Statement of Cindy Pearson, Executive Director, National Women's Health Network

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Food and Drug Administration Joint Meeting of the Bone, Reproductive and Urologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee Meeting

My name is Cindy Pearson, and I am the Executive Director of the National Women's Health Network. The National Women's Health Network is a nonprofit advocacy organization that works to improve the health of all women. We are supported by our members and by choice, we do not accept financial support from drug companies or medical device manufacturers. We bring the voices, concerns and needs of women consumers to policy and regulatory tables.

Since the Network's founding 40 years ago, we have brought the voices of women to the FDA, advocating for medical products that meet women's real life needs and a drug development process that reflects women's lived experiences.

We are pleased to have the opportunity today to comment on flibanserin's third application for FDA approval. We have followed and commented on the regulatory assessments of flibanserin for many years now. After careful review of Sprout Pharmaceutical's most recent submission, we respectfully submit the following for consideration by the Advisory Committee today.

As we all know, despite over 15 years of research and development on female sexual dysfunction there still is no empirical standard that establishes a single, normal level of sexual desire for women. The Network advocates for sexual health research to advance understanding of, and solutions to, women's problems with sex, and we recognize that a lack of sexual desire can be a real and distressing problem for women. We also believe that it may be possible to develop a drug that is effective in treating some of women's sexual problems. However, based on our review of the overall safety and efficacy profile of flibanserin, it is clear that this drug is not it.

We know that some women have told the FDA that they would like to see flibanserin approved. While we respectfully acknowledge that each woman's individual experience is valid, we must caution that need does not create proof. Though Sprout was able to show marginally statistically significant increases in sexual desire and decreases in distress (each are less than half a point), the clinical significance of these gains is not established. Given the marginal efficacy of this drug, the safety and risk profile become even more important when considering an indication for use in healthy women.

Approval of flibanserin must be based on careful consideration of a risk-benefit analysis. That analysis should be based solely on evidence proving that effectiveness is balanced with a reasonable safety profile. So, even though some may argue that numerically small improvements in a women's sexual experience can make a positive difference for her, significant known and unknown adverse reactions and side effects may still outweigh a drug's benefits. Given the reported adverse events and the higher dropout rate in the flibanserin arm in all three pivotal trials, many unresolved questions remain about the seriousness, severity, duration, and frequency of side effects with flibanserin.

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The data clearly show that taking flibanserin increases the likelihood of low blood pressure, fainting, and other potentially serious adverse events. In an effort to mitigate these adverse reactions, Sprout has changed the prescribed dosing to right before bedtime. Altering the timing of the dose, however, does not make the dangers of this drug disappear. Even more concerning is the clear omission of evidence-based research in making this conclusion. If the risks of taking this drug are so easily remedied by changing the timing of its administration, why was this strategy not considered during earlier trials? Even with this unproven risk mitigation strategy that changes the timing of dosing, there remain serious problems with this drug's application. The briefing document provided for today's meeting represents a body of evidence of documented adverse reactions that cannot be wished away by advising women to take flibanserin at night.

After expressing concerns "regarding the additive sedative and hypotensive effects of concomitant use of alcohol" in its 2013 *Complete Response letter*, the FDA recommended that Sprout Pharmaceuticals conduct a study of drug-drug interactions between alcohol and flibanserin. Inexplicably, in their 25 person study, Sprout included 2 women. Two! Sprout claims that they had "difficulty recruiting female subjects who were moderate drinkers." This study is a true example of gender bias and sexism in research, and is an insult to women. The fact that Sprout Pharmaceuticals has insinuated that sexism is driving the FDA's handling of the previous flibanserin applications is laughable considering their blatant exclusion of women in the study dedicated to measuring the effects of alcohol and flibanserin combined.

Women absorb and metabolize alcohol differently than men. An alcohol-flibanserin interaction study primarily tested on men is clinically irrelevant for the purposes of evaluating its safety in women. For the purposes of an evidence-based assessment of the risks to women of drinking alcohol while taking flibanserin, the study has not yet been done.

In the real world, alcohol consumption is common and risk mitigation is simply not enough to keep people safe. Taking the drug at night may help to avoid a car crash, but there is no known intervention or REMS that can make people abstain from alcohol in the long term.

Sprout Pharmaceuticals has not provided enough data for women to make an informed decision on whether or not to take flibanserin. The questions regarding alcohol use, night time dosing, and drug-drug interactions, particularly the large category of CYP3A4 drugs (including hormonal birth control, migraine medications and antifungals used to treat yeast infections) cannot be left unanswered. We recommend that the committee today votes no on approving this drug without further studies assessing its safety profile.

Women need and want answers to our sexual problems, and the Network strongly supports sexual health research that explores both biomedical and non-biomedical solutions to these problems. Flibanserin offers too little efficacy at too high a price to pay for our safety. We urge this committee to recommend against approval.