

SUMMARY OF FLIBANSERIN PHASE III CLINICAL TRIALS

At the 12th Congress of the European Society for Sexual Medicine (ESSM), Boehringer Ingelheim is presenting eight abstracts from the flibanserin Phase III clinical trial program. These abstracts include: one on the design of the trials; three North American trials (DAISY[®], DAHLIA[®], and VIOLET[®]); one European trial (ORCHID[®]); two pre-specified pooled analyses of the 100mg dose; and one assessing safety and tolerability of all the dosages studied.

TRIAL DESIGN

All the trials were similarly designed – randomized, double-blind, parallel-group – assessing the efficacy, safety and tolerability of varying doses of flibanserin. Collectively, the trials involved nearly 5,000 pre-menopausal women (18 or older) with a primary diagnosis of generalized-acquired Hypoactive Sexual Desire Disorder (HSDD)*. Participants were followed during a four-week baseline period and then during a 24-week treatment period. The trial included primary endpoints and secondary endpoints measuring the following areas related to HSDD:

Sexual Activity

- **Sexually Satisfying Events:** Classifying a Sexually Satisfying Event (SSE) consists of identifying the sexual event (defined as sexual intercourse, oral sex, masturbation or genital stimulation by the partner) and establishing if the event was satisfying for the individual. Women in the clinical trial were asked, “Did you have sex in the last 24 hours?” If they answered “yes,” then they were asked, “Was the sex satisfying for you?”

Desire

- **Electronic Diary:** A woman’s level of desire was assessed daily and recorded using an electronic diary (eDiary). The eDiary prompted the question, “Indicate your most intense level of sexual desire in the last 24 hours” and required a response on a scale of one (no desire) to four (strong desire).
- **Female Sexual Function Index (FSFI) Desire Domain:** The FSFI is an independently developed and validated measure assessing the quantity of female sexual functioning over a four-week recall period. Desire is one of six domains assessed in the questionnaire.

Sexual Functioning

- **FSFI Total Score:** The questionnaire assesses six domains of sexual functioning including sexual desire, arousal, lubrication, orgasm, satisfaction and pain.

Distress

- **Female Sexual Distress Scale-Revised (FSDS-R):** The FSDS-R is a 13-item questionnaire designed to assess and quantify the change in frequency of reported personal distress associated with sexual dysfunction or disorder. Question 13 of the FSDS-R specifically assesses distress due to low sexual desire by asking, “How often did you feel bothered by your low sexual desire?” The total score ranges from 0 to 52 with higher scores indicating more sexual distress and a total score of ≥11 indicating the presence of sexual distress. In order to be included in the Phase III clinical trials, women had to score ≥15 on the FSDS-R scale.

Overall Improvement

* HSDD is a form of female sexual dysfunction. As defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR), HSDD is the persistent lack (or absence) of sexual fantasies or desire for any form of sexual activity causing marked distress or interpersonal difficulty and not better accounted for by another disorder (except another sexual dysfunction), direct physiological effects of a substance (including medications), or a general medical or psychiatric condition.

CLINICAL TRIAL DATA

	PHASE III TRIAL	ABSTRACT DETAILS	DOSAGE STUDIED [†]	DESIGN	NUMBER OF PATIENTS	ENDPOINTS	RESULTS
North America	VIOLET	Sunday, 11/15 Poster All day	<ul style="list-style-type: none"> • 50mg qhs • 100mg qhs 	Phase III, randomized, double-blind, parallel-group 24-week treatment period	Flib: 585 Pla: 295	<p><i>Primary:</i> Change from baseline to study end in SSE and eDiary desire score</p> <p><i>Secondary:</i> Change in FSDS-R total and item 13, FSFI total and desire domain; safety parameters were also monitored</p>	100mg significantly improved SSE and all secondary parameters; improvements in eDiary score were not statistically significant
	DAHLIA	Monday, 11/16 Oral presentation 1:30-3 pm	<ul style="list-style-type: none"> • 25mg bid • 50mg bid • 50mg qhs 		Flib: 1,036 Pla: 349		Neither the 25mg nor the two 50mg doses were statistically superior to placebo on the co-primary endpoints
	DAISY	Tuesday, 11/17 Highlighted Poster 10-10:30 am	<ul style="list-style-type: none"> • 25mg bid • 50mg qhs (2wks) then 50mg bid • 50mg qhs (2wks) then 100mg qhs 		Flib: 1,183 Pla: 398		100mg significantly improved SSE and all secondary parameters; improvements in eDiary score were not statistically significant
Europe	ORCHID	Monday, 11/16 Oral presentation 1:30-3 pm	<ul style="list-style-type: none"> • 50mg qhs • 50mg qhs (2wks) then 100mg qhs 		Flib: 627 Pla: 318	<p><i>Primary:</i> Change in SSE</p> <p><i>Secondary:</i> Change in eDiary desire, FSDS-R total and item 13, FSFI total and desire domain; safety parameters were also monitored</p>	100mg significantly improved eDiary and distress (FSDS-R and Item 13). There was a trend toward improvement in SSE, FSFI desire, and FSFI total score

NOTE: All times noted above are Central European Standard Time (CEST)

[†]BID = Twice daily; QHS = Once daily at bedtime

	PHASE III TRIAL	ABSTRACT DETAILS	DOSAGE STUDIED [‡]	DESIGN & DURATION	NUMBER OF PATIENTS	ENDPOINTS	RESULTS
Pre-specified Pooled Analyses	VIOLET & DAISY	Sunday, 11/15 Poster All day	100mg qhs	Pooled data	Flib: 685 Pla: 693	Change in: <ul style="list-style-type: none"> • SSE • eDiary desire score • FSDS-R total and item 13 • FSFI total and desire domain Safety parameters were also monitored	100mg significantly improved all primary and secondary measures versus placebo
	VIOLET, DAISY & ORCHID	Sunday, 11/15 Poster All day	100mg qhs		Flib: 962 Pla: 984		
Safety Analysis	VIOLET, DAISY, DAHLIA & ORCHID	Monday, 11/16 Oral presentation 1:30 – 3 pm	<ul style="list-style-type: none"> • 25mg bid • 50mg qhs • 50mg bid • 100 qhs 	Analysis of safety and tolerability from all trials	Flib: 3,431 Pla: 1,360	<ul style="list-style-type: none"> • Adverse events • Blood pressure and pulse • Weight • Laboratory tests • Electrocardiograms • Physical exams • Pelvic exams 	<ul style="list-style-type: none"> • No significant safety concerns up to 100mg/day • Most commonly reported AEs included sleepiness, dizziness, fatigue, anxiety, dry mouth, nausea and insomnia, occurring in between two to 12 percent of women taking flibanserin • AEs were generally mild to moderate, and resolved with continued treatment in most cases

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