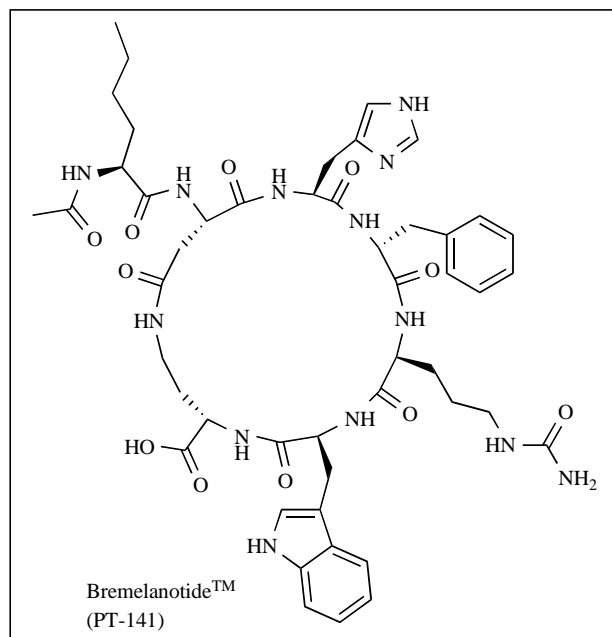


## Molecule of the Month

**Pharmaceutical aphrodisia.** Almost a decade ago, 43% of women and 31% of men in the United States were believed to suffer from one form or another of sexual dysfunction [1]. Viagra™ and other phosphodiesterase type 5 (PDE5) inhibitors have provided viable pharmacological treatment options for men over the past decade. However, these drugs lack efficacy in women, and similarly successful drug treatments for female sexual dysfunction have yet to emerge [2]. Furthermore, despite the high efficacy and widespread tolerability of PDE inhibitors in men, these drugs are not



without drawbacks. Headache and vision-related side effects are present in some individuals, and these drugs are contraindicated in patients concurrently taking nitrates or related drugs that may carry hypotension risks [3]. Additionally, it is estimated that half of men prescribed sildenafil (Viagra™) subsequently cease use over time [4]. Bremelanotide (formerly PT-141), a drug currently under development by Palatin Technologies [5], could prove a novel and effective treatment for female and male sexual dysfunction. The main reason underlying the drug's potential efficacy in both sexes lies in its CNS-acting mechanism. Bremelanotide is a cyclic heptapeptide melanocortin analog, which acts as an agonist at the primarily CNS-expressed melanocortin receptors, MC3-R and MC4-R [6, 7]. The mechanism by which melanocortin receptor activation mediates sexual arousal and behavior is not well established; however, it likely involves an increase in nitric oxide signaling in the CNS [7]. Central activation of the melanocortin receptors by known agonist such as alpha-melanocyte-stimulating hormone (alpha-MSH) causes increased sexual arousal and mating behavior in animals [8]. Likewise, the synthetic melanocortin analog Melanotan-II, which is structurally similar to Bremelanotide (and is the parent compound from which the latter was derived), induces penile erection in men suffering from erectile dysfunction (ED) [9]. Rodent and non-human primate studies demonstrate a potent erection-promoting effect of Bremelanotide [10]. Women with female sexual arousal disorder given Bremelanotide (by intranasal delivery) report significantly increased sexual desire after treatment, as well as more satisfaction with their level of arousal when attempting intercourse within 24 hours [11]. In both normal and ED men, treatment with Bremelanotide causes significant

increases in erectile activity, in a dose-dependant manner [10]. Clinically and statistically effective doses of the drug (up to 20mg) are safe and well tolerated by both normal and ED patients [12]. Having completed all Phase II trials in men with promising results, Bremelanotide is set to enter Phase III for men in the first half of this year. In women, positive data from a Phase IIa trial and the recent commencement of a Phase IIb trial suggest that entry to Phase III for women may also be on the horizon. If approved, Bremelanotide would be the first FDA-approved synthetic aphrodisiac. This novel therapy could potentially address the substantial need for an effective female sexual dysfunction treatment as well as offer an alternative to traditional PDE inhibition in ED men.

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