

# TX-001HR Improved Quality of Life in Menopausal Women with Vasomotor Symptoms

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# Disclosures

- **Consultant/Advisory board:** AbbVie, Allergan, AMAG, Amgen, Apotex, Ascend Therapeutics, Azure Biotech, JDS Therapeutics, Merck, Millendo Therapeutics, Noven, Novo Nordisk, Nuelle, Perrigo Company, PLC, Radius Health, Regeneron, Roivant Sciences, Sanofi SA, Sebela, Sermonix, Shionogi, Sprout, Symbiotec Pharmalab, TherapeuticsMD, and Valeant
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- **Stockholder:** Sermonix Pharmaceuticals

# Menopausal VMS Treatment

- Vasomotor symptoms (VMS) in menopausal women can
  - Be bothersome<sup>1-3</sup>
  - Negatively impact quality of life,<sup>1,4</sup> sleep,<sup>1,5</sup> and work productivity<sup>4,6</sup>
- **REPLENISH trial**
  - TX-001HR (TherapeuticsMD, Boca Raton, FL) is an investigational combination of 17 $\beta$ -estradiol and progesterone in a single oral softgel capsule
  - One of the secondary endpoints was to determine the effects of four TX-001HR (E2/P4) doses versus placebo on quality of life when used for the treatment of moderate-to-severe VMS

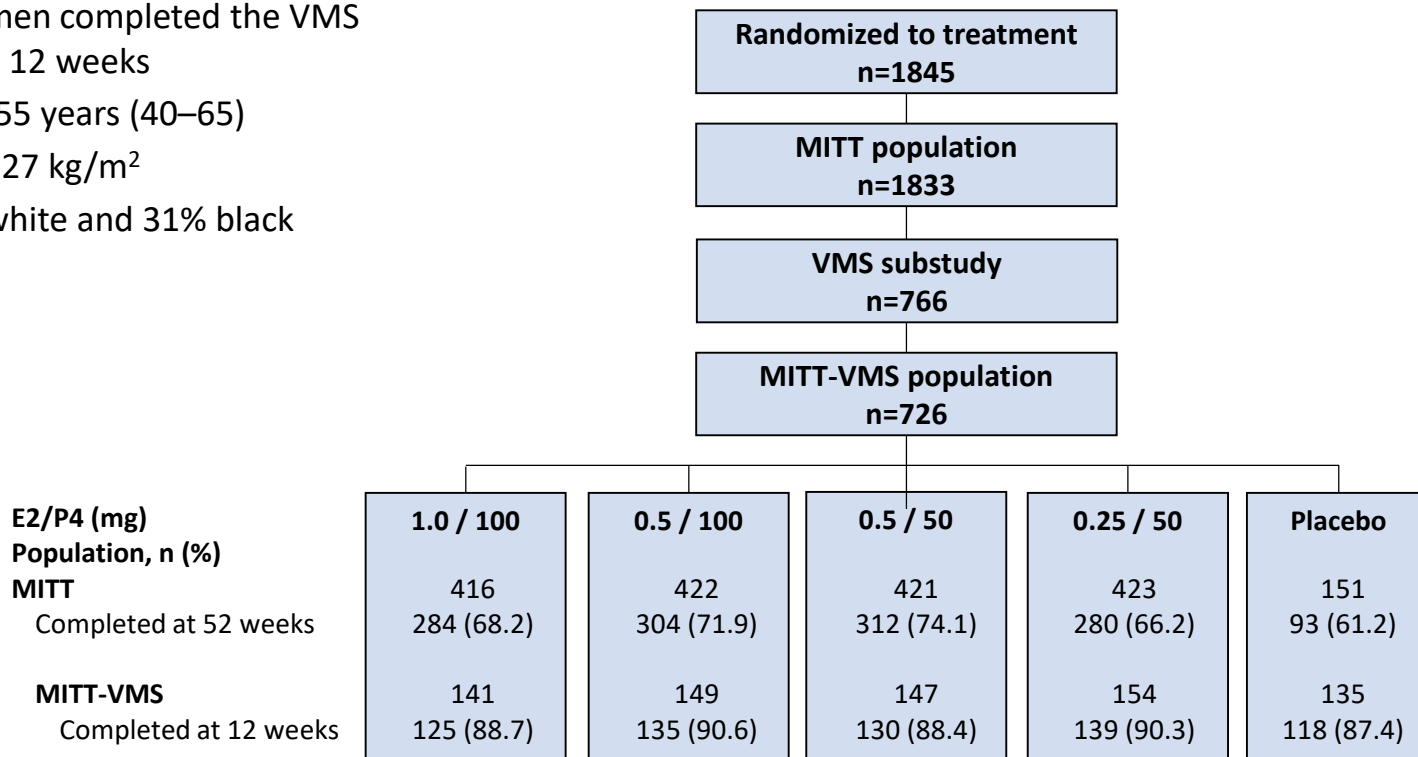
E2: estradiol; P4: progesterone.

# MENQOL Questionnaire

- Questionnaire consists of 29 items (symptoms), and if experienced were rated using a 7-item Likert scale ranging from “Not at all bothered” to “Extremely bothered”
  - Items are grouped to form 4 domains: vasomotor (3 items), psychosocial (7 items), physical (16 items) and sexual (3 items)
- Subjects were administered the MENQOL questionnaire at baseline, week 12 and at months 6 and 12
  - Baseline changes in the MENQOL overall and subdomain scores were assessed in the VMS substudy population
- Pearson correlations were assessed between changes in MENQOL scores and changes in moderate-to-severe VMS frequency at 12 weeks
- Changes in MENQOL were used to calculate clinically important changes

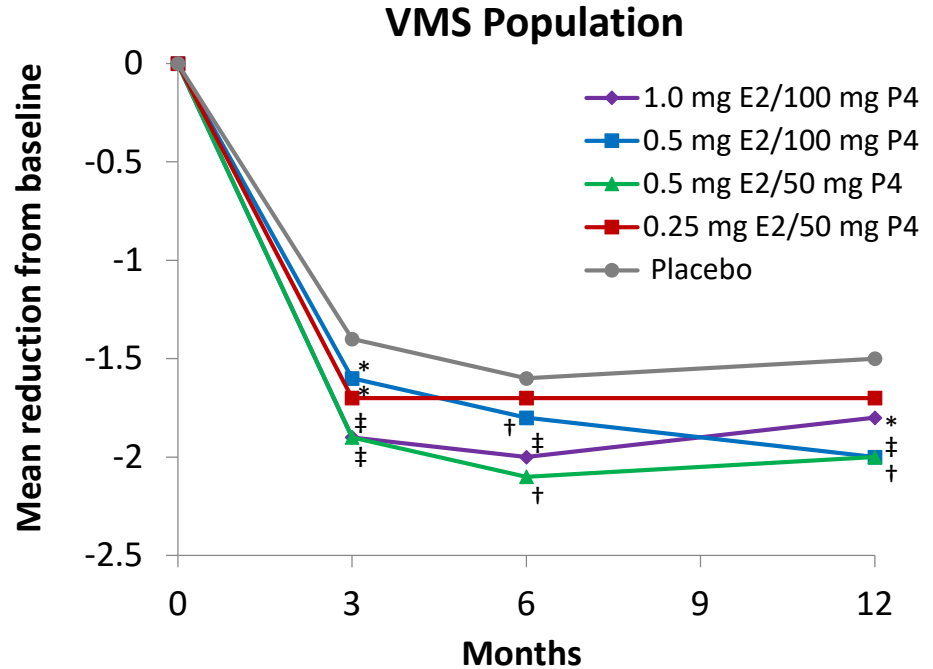
# Disposition and Demographics

- 89% of women completed the VMS substudy at 12 weeks
- Mean age: 55 years (40–65)
- Mean BMI: 27 kg/m<sup>2</sup>
- 67% were white and 31% black



# Improvements in MENQOL Overall Score

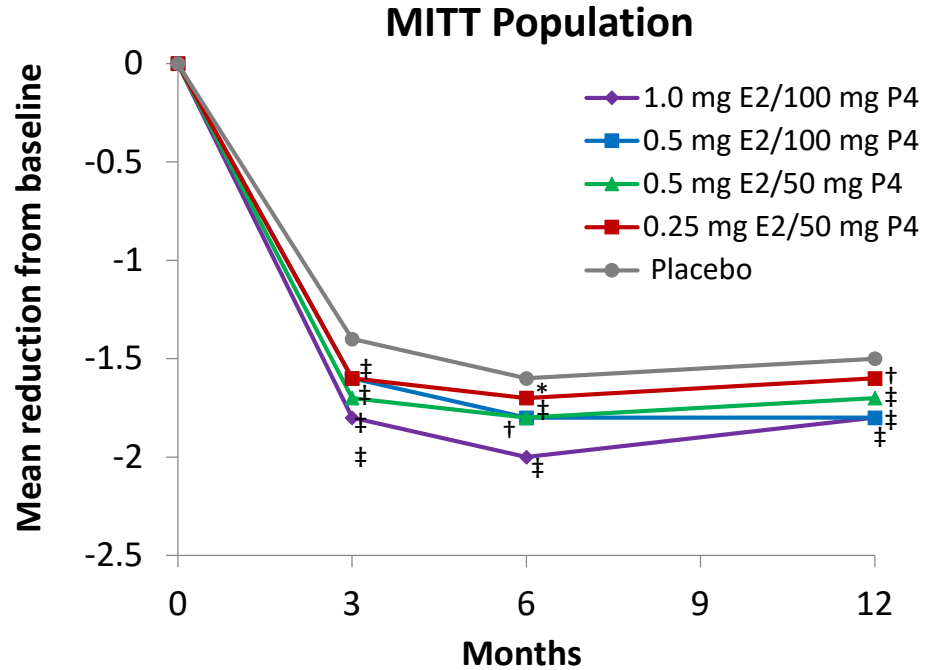
- At 12 weeks, statistically significant improvements in the MENQOL overall score were observed for all active treatment groups versus placebo
- At 6 and 12 months, the overall scores for the 3 highest doses were statistically significantly improved over placebo
- Overall scores ranged from 4.3–4.7 at baseline and were 2.3–2.8 with TX-001HR and 3.1 with placebo at month 12



\* $P < 0.05$ ; † $P < 0.01$ ; ‡ $P < 0.001$  vs placebo.

# Improvements in MENQOL Overall Score

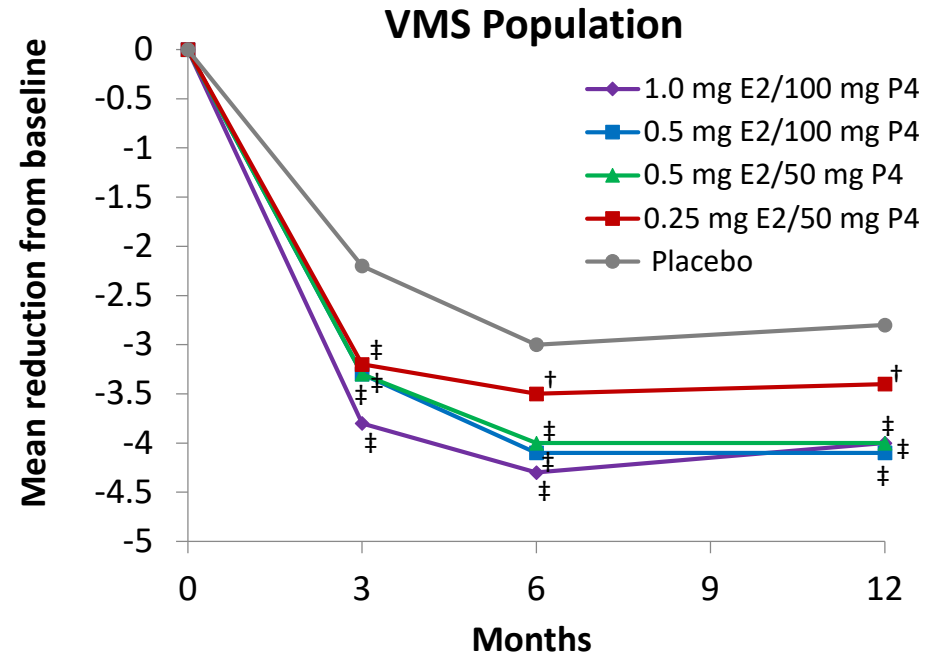
- Similar results were observed in the MITT (all subjects) vs VMS population
  - Significant improvements in the MENQOL overall score for all active TX-001HR groups versus placebo at all timepoints



\* $P < 0.05$ ; † $P < 0.01$ ; ‡ $P < 0.001$  vs placebo.

# Improvements in MENQOL VMS Domain

- Improvements in MENQOL vasomotor domain score from baseline were significantly greater with all TX-001HR doses versus the placebo at all timepoints
- Vasomotor domain scores ranged from 6.9–7.2 at baseline and were 2.8–3.6 with TX-001HR and 4.4 with placebo at month 12
- No statistically significant differences were noted between groups in the physical, psychosocial, or sexual domains

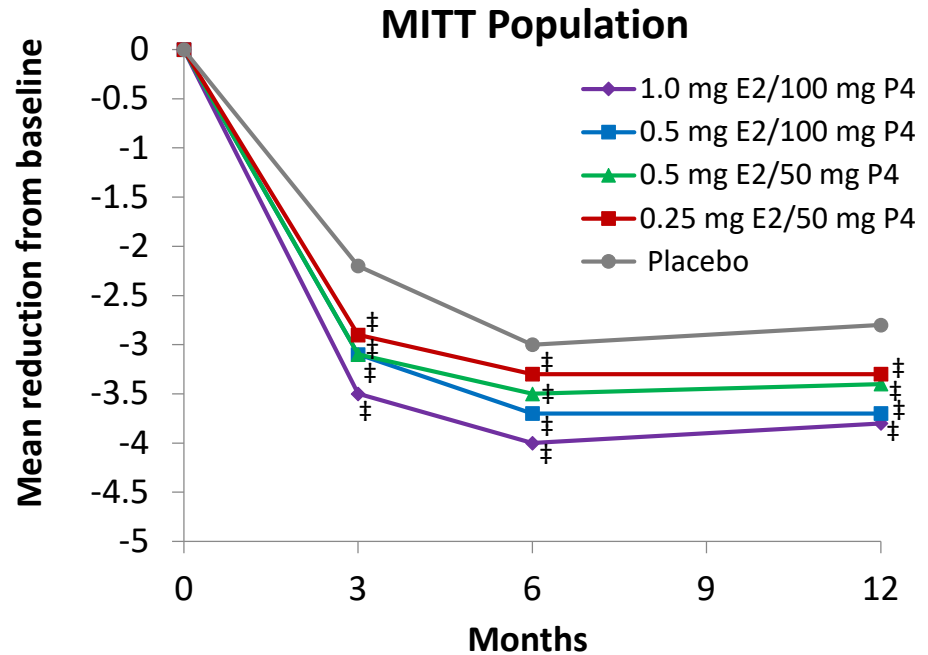


\* $P < 0.05$ ; † $P < 0.01$ ; ‡ $P < 0.001$  vs placebo.



# Improvements in MENQOL VMS Domain

- Similar results were observed in the MITT (all subjects) vs VMS population
  - Significant improvements in the MENQOL VMS domain score for all active TX-001HR groups versus placebo at all timepoints



\* $P < 0.05$ ; † $P < 0.01$ ; ‡ $P < 0.001$  vs placebo.

# Changes in Moderate-to-Severe VMS Frequency Correlated with Changes in MENQOL

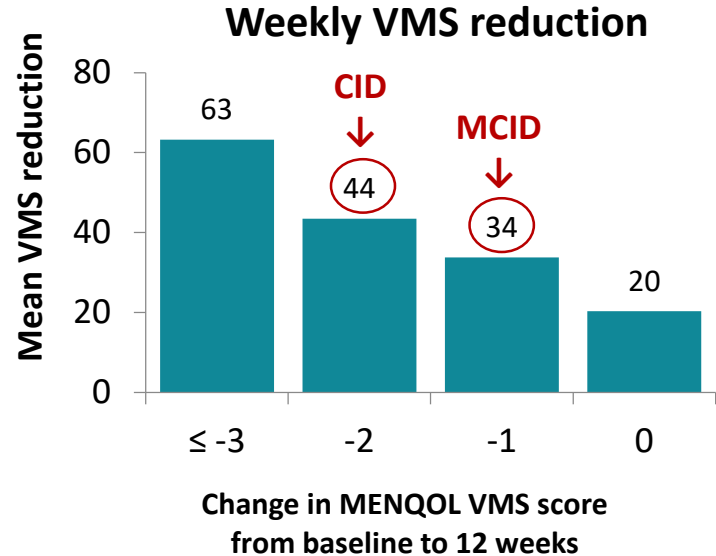
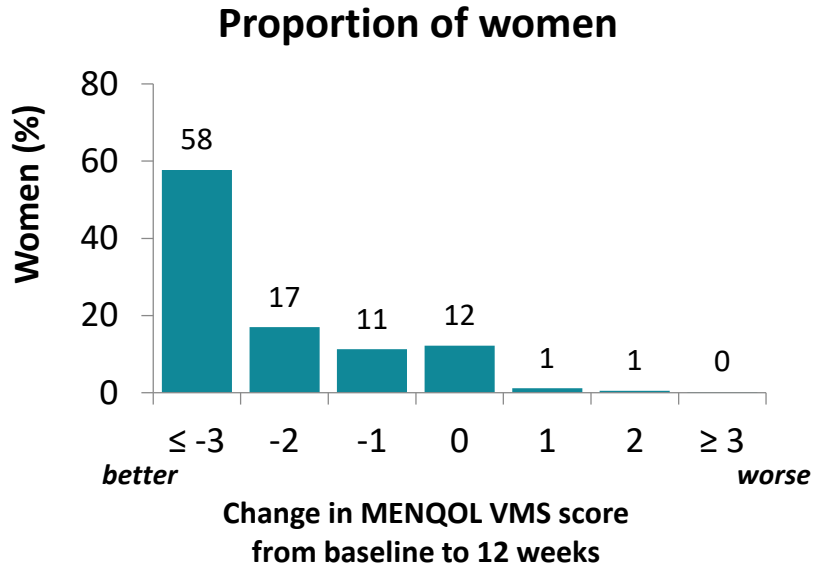
- Independent of treatment, the largest correlation observed was between changes in moderate-to-severe VMS frequency and changes in the MENQOL VMS domain score at 12 weeks ( $r=0.561$ )
  - Improvements in VMS frequency were associated with improvements in MENQOL VMS scores and other menopausal-related quality of life scores

Change in VMS frequency vs change in MENQOL domains*	r	P-value
Overall	0.397	<0.0001
<b>Vasomotor</b>	<b>0.561</b>	<0.0001
Physical	0.260	<0.0001
Psychosocial	0.183	<0.0001
Sexual	0.159	<0.0001

\*Change between baseline and week 12.

# Threshold Calculations for MENQOL Responder Analysis

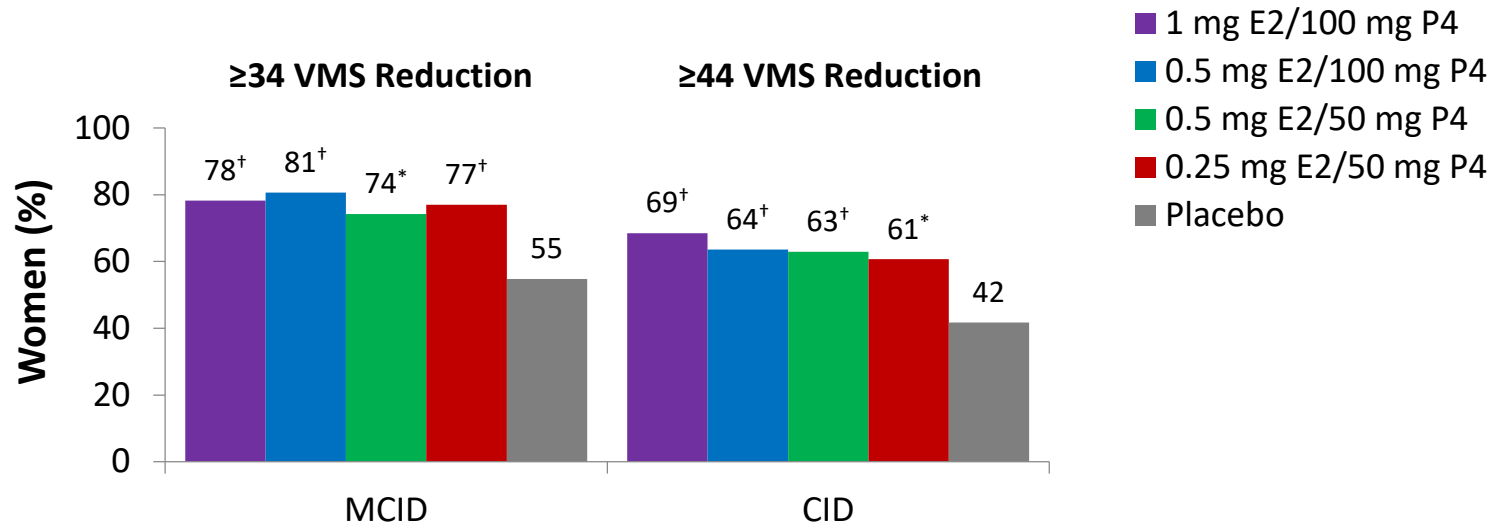
- 86% had improvement in their MENQOL VMS score
- Women with MCID had a weekly improvement of 34 fewer VMS, while those with CID had a weekly improvement of 44 fewer VMS



CID: clinically important difference defined as change of -2 in weekly VMS;  
MCID: minimal clinically important difference defined as change of -1 in weekly VMS.

# MENQOL-based Clinical Meaningfulness Analysis

- Significantly more MENQOL-responders had MCID and CID with TX-001HR than with placebo at week 12



\* $P < 0.01$ ; <sup>†</sup> $P \leq 0.001$  vs placebo.

CID: clinically important difference; MCID: minimal clinically important difference.

MENQOL-responders defined as a reduction in frequency of moderate-to-severe VMS from baseline of  $\geq 34$  as MCID and  $\geq 44$  as CID at week 12.

# Conclusions

- All doses of TX-001HR provided clinically significant improvements in quality of life (measured by MENQOL) from baseline to 12 weeks versus placebo
  - These significant improvements were maintained up to 12 months
- TX-001HR, if approved, may provide the first oral hormone therapy formulation combining the physiologic steroids E2 and P4 for the treatment of moderate-to-severe VMS in menopausal women with an intact uterus
  - TX-001HR may be an option for the estimated millions of women currently using less regulated and unapproved compounded bioidentical HT