EB613 (Oral PTH[1-34] Tablets) Increases BMD Over 6 Months in Early Postmenopausal Women with Low Bone Mass or Osteoporosis: A Phase 2 Randomized Trial

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OBJECTIVE

- Despite the superior benefits of bone-building (anabolic) agents and clinical guidelines recommending their use, these therapies are still underutilized, with only a minority of eligible patients receiving them. Current patient acceptance of anabolic agents is limited by the requirement for dosing by injection and their high cost. An oral anabolic tablet has the potential to address this substantial treatment gap.
- EB613 is being developed by Entera Bio Ltd. as a first-in-class, osteoanabolic, once-daily oral PTH(1-34) tablet treatment for postmenopausal women with osteoporosis at increased risk for fracture.
- EB613 was evaluated in a placebo controlled, dose ranging 6-month Phase 2 trial (NCT04003467) in 161 postmenopausal women aged 50 to 74, presenting with low bone mass or osteoporosis. Phase 2 data showed that EB613 significantly increased bone mineral density (BMD) at the lumbar spine (LS), total hip (TH), and femoral neck (FN) in a dose dependent manner, with a dual mechanism of elevated bone formation (PINP) and decreased bone resorption (CTx) (Tripto-Shkolnik et al., 2024[1]), meeting primary and secondary endpoints. The safety and efficacy of EB613 will be further confirmed in the upcoming Phase 3 trial.
- Here, we further analyze the results of the EB613 Phase 2 trial, focusing on BMD outcomes relative to time since menopause.

DESIGN

- In this post-hoc analysis, we evaluated all Phase 2 trial subjects (per protocol) from the EB613 2.5 mg dose group (n = 21), which is selected as the treatment dose in the upcoming Phase 3 trial, and placebo group (n = 38) by time since last menstrual period (LMP, ≤10 years and >10 years). Demographics are presented in Table 1.
- Percent changes in BMD from baseline to Month 6 at the LS, TH, and FN were evaluated.
- Statistical significance between EB613 and placebo groups was assessed by *t-test*.

Table 1. *Demographics*

	Mean (SD) age, years (n = number of subjects)	
	EB613	Placebo
Overall	61.0 (4.5) (n = 21)	59.8 (5.3) (n = 38)
≤10 years LMP	57.9 (4.4) (n = 8)	56.9 (3.5) (n = 19)
>10 years LMP	62.9 (3.5) (n = 13)	62.8 (5.2) (n = 19)

LMP – last menstrual period; SD – standard deviation

RESULTS

As shown in Table 2, at 6 months, in subjects with LMP ≤10 years, on EB613 (n = 8) vs placebo (n = 19), BMD increased at the LS 3.1% (p = 0.05), at the TH 2.3% (p = 0.03), and at the FN 2.0% (NS). In subjects with LMP >10 years, on EB613 (n = 13) vs placebo (n = 19), BMD increased 3.2% at the FN (p = 0.02), 2.5% at the LS (p = 0.08), and 1.5% at the TH (NS).

Table 2. *Percent change BMD from baseline to month 6*

	Mean % change (SD)		Placebo adjusted mean % change	Group difference p-value
	EB613	Placebo		
Parameter				
Overall	n = 21	n = 38		
Lumbar spine	2.6 (4.2)	-0.2 (3.4)	2.7	<0.01
Total hip	1.3 (2.8)	-0.5 (2.8)	1.8	0.02
Femoral neck	2.0 (2.5)	-0.8 (3.8)	2.8	<0.01
≤10 years LMP	n = 8	n = 19		
Lumbar spine	3.0 (4.9)	-0.1 (2.9)	3.1	0.05
Total hip	1.7 (2.0)	-0.6 (2.4)	2.3	0.03
Femoral neck	1.4 (3.3)	-0.7 (3.4)	2.0	0.17
>10 years LMP	n = 13	n = 19		
Lumbar spine	2.3 (3.9)	-0.2 (3.9)	2.5	0.08
Total hip	1.1 (3.2)	-0.4 (3.2)	1.5	0.19
Femoral neck	2.4 (1.8)	-0.9 (4.3)	3.2	0.02

LMP – last menstrual period; SD – standard deviation
EB613 vs placebo group difference p-value was determined by t-test

CONCLUSION

- Six-month treatment with EB613 in early postmenopausal women consistently increased BMD at spine and total hip, and in increments that are similar to those in women >10 years from their LMP and generally in line to the overall population.
- The safety and efficacy of EB613 will be further assessed in the upcoming Phase 3 trial. EB613 shows strong potential as the first oral anabolic tablet treatment option for postmenopausal women with osteoporosis who are at high risk for fracture, offering a promising new approach to address this unmet need.

REFERENCE

1. Tripto-Shkolnik, et al. "Oral daily PTH (1-34) tablets (EB613) in postmenopausal women with low BMD or osteoporosis: a randomized, placebo-controlled, 6-month, phase 2 study." JBMR 39(6) 2024: 672-682.

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