AbbVie Announces Positive Topline Results from Phase 3 Extension Study Evaluating Investigational Elagolix in Women with Uterine Fibroids

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- Study results (ELARIS UF-EXTEND) showed elagolix, in combination with add-back therapy, reduced heavy menstrual bleeding for up to 12 months
- Results were consistent with two pivotal Phase 3 studies (ELARIS UF-I and ELARIS UF-II) and no new safety signals were identified
- Data from the pivotal studies will be presented at a medical conference later this year

NORTH CHICAGO, Ill., Aug. 22, 2018 /PRNewswire/ -- AbbVie (NYSE: ABBV), a research-based global biopharmaceutical company, in cooperation with Neurocrine Biosciences, Inc. (NASDAQ: NBIX), announced that results from the Phase 3 ELARIS UF-EXTEND extension study (MI2-816) showed at month 12 that elagolix (300 mg twice daily), in combination with low-dose hormone (add-back) therapy (estradiol 1.0 mg / norethindrone acetate 0.5 mg), reduced heavy menstrual bleeding with 87.9 percent of women with uterine fibroids achieving clinical response.

This result is consistent with that observed in the two pivotal Phase 3 studies, ELARIS UF-I and ELARIS UF-II, in which 68.5 percent and 76.2 percent of women with uterine fibroids who received elagolix with add-back therapy for six months achieved clinical response, respectively. Clinical response was defined as menstrual blood loss volume of less than 80 mL and a 50 percent or greater reduction in menstrual blood loss volume from baseline to their final month. Secondary endpoint results in the extension study were also consistent with that observed in the pivotal studies.[1]

Uterine fibroids are the most common type of benign abnormal growth in a woman's pelvis.[2] Most American women will develop fibroids at some point in their lives.[2,5] Fibroids can be asymptomatic, but in approximately 25 percent of women,[3] they can cause symptoms, such as heavy menstrual bleeding, painful periods, vaginal bleeding at times other than menstruation, and anemia.[2] African American women are more likely to experience fibroids and do so at a younger age.[4]

"Women with uterine fibroids are in need of additional medical management options that could help address unresolved symptoms," said Dawn Carlson, M.D., M.P.H., vice president, general medicine development. "The results from this extension study provide additional information on the use of elagolix for up to 12 months in the management of heavy menstrual bleeding associated with uterine fibroids."

The safety profile in ELARIS UF-EXTEND was consistent with previously reported topline results from the pivotal Phase 3 studies and no new safety signals were identified. The most frequent adverse events reported (≥ 5 percent) were hot flush, night sweats, nausea, headache and nasopharyngitis. Reduction of bone mineral density (BMD) was also observed. Evaluation of BMD at 12 months showed women with heavy menstrual bleeding associated with uterine fibroids who received elagolix in combination with add-back therapy had less mean percent change from baseline in BMD compared to women who received elagolix alone.[1] Safety data will continue to be collected and analyzed.

Data from the pivotal Phase 3 studies will be presented at a medical conference later this year and the ELARIS UF-EXTEND Phase 3 study data will be presented at a future medical conference. Data from the Phase 3 program will support regulatory submission for elagolix in uterine fibroids, anticipated in 2019.

Elagolix in uterine fibroids is investigational and has not been proven safe and effective.

Overview of the Elagolix Phase 3 Uterine Fibroids Program

The elagolix Phase 3 uterine fibroid program evaluated nearly 800 premenopausal women with heavy menstrual bleeding associated with uterine fibroids in two pivotal studies at approximately 100 sites in the United States and Canada. The replicate studies evaluated the safety, tolerability and efficacy of elagolix alone (300 mg twice daily or BID) and in combination with low-dose hormone (add-back) therapy (estradiol 1.0 mg / norethindrone acetate 0.5 mg) in women with uterine fibroids for six months. The primary endpoint assessed the reduction in heavy menstrual bleeding compared to placebo as measured by the alkaline hematin method, an objective measurement of total menstrual blood loss based on quantitation of menstrual blood collected on sanitary products.

ELARIS UF-EXTEND is a Phase 3 randomized, double-blind, multicenter, extension study designed to evaluate the efficacy and safety of elagolix alone and in combination with add-back therapy in premenopausal women with heavy menstrual bleeding associated with uterine fibroids for an additional six months (up to 12 months total). Subjects who received elagolix 300 mg twice daily or elagolix 300 mg twice daily in combination with add-back therapy in the pivotal studies continued to receive the same treatment while subjects who received placebo in the pivotal studies were randomized in an equal ratio to one of the two treatment groups (elagolix 300 mg twice daily or elagolix 300 mg twice daily in combination with add-back therapy).

An overview of the results from the elagolix Phase 3 uterine fibroids program is below.[1]

Primary Endpoint Results at Final Month Across the Elagolix Phase 3 Uterine Fibroids Program		
Study	**Responder Rate**	
	Elagolix 300 mg BID + Add-Back Therapy	**PBO**
ELARIS UF-I	68.5% (p<0.001) n=206	8.7% n=102
ELARIS UF-II	76.2% (p<0.001) n=189	10.1% n=94

ELARIS UF-EXTEND	87.9% n=206	N/A

About Uterine Fibroids

Uterine fibroids (also called leiomyomas or myomas) are non-cancerous, hormonally-responsive muscle tissue tumors of the uterus.[3] Fibroids are the most common type of abnormal growth in a woman's pelvis and can affect up to 70 percent of Caucasian women and up to 80 percent of African American women by age 50.[2,5] Fibroids can range in size, shape, number and location.[2] Fibroids can be asymptomatic, but in some women, fibroids can cause symptoms such as heavy menstrual bleeding, painful periods, vaginal bleeding at times other than menstruation, anemia, pain in the abdomen or lower back, pain during sex, difficulty urinating or frequent urination, constipation, rectal pain or difficulty getting pregnant.[2] Treatment options for uterine fibroids include surgery (hysterectomy, myomectomy), hysteroscopy, endometrial ablation, uterine artery embolization, magnetic resonance imaging-guided ultrasound and medical management with treatments such as oral contraceptives, progestins, selective progesterone receptor modulators, and GnRH agonists.[2] Fibroids are the leading indication for hysterectomy in the United States.[5]

About Elagolix

Elagolix is an orally-administered, nonpeptide, small molecule gonadotropin-releasing hormone (GnRH) receptor antagonist that inhibits endogenous GnRH signaling by binding competitively to GnRH receptors in the pituitary gland.[6] Administration results in dose-dependent suppression of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), leading to decreased blood concentrations of ovarian sex hormones, estradiol and progesterone.[6] 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 studies, totaling more than 3,700 subjects. U.S. regulatory submission for elagolix in uterine fibroids is anticipated in 2019.

About ORILISSA™ (elagolix)

ORILISSA is approved by the U.S. Food and Drug Administration (FDA) for the management of moderate to severe pain associated with endometriosis. The recommended duration of use for ORILISSA is up to 24 months for the 150 mg once daily dose and up to six months for the 200 mg twice daily dose, as it causes a dose-dependent decrease in bone mineral density (BMD). BMD loss is greater with increasing duration of use and may not be completely reversible after stopping treatment. For women with moderate hepatic impairment, the recommended dosage is 150 mg once daily for up to six months. ORILISSA is recommended to be taken orally at approximately the same time each day, with or without food.[6]

Please click here for full Prescribing Information, including the Medication Guide.

USE:
ORILISSA is a prescription medicine used to treat moderate to severe pain associated with endometriosis. It is not known if ORILISSA is safe and effective in children under 18 years of age.

IMPORTANT SAFETY INFORMATION:
What is the most important information I should know about ORILISSA?
Take ORILISSA exactly as your healthcare provider tells you.

ORILISSA may cause serious side effects, including:

- **Bone Loss (decreased Bone Mineral Density (BMD))**
  While you are taking ORILISSA, your estrogen levels will be low. This can lead to BMD loss. Your BMD may improve after stopping ORILISSA but may not recover completely. It is unknown if these bone changes could increase your risk for broken bones as you age. Your healthcare provider may order a DXA scan to check your BMD.
- **Effects on Pregnancy**
  Do not take ORILISSA if you are trying to become or are pregnant as your risk for early pregnancy loss may increase. **If you think you are pregnant**, stop taking ORILISSA right away and call your healthcare provider. ORILISSA may change your menstrual periods (irregular bleeding or spotting, a decrease in menstrual bleeding, or no bleeding at all), making it hard to know if you are pregnant. Watch for other signs of pregnancy such as breast tenderness, weight gain and nausea. ORILISSA does not prevent pregnancy. You will need to use effective hormone-free birth control (such as condoms or spermicide) while taking ORILISSA and for one week after stopping ORILISSA. Birth control pills that contain estrogen may make ORILISSA less effective. It is unknown how well ORILISSA works while on progestin-only birth control.

Do not take ORILISSAif you:

- are or may be pregnant, have osteoporosis, have severe liver disease, or take medicines known as strong OATP1B1 inhibitors such as cyclosporine or gemfibrozil. If you are unsure if you are taking one of these medicines, ask your healthcare provider.

What should I tell my healthcare provider before taking ORILISSA?

Tell your healthcare provider of all your medical conditions, including if you:

- have or have had broken bones, have other conditions or take medicine that may cause bone problems, have or have had depression, mood problems or suicidal thoughts or behavior, have liver problems, think you may be pregnant, or are breastfeeding or plan to be. It is unknown if ORILISSA passes into breastmilk. Talk to your healthcare provider about the

best way to feed your baby if you take ORILISSA.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. **Especially tell your healthcare provider if you take** birth control pills. Your healthcare provider may advise you to change the pills you take or your method of birth control**.**

What are the possible side effects of ORILISSA?

ORILISSA can cause serious side effects including:

- **suicidal thoughts, actions, or behavior, and worsening mood**. Call your healthcare provider right away, or call 911 if an emergency, if you have any of these symptoms, especially if they are new, worse, or bother you: thoughts about suicide or dying, try to commit suicide, new or worse depression or anxiety, or other unusual changes in behavior or mood. You or your caregiver should pay attention to any changes, especially sudden changes in your mood, behaviors, thoughts, or feelings.
- **abnormal liver tests.** Call your healthcare provider right away if you have any of these signs and symptoms of liver problems: yellowing of the skin or the whites of the eyes (jaundice), dark amber-colored urine, feeling tired, nausea and vomiting, generalized swelling, right upper stomach area pain, bruising easily.

The most common side effects of ORILISSA include: hot flashes or night sweats, headache, nausea, difficulty sleeping, absence of periods, anxiety, joint pain, depression and mood changes.

These are not all the possible side effects of ORILISSA. This is the most important information to know about ORILISSA. For more information, talk to your healthcare provider.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away. Call your healthcare provider for medical advice about side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

If you cannot afford your medication, contact www.pparx.org for assistance.

About AbbVie

AbbVie is a global, research and development-based 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 are, or may be considered, 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," of AbbVie's 2017 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 Data on File, ABVRRTI66805

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Contact(s)

U.S.
Media
Toni Haubert
+1 (847) 936-5382
antoinette.haubert@abbvie.com

Investors

Liz Shea
+1 (847) 935-2211
liz.shea@abbvie.com