AbbVie Announces Positive Phase 3 Extension Study Data for Investigational Oral Treatment Elagolix for Management of Endometriosis with Associated Pain

November 1, 2017

- In two extension studies, elagolix demonstrated sustained reduction in average monthly menstrual pelvic pain, non-menstrual pelvic pain and painful intercourse

- No new safety concerns were identified with elagolix use for the 12-month treatment period

NORTH CHICAGO, Ill., Nov. 1, 2017 /PRNewswire/ -- AbbVie (NYSE:ABBV), a research and development based global biopharmaceutical company in cooperation with Neurocrine Biosciences, Inc. (NASDAQ: NBIX), announced detailed results from two replicate Phase 3 extension studies evaluating the long-term efficacy and safety of elagolix, an investigational, orally administered gonadotropin-releasing hormone (GnRH) antagonist, being evaluated for the management of endometriosis with associated pain. In the extension studies, elagolix demonstrated sustained reduction in average monthly menstrual pelvic pain and non-menstrual pelvic pain in women through the 12-month treatment period. The safety and tolerability of elagolix was consistent with the anticipated effects of reduced estradiol levels and no new safety concerns were identified with elagolix use for the 12-month treatment period[1]. These results, and other additional abstracts, were presented at the American Society for Reproductive Medicine Scientific Congress & Expo (ASRM) in San Antonio.

"Endometriosis is a chronic and painful disease," said Eric Surrey, M.D., study investigator and Medical Director, Colorado Center of Reproductive Medicine. "The results presented today are positive for patients and are consistent with previous data that demonstrate elagolix has the potential to be an important non-surgical treatment option for women suffering from the most prevalent symptoms of endometriosis."

The objective of the extension studies was to evaluate the long-term safety and efficacy of elagolix for the management of endometriosis with associated pain. The efficacy endpoints of the pivotal studies were the proportion of responders based on the average monthly menstrual pain (dysmenorrhea) and non-menstrual pelvic pain scores, as measured by the Daily Assessment of Endometriosis Pain scale.[1, 4] The reductions in dysmenorrhea and non-menstrual pelvic pain following six months of elagolix treatment were maintained over six additional months of treatment (12 months total) across both extension studies for both 150 mg once daily (QD) and 200 mg twice daily (BID) doses.[1] More than 50 percent of women were responders for dysmenorrhea and non-menstrual pelvic pain at both doses.[1] The responder rate for painful intercourse (dyspareunia) after 12 months was higher with the 200 mg BID dose than with 150 mg QD dose[2], which reflects a dose-dependent effect similar to the effect reported in pivotal studies.[1, 3,4]

"An estimated one in 10 women of reproductive age have endometriosis," said Shao-Lee Lin, M.D., Ph.D., vice president, therapeutic areas and international development, AbbVie. "There have been few recent scientific advancements for women suffering from endometriosis and physicians are in need of additional treatment options to help manage this debilitating disease."

Safety assessments in the extension studies included evaluation of adverse events, along with clinical laboratory tests and changes in bone mineral density.[1,6] The safety profile of elagolix was consistent with the partial hormone suppression associated with its mechanism of action. The proportion of women with new incidences of hot flush ranged between 4-8 percent across both studies and doses.[1] A dose-dependent average decrease from baseline in bone mineral density (0.6% and 1.1% with 150 mg QD in EM-III and EM-IV, respectively; and 3.6% and 3.9% with 200 mg BID in EM-III and EM-IV, respectively) was observed at month 12.[6] After 12 months of treatment, one woman on the 200 mg BID dose had a BMD z-score below -2.0,which is the age-adjusted normal threshold.[15] All of the women on the 150 mg QD dose had a BMD z-score within the age-adjusted normal threshold.[15] Findings were consistent across both Phase 3 extension trials and no new safety concerns were identified with long-term elagolix use.

AbbVie conducted multiple oral presentations at ASRM highlighting the results of the Phase 3 extension studies[1,2,6,7], as well as research on the direct healthcare utilization and costs associated with endometriosis among women with Medicaid insurance in the United States.[8] AbbVie also presented efficacy and safety data from a Phase 2b clinical trial evaluating elagolix alone or in combination with add-back therapy (estradiol/norethindrone acetate) compared to placebo in women with uterine fibroids.[9,10]

Trial Design

Elaris EMIII and Elaris EMIV are two extension studies of the six month pivotal, Phase 3 studies (Elaris EM-I and Elaris EM-II) that evaluated an additional six months of treatment, for an overall treatment period of 12 months, with two elagolix doses (150 mg once daily and 200 mg twice daily).[4] Study participants were women, age 18-49, with surgically diagnosed endometriosis and moderate to severe endometriosis-associated pain at baseline during the pivotal trials. Baseline values for these analyses were assessed prior to dosing in the pivotal studies[1,3].

About Endometriosis
Endometriosis occurs when tissue similar to that normally found in the uterus begins to grow outside of the uterus, leading to long-term pelvic pain (during or between periods), pain with intercourse and other painful symptoms.[11] These growths are called lesions and can occur on the ovaries, the fallopian tubes, or other areas near the uterus, such as the bowel or bladder.[11,12] Estrogen fuels the growth of lesions.[12] There is no cure for endometriosis,[13] and the associated pain is currently managed with oral contraceptives, progestins, danazol, nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, and GnRH agonists, many of which are not specifically indicated for the treatment of endometriosis.[11,14] In more extensive cases, surgical interventions (e.g., laparotomy or laparoscopy) are often pursued, and may not be curative for all individuals.[14]

About Elagolix
Elagolix, a gonadotropin-releasing hormone (GnRH) receptor antagonist, is an orally administered, short-acting molecule that blocks endogenous GnRH signaling by binding competitively to GnRH receptors in the pituitary gland. Administration results in readily reversible, dose-dependent inhibition of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) secretion, leading to reduced ovarian production of the ovarian sex hormones, estradiol and progesterone, while on therapy. Elagolix is currently being investigated in diseases that are mediated by ovarian sex hormones, such as uterine fibroids and endometriosis. To date, elagolix has been studied in over 40 clinical trials totaling more than 3,000 subjects. The FDA granted priority review for AbbVie's NDA for endometriosis in Q4 2017. Phase 3 trials of elagolix for the management of uterine fibroids are ongoing.

About AbbVie
AbbVie is a global, research-driven biopharmaceutical company committed to developing innovative advanced therapies for some of the world's most complex and critical conditions. The company's mission is to use its expertise, dedicated people and unique approach to innovation to markedly improve treatments across four primary therapeutic areas: immunology, oncology, virology and neuroscience. In more than 75 countries, AbbVie employees are working every day to advance health solutions for people around the world. For more information about AbbVie, please visit us at www.abbvie.com. Follow @AbbVieUS on Twitter, Facebook or LinkedIn.

Forward-Looking Statements
Some statements in this news release may be forward-looking statements for purposes of the Private Securities Litigation Reform Act of 1995. The words "believe," "expect," "anticipate," "project" and similar expressions, among others, generally identify forward-looking statements. AbbVie cautions that these forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those indicated in the forward-looking statements. Such risks and uncertainties include, but are not limited to, challenges to intellectual property, competition from other products, difficulties inherent in the research and development process, adverse litigation or government action, and changes to laws and regulations applicable to our industry. Additional information about the economic, competitive, governmental, technological and other factors that may affect AbbVie's operations is set forth in Item 1A, "Risk Factors," in AbbVie's 2015 Annual Report on Form 10-K, which has been filed with the Securities and Exchange Commission. AbbVie undertakes no obligation to release publicly any revisions to forward-looking statements as a result of subsequent events or developments, except as required by law.

[1] Surrey, E., Taylor, H.S., Giudice, L.C., Singh, S., Abrao, M.S., Lessey, B.A., Duan, W.R., Peloso P.M., Schwefel, B. Chwalisz, K. Long-term safety and efficacy of elagolix treatment in women with endometriosis associated pain: primary results from two phase 3 extension studies. *Fert. Sterl*. 2017; 108: e95.

[2] Taylor H.S, Johnson N., Carr B., Leyland N., Rechberger T., Duan W.R., Peloso P.M., Soliman A.M., Schwefel B., Chwalisz K. Maintenance of endometriosis-associated pain reduction and quality of life improvement in phase 3 extension studies with elagolix. *Fert. Sterl.* 2017; 108: e96.

[3] Taylor, H. S. ,Giudice, L. C., Lessey, B. A.,Abrao, M. S., Kotarski, J., Archer, D. F., Diamond, M. P., Surrey, E., Johnson, N. P., Watts, N. B., Gallagher, J. C., Simon, J. A., Carr, B. R., Dmowski, W. P., Leyland, N., Rowan, J. P., Duan, W. R., Ng, J., Schwefel, B., Thomas, J. W., Jain, R. I., Chwalisz, K. Treatment of Endometriosis-Associated Pain with Elagolix, an Oral GnRH Antagonist. N Engl J Med. 377:28-40, 2017.

[4] Surrey, E. et. al. Use of elagolix for the management of endometriosis-associated pain: secondary efficacy results from two randomized, placebo-controlled studies. *Fertil Steril.* 2016; 106: e268-e269.

[5] Taylor, H.S. et. al. The impact of elagolix on quality of life in women with endometriosis-associated pain: results from two randomized, placebo controlled studies using the endometriosis health profile questionnaire. *Fertil Steril.* 2016; 106: e93.

[6] Archer D.F., Watts N., Gallagher C., Surrey E., Leyland N., Duan W.R., Schwefel B., Peloso P.M., Chwalisz K. Long-term effect of elagolix on bone mineral density: results from two phase three extension studies in women with endometriosis-associated pain. *Fert. Sterl*. 2017; 108: e95.

[7] Lessey B.A., Diamond M.P., Agarwal S., Dmowski P., Duan W.R., Thomas J.W., Chwalisz K. Long-term effect of elagolix on the endometrium: results from two phase 3 extension studies in women with endometriosis-associated pain *Fert. Sterl*. 2017; 108: e45.

[8] Soliman, A.M, Surrey, E., Bonafede, M., Nelson J.K., Vora J.B., Agarwal S. Direct healthcare utilization and costs associated with endometriosis among women with Medicaid insurance. *Fert. Sterl.* 2017; 108: e96.

[9] Simon J.A., Stewart E.A., Owens C., Duan W.R, Gao J. Chwalisz K. Elagolix treatment in women with heavy menstrual bleeding-associated with uterine fibroids: efficacy and safety results from a phase 2b study. *Fert. Sterl*. 2017; 108: e26.

[10] Diamond M., Soliman A.M., Gao J., Owens C., Chwalisz K., Archer D.F. Elagolix improves quality of life in women with heavy menstrual bleeding associated with uterine fibroids: evidence from a phase 2b randomized trial. *Fert. Sterl*. 2017; 108: e27.

[11] The American College of Obstetricians and Gynecologists. ACOG Education Pamphlet AP013: Endometriosis. Washington, DC: September 2008. ISSN 1074-8601.

[12] Giudice LC. Clinical practice: Endometriosis. New England Journal of Medicine. 2010; 362:2389–2398.

[13] Greene, AD, Lang, SA, Kendziorski, JA, Sroga-Rios, JM, Herzog, TJ, Burns, KA. Endometriosis: where are we and where are we going? Reproduction. 2016; 152 (3):R63-78.

[14] Mayo Clinic. Diseases & Conditions: Endometriosis Fact Sheet. http://www.mayoclinic.org/diseases-conditions/endometriosis/diagnosis-treatment/treatment/txc-20236449. Accessed June 1, 2017.

[15] Data on File, AbbVie Inc. ABVRRTI 65242

Contact(s)

Media
Toni Haubert
antoinette.haubert@abbvie.com
(847) 936-5382

Investors
Liz Shea
liz.shea@abbvie.com
(847) 935-2211