Effects of TX-001HR on Uterine Bleeding Rates in Menopausal Women with Vasomotor Symptoms

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Objective
Uterine bleeding can be associated with endometrial pathology. Recent evidence (Eden 2007, Davis 2014, Dezman 2015, Gass 2015) suggests a potential increase in uterine bleeding and endometrial cancer with compounded bioidentical hormone therapy (CBHT). The objective was to evaluate uterine bleeding with TX-001HR, an investigational, single, oral softgel capsule combination of 17β-estradiol/ progesterone (E2/P4) designed to treat moderate-to-severe vasomotor symptoms (VMS) in menopausal women, while protecting the endometrium.

Methods
The REPLENISH trial evaluated TX-001HR in menopausal women (40–65 years) with VMS and an intact uterus. Women with moderate-to-severe hot flushes (≥7/day or ≥50/wk) were randomized (1:1:1:1:1) to daily E2/P4 (mg/mg) 1/100, 0.5/100, 0.5/50, 0.25/50 or placebo (VMS substudy); all others were randomized (1:1:1:1) to E2/P4 doses only. Women (n=1835) were to complete daily bleeding (requiring sanitary protection) and spotting (not requiring sanitary protection) diaries up to 12 months to determine bleeding profiles from thirteen 28-day cycles.

Results
Cumulative amenorrhea (no bleeding or spotting) rates increased over time and were high from cycle 1 to 13 with TX-001HR (56–73%; placebo 81%). The percentage of women with no bleeding was high (74–90%) with TX-001HR. Few vaginal bleeding adverse events (1.0–4.6% TX-001HR vs 0.7% placebo) were reported and discontinuation due to bleeding was low (0.4%–1.4% vs 0%).

Conclusion
TX-001HR was associated with high amenorrhea rates and improved uterine bleeding and spotting over time, complementing adequate endometrial protection (reported separately). The amenorrhea rates reported here with E2/P4 are higher than historical comparison of HT that contains synthetic progestins. If approved, TX-001HR may provide the first oral E2/P4 combination to treat moderate-to-severe VMS in menopausal women with an intact uterus, including the millions using unapproved and inadequately studied CBHT.