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Advancing Oral Anabolic Treatments for Osteoporosis: Pre-Clinical Data for Next-Gen EB613 Tablet Utilizing N-Tab™ Proprietary Technology

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BACKGROUND

EB613 is being developed as a first-in-class, osteoanabolic, once-daily oral PTH(1-34), teriparatide, tablet treatment for postmenopausal women with osteoporosis. EB613 was evaluated in a placebo controlled, dose ranging, 6-month Phase 2 study (NCT04003467) in 161 postmenopausal women with osteoporosis, demonstrating dose-dependent increases in bone mineral density (BMD) at the lumbar spine, total hip, and femoral neck through a dual mechanism of enhanced bone formation and reduced bone resorption (Tripto-Shkolnik et al., 2024), meeting primary and secondary endpoints. The safety and efficacy of EB613 will be further evaluated in the planned Phase 3 study.

Here, we report on the development of a next-generation of EB613 (Next-Gen EB613), based on Entera's proprietary N-Tab™ technology platform. Next-Gen EB613 is being developed as a single tablet, fixed dose, daily treatment, while maintaining the desirable pharmacokinetic (PK) profile of current EB613 tablets.

RESULTS

The PK profile following administration of a single 1.5 mg Next-Gen EB613 tablet was similar to that of 3*0.5 mg EB613 tablets in a large-animal model. AUC_{last} and T_{max} were identical (1.2 min*ng/ml and 20 min, respectively) and C_{max} was comparable between the two formulations (Table and Figure). Additionally, the Next-Gen EB613 tablet showed a trend of lower variability in both C_{max} and AUC parameters (Table).

***Table**. Pharmacokinetic parameters following administration of EB613 tablets vs Next-Gen EB613 single tablet in minipigs (Geometric mean ±SD for C_{max} and AUC; Median with range for T_{max})*

Formulation	Dosage Form	C_{max} (pg/ml)	AUC_{last} (min*pg/ml)	T_{max} (min)
EB613	3*0.5 mg	65.2 (5.9)	1217 (9.9)	20 (10-45)
Next-Gen EB613	1*1.5 mg	47.9 (3.2)	1195 (5.1)	20 (5-30)

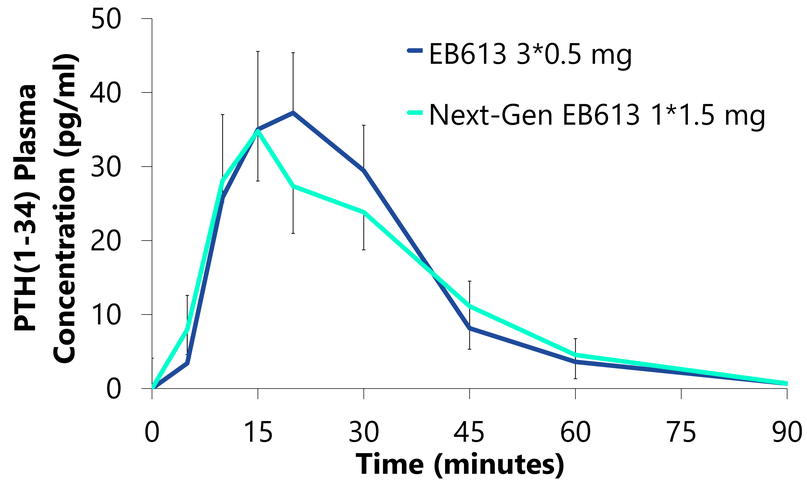

***Figure**. Pharmacokinetics following administration of EB613 tablets vs Next-Gen EB613 single tablet in minipigs (n=5; cross-over study; Geometric mean ±SD)*

METHODS

In a cross-over PK study, five (3 male and 2 female) minipigs [mean (SD) weight of 63 (±5) kg] were orally administered 1.5 mg PTH(1-34) as 3*0.5 mg clinically validated EB613 tablets vs a single 1.5 mg Next-Gen EB613 tablet on two randomized visits. To note, 1.5 mg is the planned starting dose in the upcoming Phase 3 study of EB613. Blood samples were taken via indwelling cannula at pre-determined time points and plasma PTH(1-34) was quantified by a commercial ELISA kit.

CONCLUSIONS

A single Next-Gen EB613 oral tablet demonstrated a pharmacokinetic profile comparable to the current EB613 multi-unit dosage form. These results strongly support clinical development of the single tablet dosage form for patients with osteoporosis. A Phase 1 trial is planned to initiate in late 2025.

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