TX-001HR is Associated with a Clinically Meaningful Effect on Vasomotor Symptoms

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Objective
To determine the clinical meaningfulness of reductions in moderate-to-severe vasomotor symptoms (VMS) with TX-001HR in menopausal women with an intact uterus. TX-001HR is an investigational combination of 17β-estradiol and micronized progesterone (E2/P4) in a single, oral, softgel capsule.

Methods
The REPLENISH placebo-controlled, randomized trial evaluated TX-001HR in menopausal women (40-65 years) with an intact uterus. Women with hot flushes (≥7/day or ≥50/wk) were randomized to daily E2/P4 (mg/mg) 1/100, 0.5/100, 0.5/50, 0.25/50 or placebo (VMS substudy, n=726); others were randomized to E2/P4 doses only. Participants rated their VMS using the anchor-based Clinical Global Impression (CGI) score with a 7-level scale ranging from "very much improved" to "very much worse." CGI responses were further categorized as clinically meaningful (much or very much improved), minimally improved, and no change or worse (no change to very much worse). Response thresholds were determined by nonparametric discriminant analyses to define clinical responders.

Results
As assessed by the CGI, significantly more women experienced a clinically meaningful response at wk 4 to TX-001HR (50%–63%) vs placebo (33%) and at wk 12 (73%–82% vs 53%). Response thresholds were determined to be weekly reductions in frequency of ≥36 moderate-to-severe VMS at wk 4 and ≥39 at wk 12. Overall, significantly more clinical responders based on the response thresholds were found with TX-001HR (46%–59%) than with placebo (33%) at wk 4 and at wk 12 (68%–73% vs 52%).

Conclusion
TX-001HR provides clinically meaningful improvements in VMS frequency in menopausal women as determined by CGI. A consistency of effect of TX-001HR was observed with statistically significant and clinically meaningful improvements in the MENQOL questionnaire (reported elsewhere). If approved, TX-001HR may provide a new oral option to treat moderate-to-severe VMS in menopausal women with an intact uterus.