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Flibanserin Demonstrates Efficacy and Tolerability in Pivotal Phase III Trials in Pre-Menopausal Women with Hypoactive Sexual Desire Disorder (HSDD)

Results support flibanserin as a potential treatment for HSDD, an under-recognised women's sexual health condition

For medical media, outside the US only

Data from pooled, pivotal Phase III clinical trials demonstrate that flibanserin 100mg taken once daily at bedtime significantly increased the number of Satisfying Sexual Events (SSEs) and sexual desire while significantly decreasing the distress associated with Hypoactive Sexual Desire Disorder (HSDD). Flibanserin is an investigational compound that is being developed by Boehringer Ingelheim for the treatment of pre-menopausal women with HSDD.

Ingelheim/Germany, 16 November 2009 - HSDD is a medical condition characterised by a decrease in sexual desire associated with marked distress and/or interpersonal difficulties. Women with HSDD often feel a loss of intimacy and closeness that they used to enjoy. The condition can negatively impact a women´s life and her relationship with her partner. [1,2,3,4]

The complete flibanserin pivotal trial programme was presented today at the 12th Congress of the European Society for Sexual Medicine in Lyon, France. It included an analysis of three pivotal Phase III North American trials (DAISY®, VIOLET® and DAHLIA®) and the pivotal Phase III European data (ORCHID®). In addition results from a pooled analysis of two pivotal Phase III North American trials (DAISY® and VIOLET®) and a pooled analysis of the North American and European data (DAISY®, VIOLET® and ORCHID®) were presented, assessing the safety and efficacy of flibanserin 100mg in pre-menopausal women suffering with HSDD.

Despite studies demonstrating that HSDD is a common form of female sexual dysfunction, there is currently no approved prescription treatment for pre-menopausal women suffering from the condition said Professor Rossella Nappi, director of the Gynaecological Endocrinology & Menopause Unit at the Maugeri Foundation, University of Pavia, Italy, and primary investigator of the European pivotal trial. "Flibanserin is a novel, non-hormonal compound, that has been investigated as a treatment for pre-menopausal women with HSDD. Based on the clinical trial results presented at ESSM it has the potential to help many women suffering from their lack of sexual desire.

Pooled North American Phase III Trial Results (DAISY® and VIOLET®)
The pre-specified pooled analysis of 1,378 pre-menopausal women with HSDD shows a statistically significant increase in the frequency of SSEs per month in women taking flibanserin 100mg (from 2.8 at baseline to 4.5), versus placebo (2.7 at baseline increasing to 3.7) over the 24-week study period. Flibanserin also demonstrated statistically significant improvements in sexual desire versus placebo as measured by an electronic diary (the eDiary For HSDD Trials©). This finding was further supported by data from the desire domain of the Female Sexual Function Index (FSFI) as an independent secondary measure.

Other key secondary endpoints showed flibanserin significantly improved sexual functioning (as measured by the FSFI total score), distress related to sexual dysfunction (as measured by the Female Sexual Distress Scale-Revised, FSDS-R, score) and distress related to low sexual desire (FSDS-R Item 13 score) versus placebo.

European Phase III Trial Results (ORCHID®)
The analysis of 634 pre-menopausal women with HSDD showed women taking flibanserin 100mg had statistically significant improvements in their level of sexual desire, as measured by the eDiary. These findings were supported by a trend towards an increase in the FSFI desire domain. In addition there was a statistically significant improvement in the level of distress associated with sexual dysfunction (as measured by the FSDS-R total score) as well as distress related to low sexual desire (FSDS-R Item 13) which is the second key parameter for the diagnosis of HSDD. A

numerical increase in the number of SSEs compared to placebo supports the efficacy of flibanserin in pre-menopausal women suffering with HSDD.

North American and European Phase III Trial Results - Pooled Analysis (DAISY®, VIOLET® and ORCHID®)

A pooled analysis of pivotal data including the European study (ORCHID®) and the American Phase III trials (DAISY® and VIOLET®) reinforces the efficacy of 100mg flibanserin for the treatment of pre-menopausal women with HSDD. Results show a statistically significant improvement versus placebo in the number of SSEs, as well as a statistically significant increase in the level of sexual desire, recorded via the eDiary and the FSFI desire domain scores. Distress associated with sexual dysfunction and specifically low sexual desire was significantly reduced with flibanserin 100mg (as measured by FSDS-R score and FSDS-R Item 13 score).

Safety Analysis

Most adverse drug reactions with flibanserin 100mg were mild to moderate, emerged during the first 14 days of treatment and resolved with continued treatment. The most common adverse events (AEs) reported by more women on flibanserin than on placebo included dizziness, nausea, fatigue, somnolence and insomnia. The findings are consistent across the North American and European trials with about 14% and 16% of women on flibanserin 100mg and 8% and 5% of women on placebo discontinuing treatment due to AEs in the respective trials.

Findings from the pivotal Phase III trials show that flibanserin 100mg is effective and well-tolerated for the treatment of Hypoactive Sexual Desire Disorder in pre-menopausal women, said Elaine Jolly, Medical director, Shirley E. Greenberg Women's Health Centre of the Ottawa Hospital and Professor of Obstetrics and Gynecology, University of Ottawa, and one of the Canadian physicians participating in the Phase III trials. Flibanserin acts as an agonist at the serotonin 5-HT1A receptor and as an antagonist at the 5-HT2A receptor with preferential affinity to selective brain areas. It is believed to act on neurotransmitters within the brain that are thought to play a role in sexual response. By modulating these neurotransmitter systems, flibanserin may help to restore a balance between inhibitory and excitatory factors leading to a healthy sexual response.

Notes to Editors:

About the Pivotal Phase III Trials - Inclusion criteria, endpoints and scales

The North American and European trials were designed to study flibanserin for 24-weeks in a randomised, placebo-controlled setting and involved women with generalised acquired HSDD who were treated with flibanserin 100mg (found to be the most consistently effective dose in the individual trials) or placebo. All the women in the studies were in stable, communicative, monogamous, heterosexual relationships for at least one year and were required to use a reliable form of contraception.

In the North American pivotal trials, the co-primary endpoints were changes from four-week baseline period to week 21 to 24 in the number of SSEs and sexual desire score as recorded daily by patients using an electronic diary (the eDiary For HSDD Trials©). Both are patient reported outcome measures. In the European pivotal trial the primary endpoint was changes from baseline compared to week 24 in the number of SSEs, which were also recorded daily using the eDiary.

SSE measures the number of sexual events (defined as sexual intercourse, oral sex, masturbation or genital stimulation by the partner), and whether the event was satisfying for the woman (i.e. gratifying, fulfilling, satisfactory and/or successful), irrespective of whether women had an orgasm or whether the event was satisfying for the partner. This definition of an endpoint was based on a draft guidance document issued by the U.S. Food and Drug Administration (FDA) in 2000. [5]

Boehringer Ingelheim designed the eDiary For HSDD Trials© to meet the FDA's recommendation of measuring levels of desire on a daily basis, and to report the number of satisfying sexual events. The FSFI desire score - an independently developed and validated tool - was included as a secondary endpoint to provide an additional measurement of changes in sexual desire over a longer recall period. The tool, which has a specific desire domain, assesses both the intensity and the frequency of desire over a 4-week period. The FSDS-R is a 13-item questionnaire designed to assess and quantify the change in personal distress associated with female sexual dysfunction. All measures in the trial have undergone rigorous testing to ensure they are valid and reliable.

About Hypoactive Sexual Desire Disorder

HSDD is a form of Female Sexual Dysfunction (FSD). As defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV), HSDD is the persistent lack (or absence) of sexual fantasies or desire for any form of sexual activity marked by 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 condition. Generalised, acquired HSDD is not limited to certain types of stimulation, situations or partners, and develops only after a period of normal functioning.1 Low sexual desire with associated

distress is the most commonly reported female sexual complaint. In prevalence studies approximately 1 in 10 women reported low sexual desire with associated distress, which may be HSDD. Sexual Desire Disorders are generally under-diagnosed and there are currently no pharmacological treatments available for pre-menopausal women with HSDD. HSDD has been recognised as a medical condition for over 25 years.

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In 2008, Boehringer Ingelheim posted net sales of 11.6 billion euro while spending one fifth of net sales in its largest business segment Prescription Medicines on research and development.

Related links

www.scienceofdesire.com
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