour urine calcium excretion
- Sustained improvements in
  - Renal function
  - Patient reported outcomes
  - Skeletal health
- TransCon PTH was generally well tolerated, with no new safety signals identified and no treatment discontinuations due to treatment-emergent adverse events
- 95% of patients completed five years of treatment

TransCon PTH demonstrated sustained efficacy and safety during the 5-year trial

[a] Independence defined as a standing dose of elemental calcium ≤600 mg and active vitamin D equal to zero on the day prior to the Week 266 visit

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