AbbVie Submits New Drug Application to U.S. FDA for Investigational Oral Treatment Elagolix for the Management of Endometriosis with Associated Pain

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- In clinical studies, elagolix demonstrated superiority compared to placebo in reducing three types of endometriosis-associated pain - daily menstrual pelvic pain, non-menstrual pelvic pain and painful intercourse
- Endometriosis affects an estimated one in ten women of reproductive age and is associated with pain symptoms that can be debilitating
- If approved by the FDA, elagolix will be the first new medical management treatment option for endometriosis-associated pain in more than a decade

NORTH CHICAGO, Ill., Sept. 6, 2017 /PRNewswire/ -- AbbVie (NYSE: ABBV), a research and development based global biopharmaceutical company in cooperation with Neurocrine Biosciences, Inc. (NASDAQ: NBIX), announced that it has submitted a New Drug Application (NDA) to the U.S. Food and Drug Administration for elagolix, an investigational, orally administered gonadotropin-releasing hormone (GnRH) antagonist, being evaluated for the management of endometriosis with associated pain. In two replicate Phase 3 clinical studies, elagolix demonstrated superiority compared to placebo in reducing three types of endometriosis-associated pain – daily menstrual pelvic pain, non-menstrual pelvic pain and painful intercourse.

"The submission represents an important step forward for women suffering from endometriosis and physicians who are in need of additional medical treatment options to help manage this chronic and painful disease," said Michael Severino, M.D., Executive Vice President, Research and Development and Chief Scientific Officer, AbbVie. "Elagolix has the potential to be an important oral treatment option for women suffering from the most prevalent symptoms of endometriosis and we look forward to working with the FDA throughout the review process."

The NDA is supported by data from the largest prospective randomized endometriosis clinical trials conducted to date, which evaluated the safety and efficacy of elagolix in nearly 1,700 women with moderate-to-severe endometriosis-associated pain. The data from two replicate Phase 3 studies demonstrated that, at month three and month six, both elagolix doses (150 mg once daily and 200 mg twice daily) resulted in a statistically significant higher proportion of responders for menstrual pain (dysmenorrhea) and non-menstrual pelvic pain associated with endometriosis as measured by the Daily Endometriosis Pain Impact scale versus placebo. Significant improvements compared to placebo were also observed at month three for the 200 mg twice daily dose in scores for painful intercourse (dyspareunia). A reduction in the amount and frequency of rescue pain medication use, including nonsteroidal anti-inflammatory drugs and opioids, compared to placebo was also seen in the higher dose at month three and six. In clinical studies, elagolix treatment decreased endometrial proliferation in a dose-dependent manner after six months of treatment with no adverse endometrial findings.

The safety profile of elagolix was consistent with the partial hormone suppression associated with its mechanism of action. Findings were consistent across Phase 3 trials and prior elagolix studies. In the first Phase 3 study, the most frequently reported adverse events assessed over six months were hot flush, headache and nausea. The rates for hot flush were (7%, 24%, 42% for placebo, 150 mg once daily and 200 mg twice daily, respectively) and headache were (10%, 15%, 17% for placebo, 150 mg once daily and 200 mg twice daily, respectively). The majority of hot flushes were mild to moderate in severity. Elagolix treatment was associated with dose-dependent decreases in bone mineral density (BMD) in women with endometriosis-associated pain. After six months of treatment, all of the women had a BMD z-score above -2.0, within the normal age-adjusted range.[1,2] The second Phase 3 study demonstrated similar results.

These data were first presented at the American Society for Reproductive Medicine (ASRM) annual meeting in October 2016 and published in *The New England Journal of Medicine* in May 2017.[3] Extension studies permitted some women to be treated for an additional six months, data from which will be presented at a future meeting.

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.[4] 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.[2,5] Estrogen fuels the growth of lesions.[3] There is no cure for endometriosis,[6] 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.[3] In more extensive cases, surgical interventions (e.g., laparotomy or laparoscopy) are often pursued, and may not be curative for all individuals.[7]

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 sex hormones, estradiol and progesterone, while on therapy. Elagolix is currently being investigated in diseases that are mediated by 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. AbbVie submitted a New Drug Application to the U.S. Food and Drug Administration (FDA) for the management of endometriosis-associated pain in the third quarter of 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] The International Society for Clinical Densitometry. 2015 ISCD Official Positions – Adult. https://www.iscd.org/official-positions/2015-iscd-official-positions-adult/. Accessed August 1, 2017.

[2] Data on File, ABV RRTI 64932

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

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

[6] 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.

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

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