**The Neurobiology and Efficacy of Bremelanotide in HSDD**

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**Introduction**

- Female sexual dysfunctions are classified as dysfunctions of desire (eg, hypoactive sexual desire disorder; DSD), arousal (eg, sexual arousal disorder [SAD]), delay or absence of orgasm, or sexual pain (eg, dyspareunia or vaginismus)
- There are no existing diagnostic criteria for these disorders, particularly for younger women, for which treatment options exist
- In a 2008 study, up to 43% of women aged 18 years reported having a sexual problem: 10% also reported distress (score ≥5) on the Female Sexual Distress Scale (FSDS) 4
- In a 2012 clinical sample, the overall prevalence of HSDD was 74%, HSDD was slightly more common among pre- (50%) vs postmenopausal (44.2%) women (Figure 1)

**Mechanism of Sexual Response**

- Excitatory signals are regulated by dopamine (DA), norepinephrine (NE), oxytocin, and the melanocortins (MCs) 5–7
- The MCs (eg, melanocyte-stimulating hormone [MSH], acts on the physiological and neurobiological components of female sexual function to improve sexual arousal and desire in women with HSDD 8

**Sexual and Reward Circuitry**

- Bremelanotide (BMT) stimulates brain regions of the brain, such as the medial preoptic area (MPOA) in the hypothalamus, attention- and reward-related regions of the striatum, and the prairie vortex

**Figure 1. Prevalence of HSDD**

**Figure 2. Excitatory and Inhibitory Pathways Regulating Sexual Response**

**Figure 3. Sexual and Reward Center Girdle**

**Rat Study**

- BMT's upstream CNS effects of increasing arousal and desire are thought to result from its action as a MC receptor agonist
- Among female rats primed with estrogen and progesterone or estrogen alone, BMT significantly increased motivation of ovlustation without altering pairing or estrous behavior: BMT was directly into the lateral ventricles or mPOA, but not the ventromedial hypothalamus (Figure 4)

**Figure 4. Bremelanotide Effects on Sexual Behavior in Rats**

**Human Study**

- Among 16 premenopausal women with HSDD with or without FSDA, subcutaneous (SC) administration of BMT 1.25 mg twice daily
- Significantly increased the number of sexually satisfying events (SSEs) vs placebo when taken 45 minutes before sexual activity. Mean (standard error [SE]) change in SSEs/month was 3.7 (1.0) vs 0.2 (0.3) with placebo, respectively (P=0.007; Figure 6)

**Figure 5. Mean Change in SSEs/Month After BMT Treatment**

**Figure 6. Mean Change in FSDS-DAO Total Score After BMT Treatment**

**Conclusions**

- BMT is a novel MC receptor agonist with a potential to modulate critical brain pathways involved in sexual response
- BMT 1.25 and 1.75 mg SC, self-administered as a daily injection, improve female sexual desire and SSEs in women with HSDD
- BMT was safe and well tolerated

**Disclosures**

- Dr Pfaus has received consulting fees from Emotional Brain and Palatin Technologies, Inc.
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