Effets d’eneboparatide, nouvel agoniste du récepteur 1 de la PTH

Michel OVIZE, MD, PhD

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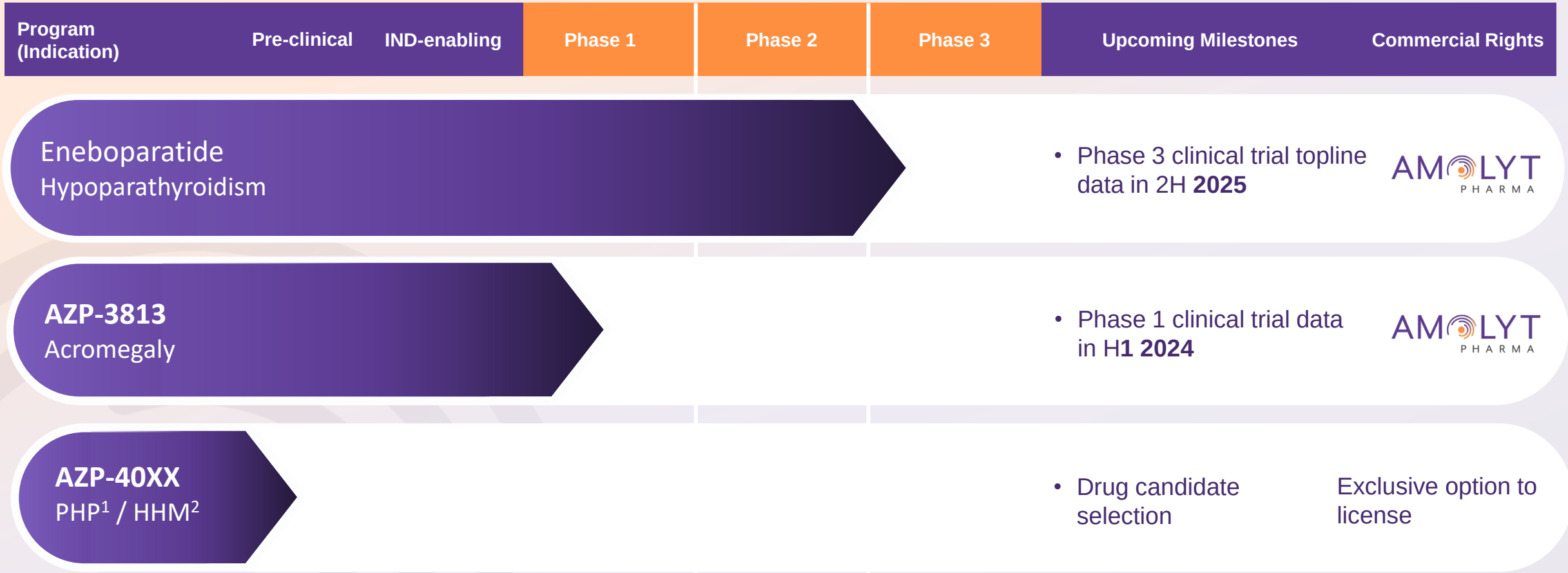
Conflict of Interest

Amolyt Pharma: Senior Medical Director

Generating Near-Term Milestones from our Product Portfolio



Additional pipeline expansion opportunities

[1] PHP: Primary Hyperparathyroidism
[2] HHM: Humoral Hypercalcemia of Malignancy

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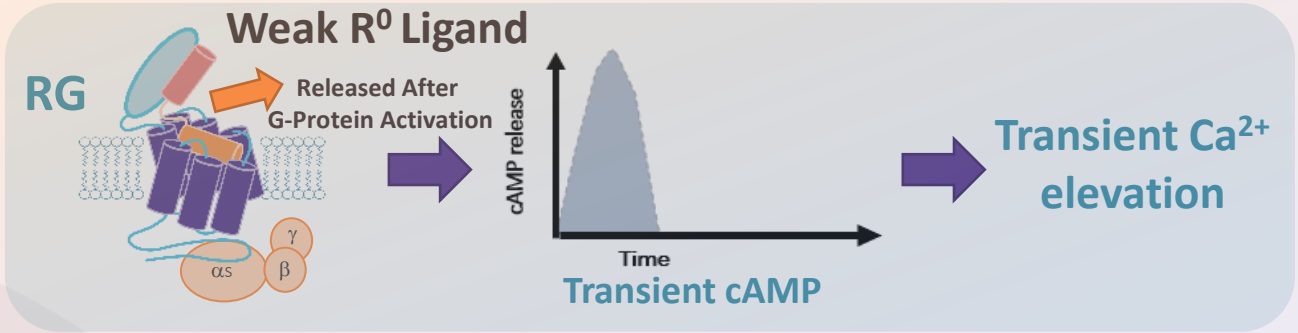
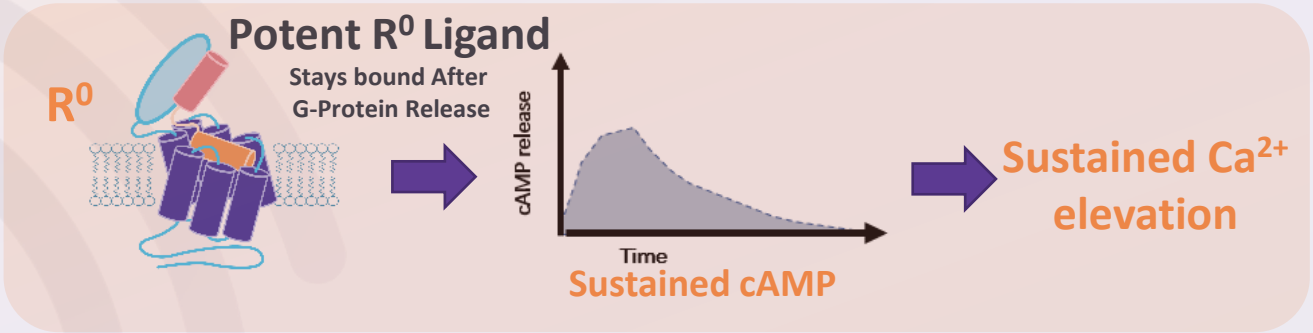
Eneboparatide Designed to Achieve Continuous Calcium Control, Restore Normal Renal Calcium Handling and Activate Normal Bone Turnover

- **Eneboparatide was specifically designed to bind with high affinity to the R^0 conformation**



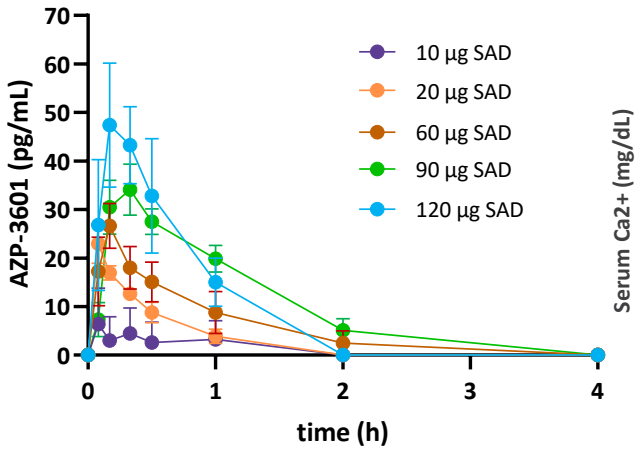


Clinical Data in Healthy Volunteers (SAD/MAD) Confirm Eneboparatide MOA

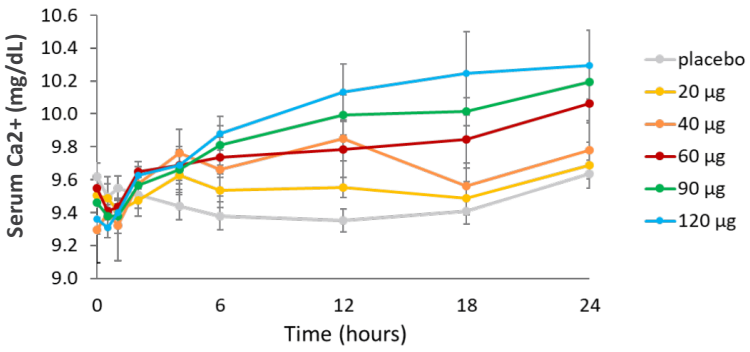
- Safety & tolerability following single and 2-week multiple ascending doses
- Efficacy as measured by sCa, uCa, bone biomarkers

Part A
Single Ascending Dose Cohort
Healthy volunteers
7 cohorts / n= 52

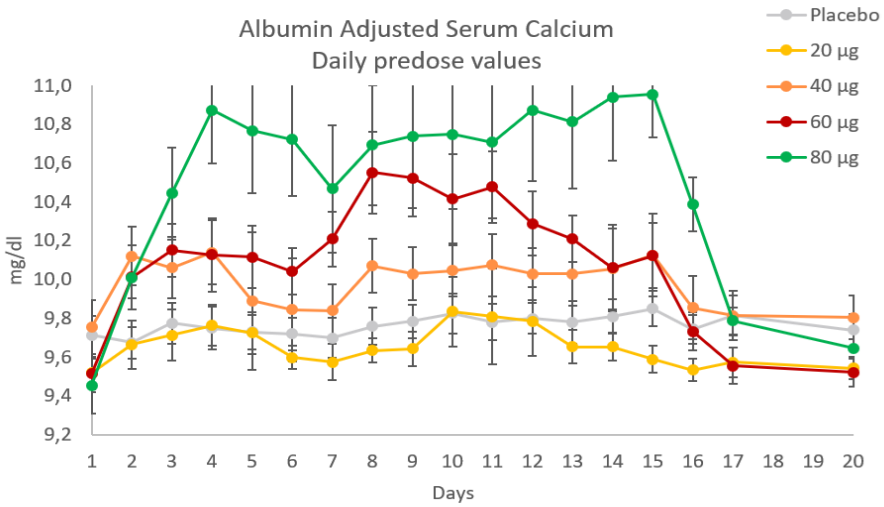
Part B
Multiple Ascending Dose Cohort
Healthy volunteers
5 cohorts / n= 50



Short PK



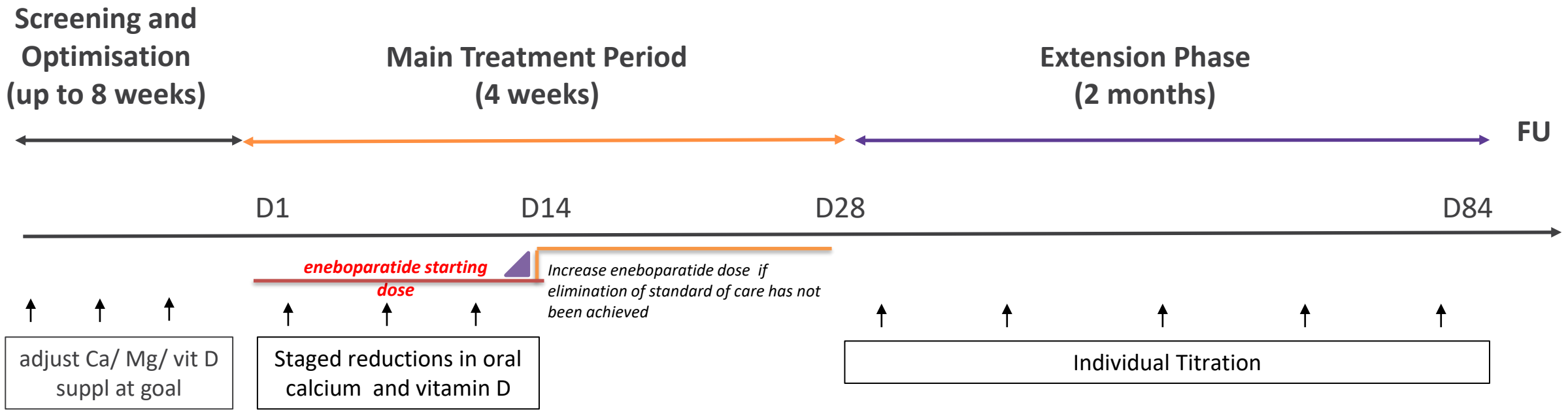
Long PD



Dose Dependent and Sustained Impact on Serum Calcium Levels

Phase 2a Trial Design

- 3-month multicenter open label study to evaluate the safety and efficacy of eneboparatide
- 2 consecutive cohorts of patients with chronic HP
  - Cohort 1: 20 µg/day as starting dose, individual titration up to 60 µg/day
  - Cohort 2: 10 µg/day as starting dose, individual titration up to 80 µg/day



Target range for serum calcium defined as 7.8 to 9 mg/dL

Baseline Characteristics

	Cohort 1 N=12	Cohort 2 N=16	All N=28
Mean age, yrs (SD), min-max	62.7 (9.7), 44-72	54 (11.2), 26-72	57.7 (11.3), 26-72
Female, n (%)	9 (75%)	12 (75%)	21 (75%)
Mean BMI, kg/m^2 (SD), min-max	28.3 (4.4), 23.0-37.1	29.1 (5.4), 19.6-38	28.8 (4.9), 19.6-38
Post-menopausal women, n (%)	7 (58.3%)	7 (43.8%)	14 (50%)
Mean time since menopause, yrs, min-max	20.1, 10-33	13.5, 2-20	17.1, 2-33
Mean time since HP diagnosis, yrs, min-max	12.8, 2-31	12.3, 3-50	12.5, 2-50
Mean time since HP diagnosis (women), yrs, min-max	13, 2-31	13, 3-50	13, 2-50
Etiology of hypoparathyroidism **Post-surgery, n (%)** **Idiopathic, n (%)** **Genetic, n (%)**	 10 (83.3%) 2 (16.7%) -	 13 (81.3%) 2 (12.5%) 1 (6.3%)	 23 (82.1%) 4 (14.3%) 1 (3.6%)
Mean oral vitamin D dose, ug/day, min-max	0.67, 0.25-1	0.60, 0.25-1	0.63, 0.25-1
Mean oral calcium dose, mg/day, min-max	1,625, 1,000-3,500	1,688, 1,000-7,800	1,661, 1,000-7,800
Mean Alb-adjusted serum calcium, mg/dL, min-max	8.67, 8.10-9.20	8.70, 7.72-9.6	8.71, 7.72-9.6
Mean 24-hour urinary calcium, mg/24h, min-max	329, 143-614	331, 57-729	330, 57-729
CKD-EPI (mL/min/1.73m^2)	71.15, 46.1-90.0 (n=10)	70, 38-109 (n=11)	70.55, 38-109 (n=21)

Eneboparatide Was Well-Tolerated with a Good Safety Profile

Adverse Event	Cohort 1 N=12 n (n/N %)	Cohort 2 N=16 n (n/N %)	Total N=28 n (n/N %)
SAEs	0	0	0
AEs	36	77	113
Mild	25 (69%)	67 (87%)	92 (81%)
Moderate	11 (31%)	10 (13%)	21 (19%)
Severe	0	0	0
ISRs	4 in 4 patients	14 in 9 patients	18 in 13 patients
Hypocalcemia	2	9*	11
Hypercalcemia	3	0	3

- Eneboparatide treatment was well tolerated
- No SAEs
- Good safety profile with no safety concerns

***Hypocalcemia was more common in Cohort 2 likely due to lower starting dose (10 μg/d)**

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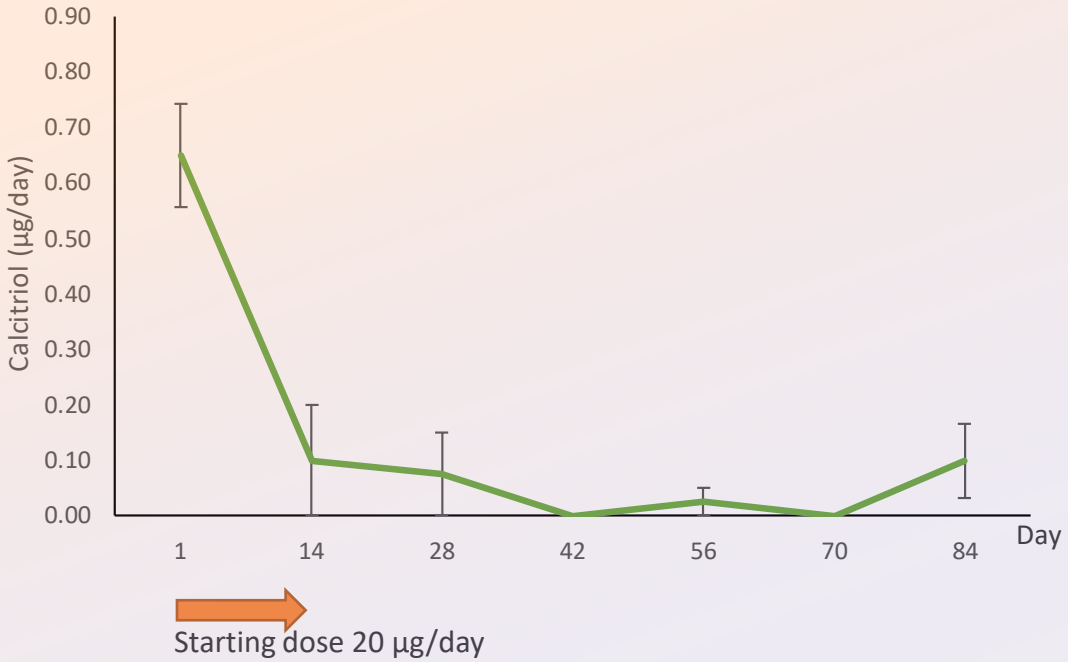
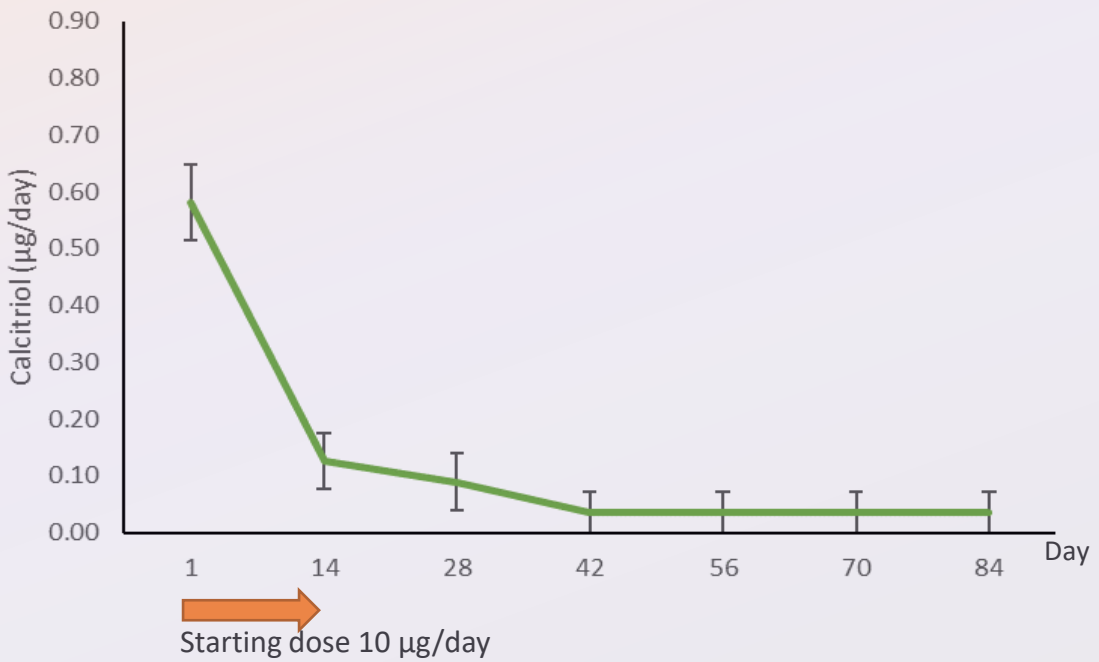
Demonstrated Potential to Eliminate Standard of Care Treatment - Calcitriol

C1 Patients who completed Extension Period, N=10



C2 Patients who completed Extension Period, N=14



For one patient, calcitriol was reintroduced at D84 instead of D85 due to a misunderstanding of the protocol

Eneboparatide enabled ***discontinuation of Vitamin D*** within two weeks of treatment initiation

Data are presented as mean ± SEM

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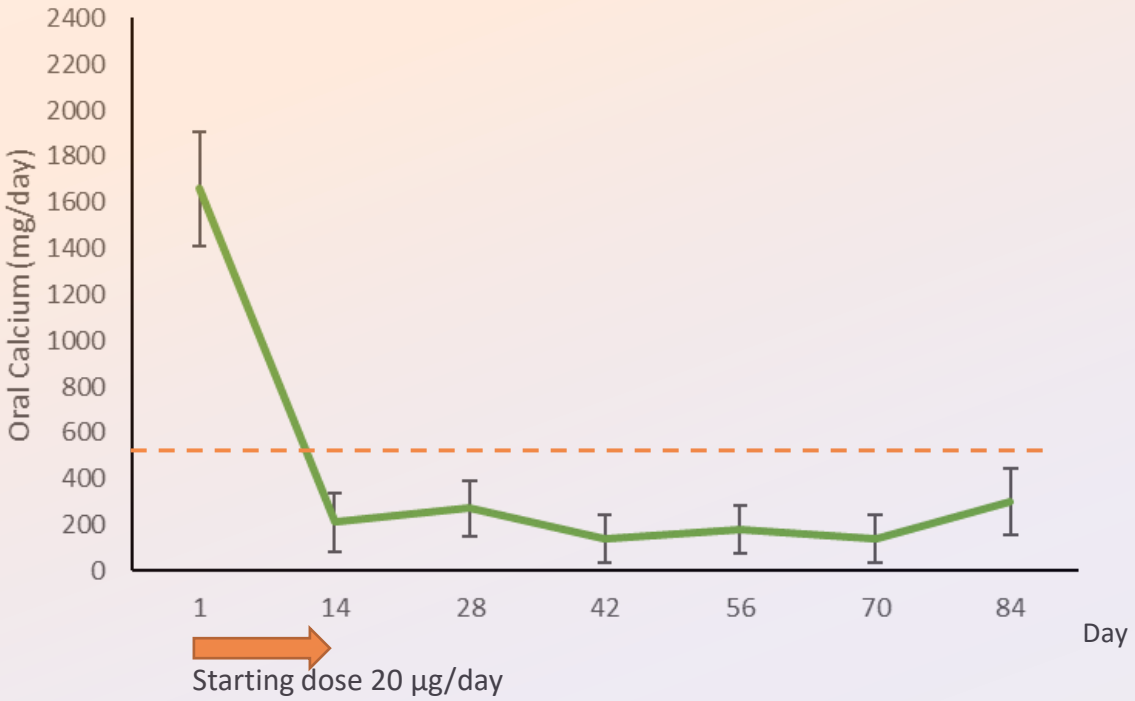
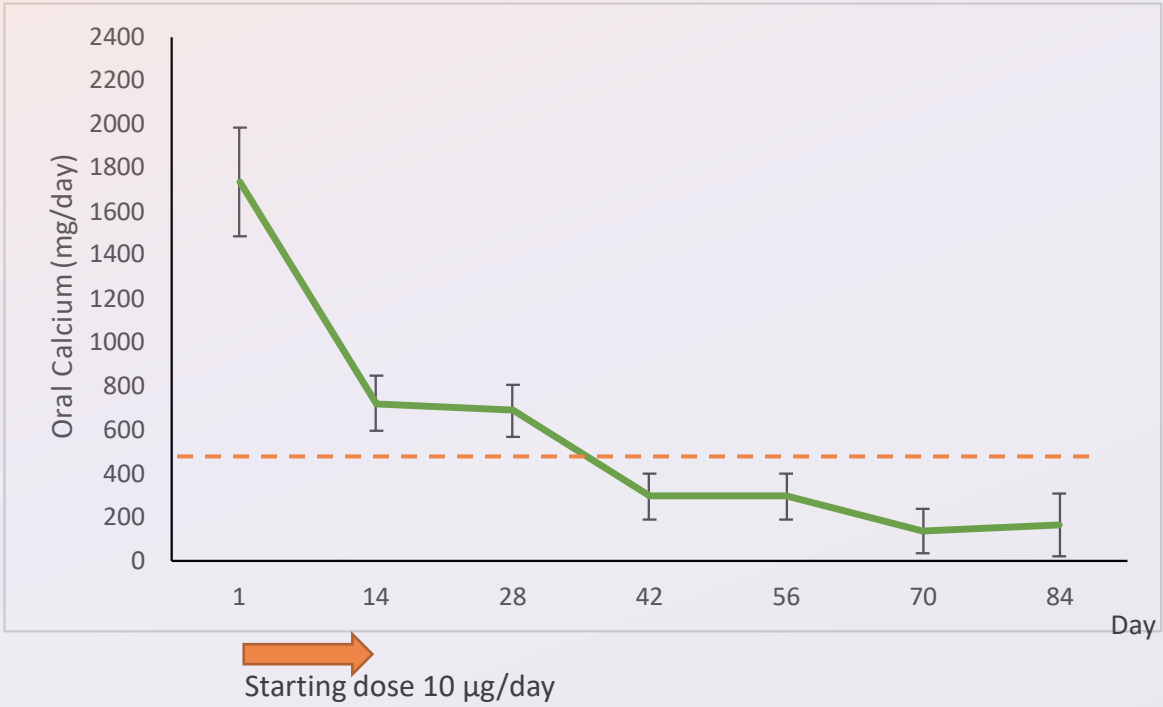
Demonstrated Potential to Eliminate Standard of Care Treatment – Oral Calcium

C1 Patients who completed Extension Period, N=10



C2 Patients who completed Extension Period, N=14



In both cohorts, eneboparatide enabled ***sustained reduction in oral calcium supplementation*** below 500mg/d. In Cohort 2, discontinuation of oral calcium supplementation was delayed and required up-titration due to the lower starting dose, supporting a ***dose-related effect***

Data are presented as mean ± SEM

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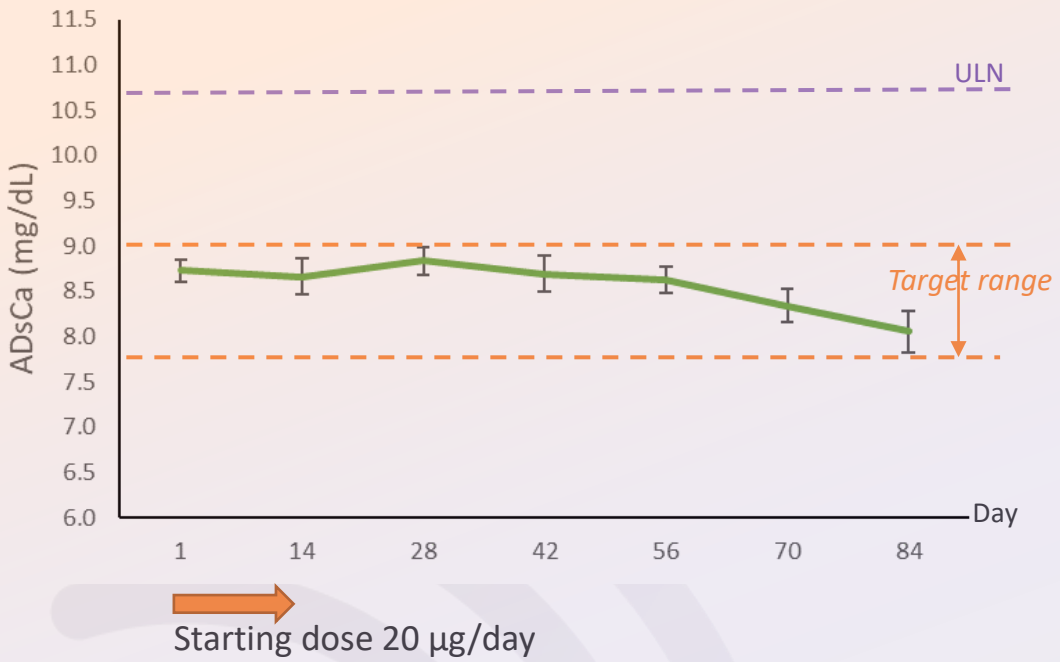
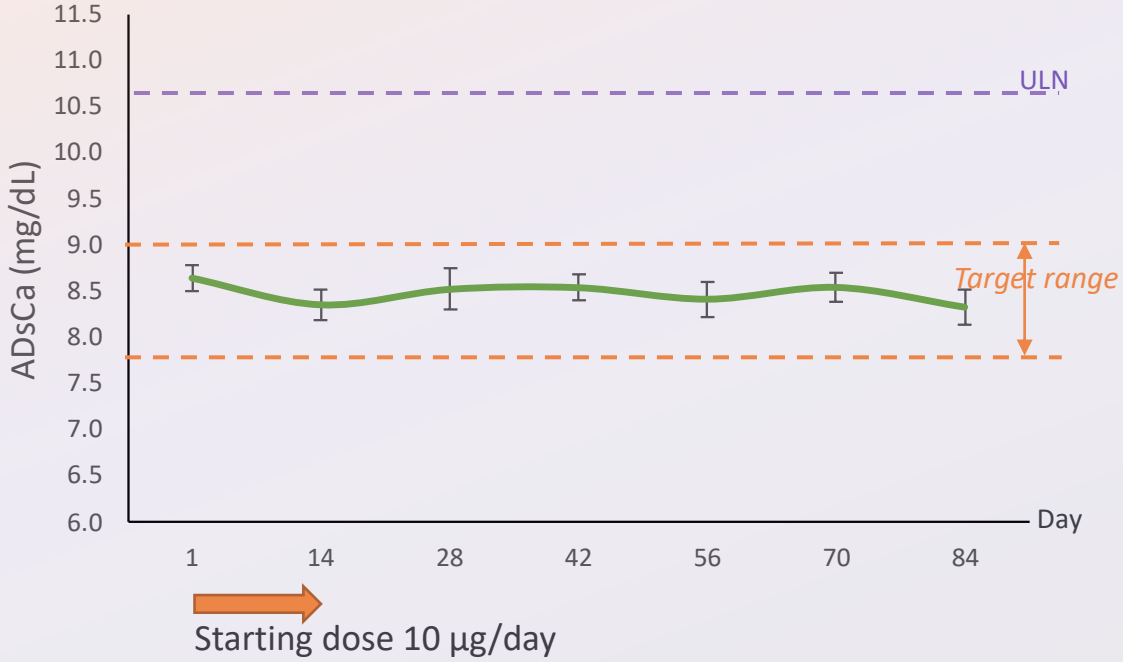
Maintained Target Mean Serum Calcium Throughout the Study Duration

C1 Patients who completed Extension Period, N=10



C2 Patients who completed Extension Period, N=14



Therapeutic Goal #1

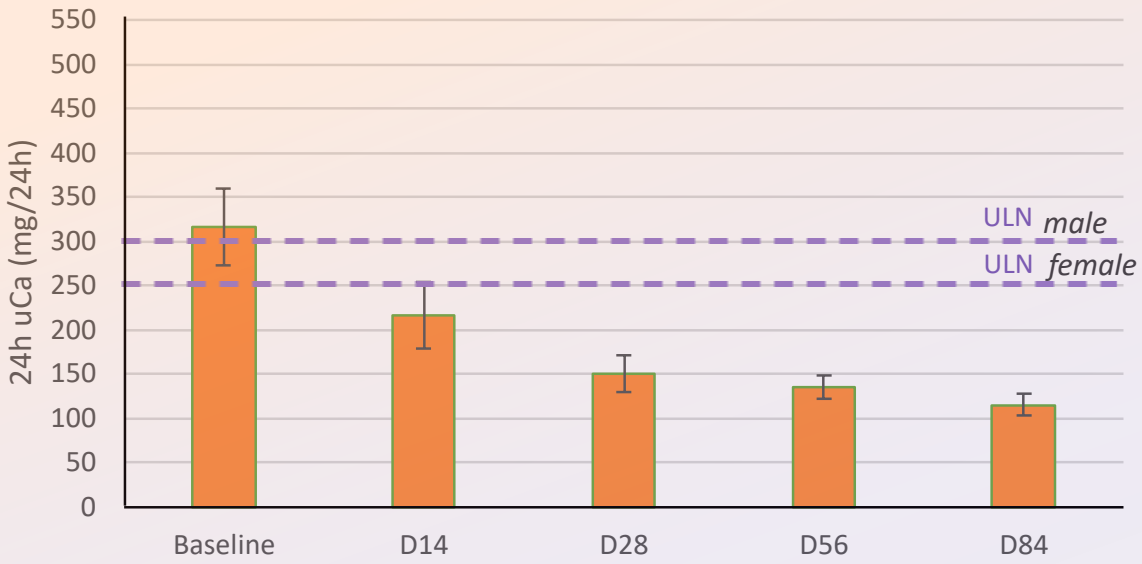
Normalization of Serum Calcium Levels and Discontinuation of SoC

ACHIEVED

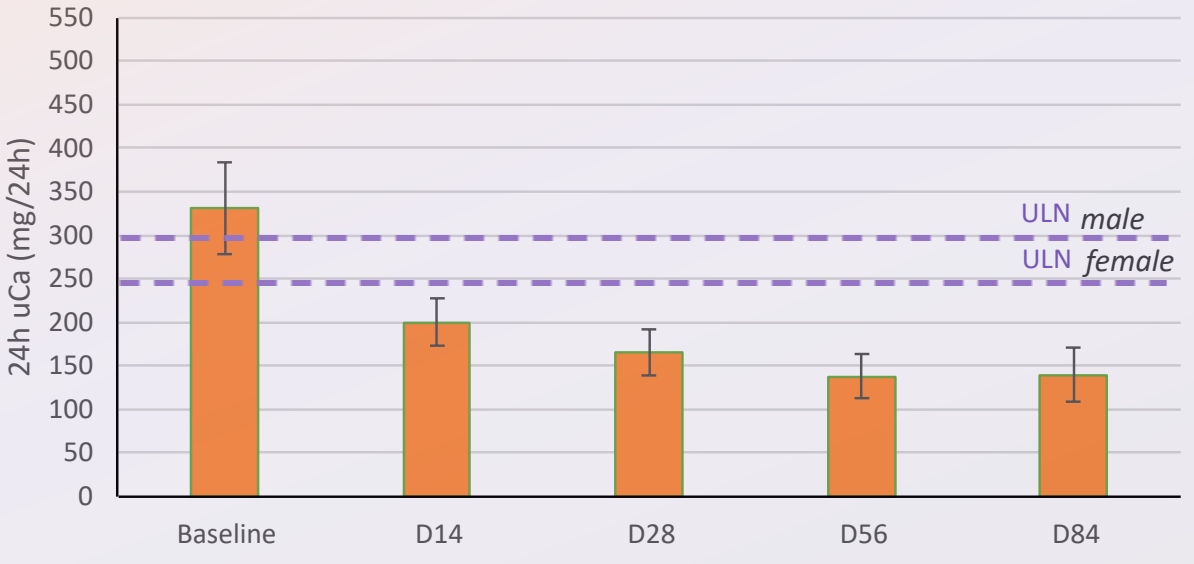
Data are presented as mean ± SEM

Induced a Rapid, Profound and Sustained Normalization of Mean 24-Hour Urine Calcium

C1 Patients who completed Extension Period, N=10



C2 Patients who completed Extension Period, N=14



Therapeutic Goal #2

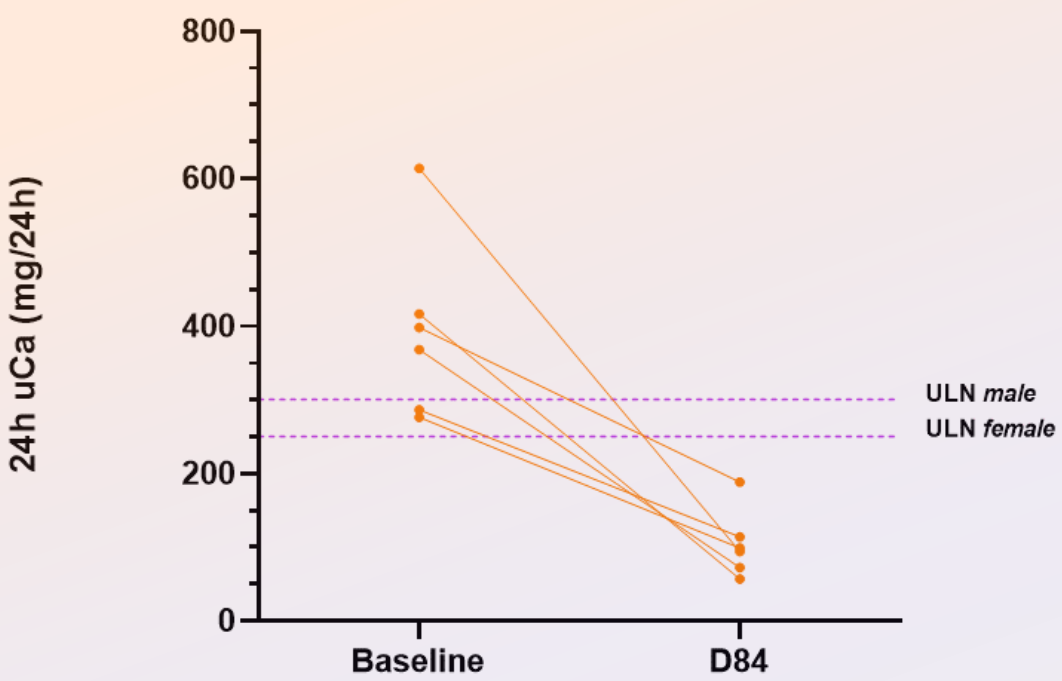
Preserve Kidney Function

ACHIEVED

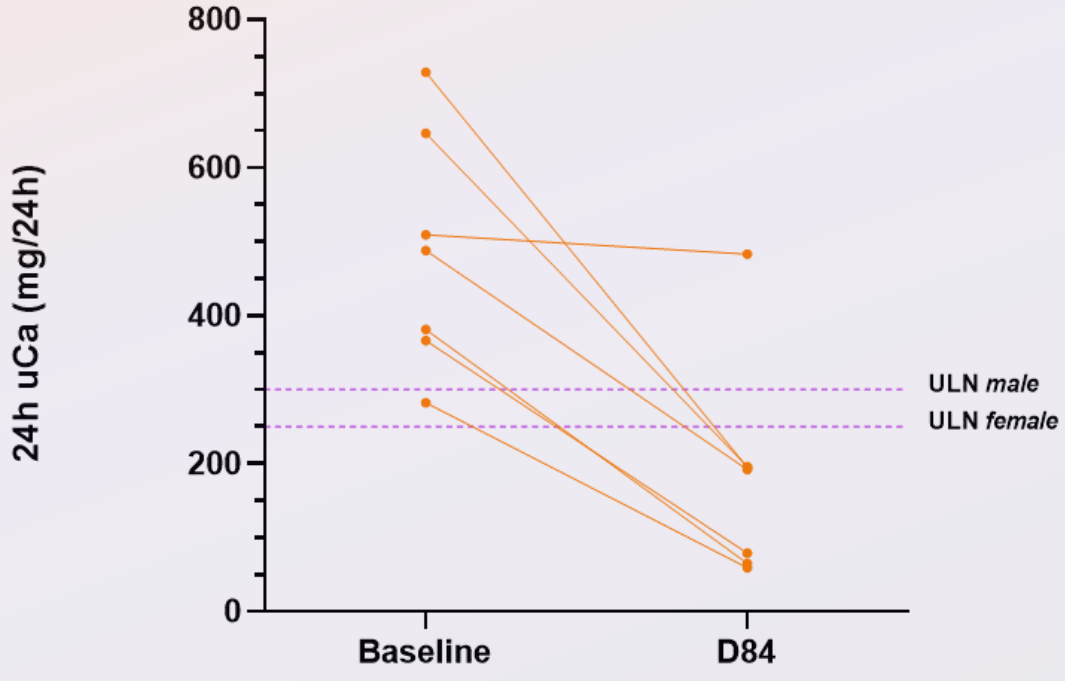
Data are presented as mean ± SEM

Mean 24h-Urinary Calcium – Patients with Elevated Urinary Ca at Baseline

C1 Patients with hypercalciuria at baseline, N=6



C2 Patients with hypercalciuria at baseline, N=7



In 12/13 (92%) patients with elevated urinary calcium at baseline, eneboparatide induced rapid, profound and sustained normalization of 24-hour urine calcium

Assessing ***normalization of urinary Ca in patients with hypercalciuric patients at baseline*** is an ***efficacy endpoint***

Showed Promising Effect on Bone for Patients at Risk of Bone Disease

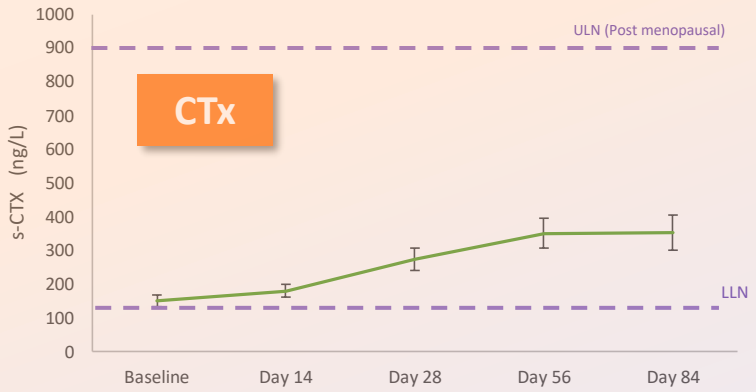
- Treatment with eneboparatide induced a gradual and mild increase in both anabolic and catabolic bone markers to the mid-normal level by 4-8 weeks
- Findings support eneboparatide's mechanism of action targets urinary calcium reabsorption rather than bone resorption
- This is a **critical differentiator** as 17-43% of patients with HP have **osteopenia or osteoporosis**; 53% are peri- or post-menopausal women

Therapeutic Goal #3

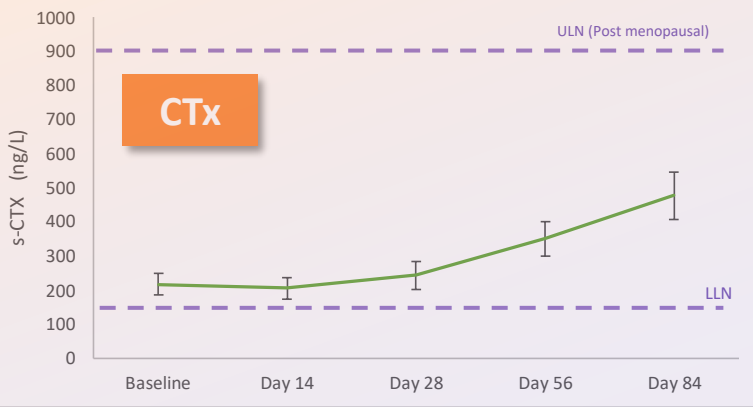
Ensure Bone Safety

ACHIEVED

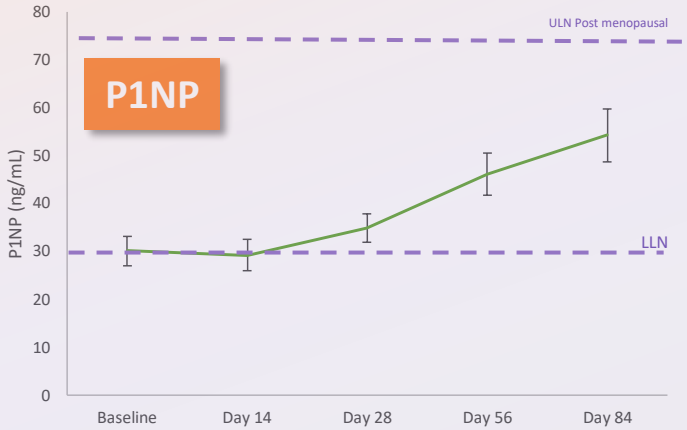
C1 Patients who completed Extension Period, N=10



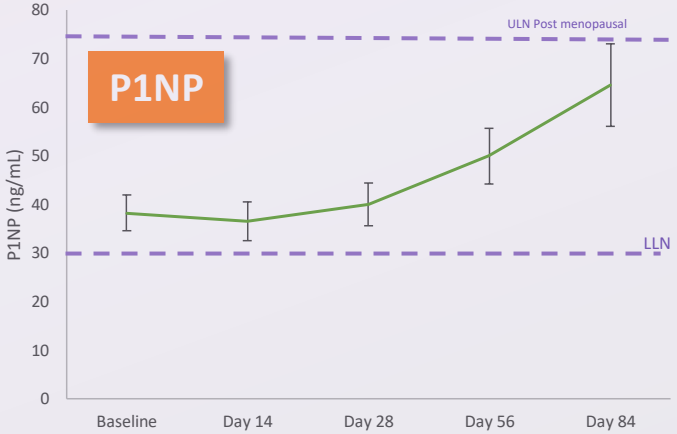
C2 Patients who completed Extension Period, N=14



C1 Patients who completed Extension Period, N=10



C2 Patients who completed Extension Period, N=14



Data are presented as mean ± SEM

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Key Takeaways

The only therapeutic, either available or in development, that can effectively address ALL THREE key therapeutic goals

1

Eneboparatide was well-tolerated at all doses administered

- No drug-related serious treatment adverse events (TEAEs) were reported
- No TEAEs leading to discontinuation of study drug

2

Subjects appeared to establish physiological calcium metabolism

- Independence from vitamin D and oral calcium achieved in most patients
- **Urinary calcium decreased and normalized in 13/14 patients with hypercalciuria**
- Bone biomarkers and BMD suggestive of restoration of balanced bone turnover

3

Next steps in Development

- Complete Phase 3 clinical trial enrolment and generate top-line data in 1H 2025

Calypso Study Design

Primary Composite Endpoint (Primary Efficacy Analysis) at Week 24

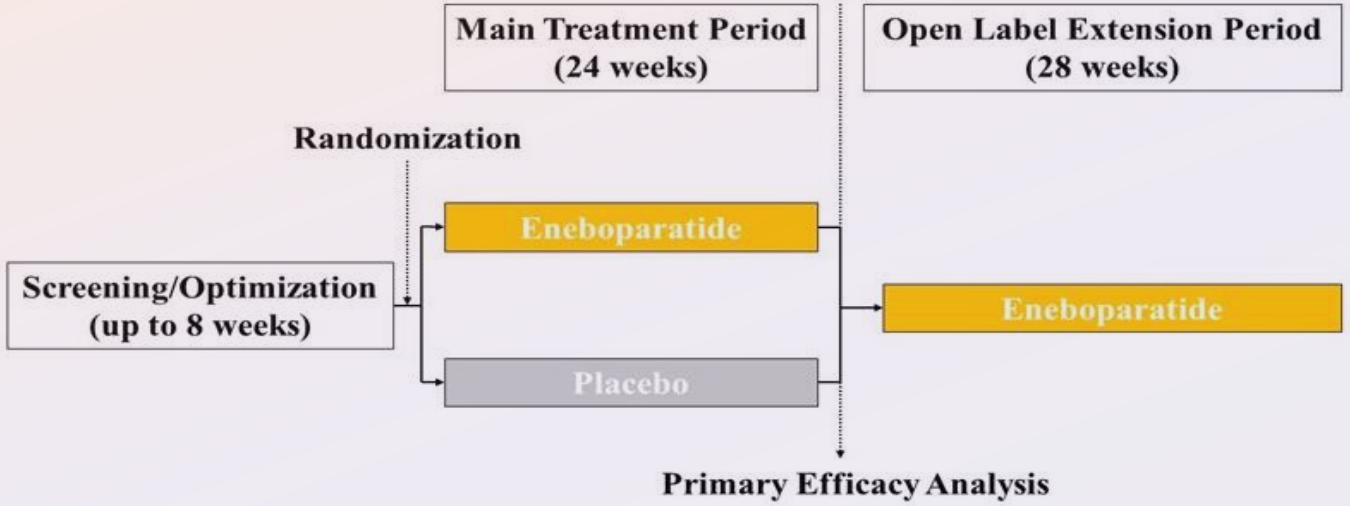
- Proportion of patients with AdsCa within the normal range and achieving independence from supplements

Key Secondary Endpoints at Week 24

- Normalization of the 24-hour urinary calcium in patients with hypercalciuria at baseline
- Disease-specific patient reported outcomes

Safety Endpoints

- Bone safety: biomarkers, BMD, TBS, HR-pQCT
- PK, ADA, AEs, Labs etc



- 165 patients to be randomized (2:1 eneboparatide : placebo)
- Minimum of 75 patients with hypercalciuria
- Stratification on etiology of chronic hypoparathyroidism (surgery vs non-surgery)