Bremelanotide Treatment Provided Clinically Meaningful Benefits in Premenopausal Women With Hypoactive Sexual Desire Disorder

Sheryl A. Kingsberg, PhD, Anita H. Clayton, MD, David Portman, MD, Robert Jordan, BS, Dennis Revicki, PhD, Laura A. Williams, MD, MPH, Julie Krop, MD

1University Hospitals Cleveland Medical Center, Cleveland, OH, USA; 2University of Virginia, Charlottesville, VA, USA; 3Sermonix Pharmaceuticals, Columbus, OH, USA; 4Palatin Technologies, Inc., Cranbury, NJ, USA; 5Evidera, Bethesda, MD, USA; 6AMAG Pharmaceuticals, Inc., Waltham, MA, USA
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Introduction

- HSDD, defined as a lack of sexual desire accompanied by personal distress, affects approximately 10% of US women\(^1\)

- The distress associated with HSDD can have a significant impact on a woman’s quality of life\(^2\)

- Bremelanotide was recently approved for treatment of HSDD based on the results of the phase 3 RECONNECT studies\(^3,4\)
  - RECONNECT was comprised of two identically designed, randomized, double-blind, placebo-controlled studies
  - After 24 weeks of as-needed treatment, bremelanotide was associated with significantly improved sexual desire and decreased related personal distress in premenopausal women with HSDD

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Objective

• The objective of this analysis was to determine whether the improvements in sexual desire and related personal distress seen with bremelanotide in the RECONNECT studies were clinically meaningful
Methods: Study Design

- Studies 301 and 302 were two identically designed, randomized, double-blind, placebo-controlled phase 3 trials.
Methods: Participants

• Eligible participants included healthy premenopausal (according to STRAW criteria\(^1\)), nonpregnant women, ≥18 years of age, currently in a stable (≥6 months) relationship, and who had been diagnosed with HSDD for ≥6 months (with or without decreased arousal)
  — HSDD was diagnosed according to DSM-IV TR criteria\(^2\)
  — Subjects must not have any FSD other than acquired HSDD

• Subjects must have had all of the following at screening:
  — FSFI total score ≤26 if diagnosed with HSDD (with or without symptoms of decreased arousal) OR diagnosed with HSDD only (without symptoms of decreased arousal)
  — FSFI desire (FSFI-D) domain score ≤5 (regardless of total FSFI score)
  — FSDS.DAO total score >18

• Participants had experienced a normal level of desire at some point in the past for ≥2 years and were willing to engage in sexual activities ≥1×/month during the study

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DSM-IV TR, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision; FSD, female sexual dysfunction; FSDS-DAO, Female Sexual Distress Scale–Desire/Arousal/Orgasm; FSFI, Female Sexual Function Index; HSDD, hypoactive sexual desire disorder; STRAW, Stages of Reproductive Aging Workshop.

Methods: Endpoints

• The co-primary efficacy endpoints were change from baseline to end of study in FSFI-D and FSDS-DAO Item 13
  — FSFI is a validated 19-item measure of female sexual function consisting of 6 domains: desire, arousal, lubrication, orgasm, satisfaction, and pain\(^1,2\)
  — FSDS-DAO is a validated 15-item instrument used to evaluate aspects of sexual-related distress\(^3,4\)

• To define responders and to determine clinically meaningful responder thresholds for the co-primary endpoints, an independent anchor analysis (GAQ) with prespecified definitions was used
  — Question 3 measured satisfaction with treatment and provided a dynamic anchor for the co-primary endpoints of the core study phase: “Compared to the start of the study [prior to taking study drug], to what degree do you think you benefited from taking the study drug?”

FSDS-DAO, Female Sexual Distress Scale—Desire/Arousal/Orgasm; FSDS-R, Female Sexual Distress Scale—Revised; FSFI, Female Sexual Function Index; GAQ, General Assessment Questionnaire.
# Results: Demographics and Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=606)</th>
<th>Bremelanotide (n=596)</th>
<th>Total (N=1202)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (SD), years</td>
<td>38.8 (7.1)</td>
<td>38.5 (7.0)</td>
<td>38.7 (7.1)</td>
</tr>
<tr>
<td>Mean BMI (SD), kg/m²</td>
<td>28.4 (7.0)</td>
<td>28.9 (7.0)</td>
<td>28.7 (7.0)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>518 (85.5)</td>
<td>511 (85.7)</td>
<td>1029 (85.6)</td>
</tr>
<tr>
<td>Black</td>
<td>70 (11.6)</td>
<td>68 (11.4)</td>
<td>138 (11.5)</td>
</tr>
<tr>
<td>Other</td>
<td>18 (3.0)</td>
<td>17 (2.8)</td>
<td>35 (2.9)</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic/Latina</td>
<td>50 (8.3)</td>
<td>49 (8.2)</td>
<td>99 (8.2)</td>
</tr>
<tr>
<td>Not Hispanic/Latina</td>
<td>556 (91.7)</td>
<td>547 (91.8)</td>
<td>1103 (91.8)</td>
</tr>
<tr>
<td>Diagnosis, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HSDD with decreased arousal</td>
<td>434 (71.6)</td>
<td>420 (70.5)</td>
<td>854 (71.0)</td>
</tr>
<tr>
<td>HSDD without decreased arousal</td>
<td>172 (28.4)</td>
<td>176 (29.5)</td>
<td>348 (29.0)</td>
</tr>
<tr>
<td>Mean duration of HSDD symptoms (SD), months</td>
<td>47.9 (44.0)</td>
<td>46.6 (42.1)</td>
<td>47.2 (43.1)</td>
</tr>
</tbody>
</table>
Results: Change in FSFI-D After 24 Weeks

• There was a statistically significant improvement in sexual desire reported by patients treated with bremelanotide compared to patients treated with placebo
  ○ Baseline FSFI-D scores were required to be ≤5

FSFI-D, Female Sexual Function Index—Desire Domain.
Results: Change in FSDS-DAO Item 13 After 24 Weeks

- There was a statistically significant improvement in personal distress related to sexual desire reported by patients treated with bremelanotide compared to patients treated with placebo.
  - Baseline FSDS-DAO Item 13 scores were required to be >18
Results: Proportion of Patients Reporting Clinically Meaningful Benefit After 24 Weeks (GAQ Question 3)

- Significantly more patients reported a clinically meaningful benefit following treatment with bremelanotide compared to patients treated with placebo.
Results: GAQ Question 3 Scores During the Core and Open-Label Extension Phases of the RECONNECT Studies

- Similar scores for clinically meaningful benefit were reported by patients who switched from placebo in the core phase to bremelanotide in the open-label extension and patients who received bremelanotide in the core and open-label extension phases.
## Results: Safety

<table>
<thead>
<tr>
<th>TEAE, n (%)</th>
<th>Bremelanotide (n=627)</th>
<th>Placebo (n=620)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>251 (40.0)</td>
<td>8 (1.3)</td>
</tr>
<tr>
<td>Flushing</td>
<td>127 (20.3)</td>
<td>2 (0.3)</td>
</tr>
<tr>
<td>Injection site</td>
<td>83 (13.2)</td>
<td>52 (8.4)</td>
</tr>
<tr>
<td>reactions*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>71 (11.3)</td>
<td>12 (1.9)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>30 (4.8)</td>
<td>1 (0.2)</td>
</tr>
</tbody>
</table>

- The majority of TEAEs in the study were mild to moderate in intensity
- Serious adverse reactions were reported in 1.1% of patients treated with bremelanotide and 0.5% of patients who received placebo
- The discontinuation rate due to TEAEs was 18% among patients treated with bremelanotide and 2% among patients treated with placebo

- Maximal, transient, and mild increases in systolic BP and diastolic BP were noted approximately 2 hours after bremelanotide dosing, and were accompanied by similarly mild decreases in pulse rates such that there would be no expected increase in overall heart rate-BP product
- No clinically significant effects on clinical laboratory tests, ECG, weight, depression or suicidal ideation, or effect on alcohol consumption were observed

*Injection site pain, unspecified injection site reactions, erythema, hematoma, pruritus, hemorrhage, bruising, paresthesia, and hypoesthesia. BP, blood pressure; ECG, electrocardiogram; TEAE, treatment-emergent adverse event.
Conclusions

• Bremelanotide demonstrated statistically significant and clinically meaningful improvements in sexual desire and related personal distress in premenopausal women with acquired, generalized HSDD
  • These statistically significant differences between treatment groups in favor of bremelanotide were supported by anchored responder analyses with prespecified definitions to support clinical meaningfulness
  • The dynamic anchor (GAQ Question 3) assessment of the co-primary endpoints yielded both clinically meaningful and statistically significant differences between treatment groups, with a 58.1% responder rate in the bremelanotide group compared to 35.6% for placebo ($P<0.0001$)

• Bremelanotide was well tolerated in this population of premenopausal women with HSDD

• The consistency of these results confirms that a clinically meaningful benefit was gained from bremelanotide treatment in premenopausal women with HSDD

GAQ, General Assessment Questionnaire; HSDD, hypoactive sexual desire disorder.