First Ever Peyronie's Disease (PD) Treatment Guidelines Support Use of XIAFLEX® in Appropriate Patients

May 19, 2015

-- Endo presents encore data of research evaluating the impact of PD on erectile function and female partners, as well as the efficacy of XIAFLEX® treatment --

DUBLIN, May 19, 2015 /PRNewswire/ -- Endo Pharmaceuticals Inc., a subsidiary of Endo International plc (NASDAQ: ENDP) (TSX: ENL), supports efforts to bring the medical community the first ever treatment guidelines for Peyronie's Disease (PD), a condition in which collagen plaque, or scar tissue, develops on the shaft of the penis, and may harden and reduce flexibility. The company also announced today that it has presented encore data at a key medical meeting evaluating the efficacy of XIAFLEX® (collagenase clostridium histolyticum) treatment for PD as well as the impact of PD on erectile dysfunction (ED) and female partners.

The new guidelines, presented on Monday by the American Urological Association (AUA) at its 110th Annual Scientific Meeting in New Orleans, recommend the use of XIAFLEX® in combination with modeling in patients with stable PD, penile curvature greater than 30 degrees and less than 90 degrees, and intact erectile function. XIAFLEX®, which is the only treatment approved by the U.S. Food and Drug Administration for PD, received a stronger recommendation than any other potential treatment option for PD, based on the strength of existing data. XIAFLEX® is indicated for adult men with PD who have a plaque that can be felt and a curve in their penis greater than 30 degrees when treatment is started.

"As the only FDA-approved PD treatment, XIAFLEX® is available to address a critical unmet need for men living with this distressing and sometimes painful condition," said Sue Hall, Executive Vice President, Chief Scientific Officer and Global Head of Research & Development and Quality at Endo. "We are pleased that the AUA has issued the first PD treatment guidelines, and that the recommendations support the use of XIAFLEX®. We believe these guidelines will serve to inform physicians as they determine the best treatment paradigm for managing this condition."

Encore Presentations of XIAFLEX® Studies
Also at the AUA conference, Endo Pharmaceuticals Inc. presented several abstracts yesterday as part of a podium session. These findings were previously presented at the 20th Annual Fall Scientific Meeting of the Sexual Medicine Society of North America (SMSNA) in Miami in November 2014, and included the following:

- ***XIAFLEX® and Earlier Treatment***: A post-hoc analysis of the Phase 3 IMPRESS (The **I**nvestigation for **M**aximal **P**eyronie's **R**eduction **E**fficacy and **S**afety **S**tudies) trials examined improvements in penile curvature and bother related to PD following treatment with XIAFLEX® or placebo in subjects with PD duration of 6 to <12 months or >/=12 months. Average improvements in penile curvature with XIAFLEX® were higher than placebo among men with PD duration of 6 to <12 months, and these findings were comparable to changes observed for men with PD duration >/=12 months. In addition, improvements in patient-reported bother were similar between the two groups. Most adverse events (AEs) in the XIAFLEX® group occurred at the injection site (penile bruising, pain, edema, contusion) and were mild to moderate in severity. The AE profiles were comparable regardless of PD duration.
- ***PD bother, pain and erectile function***: A second post-hoc analysis of the IMPRESS trials showed that men with PD experience distress, or "bother" for several reasons, including penile curvature, perceived penile shortening, and pain during intercourse. Both PD bother and pain during intercourse were found to directly impact erectile function.

"Research and treatment decisions in PD have, historically, focused on penile curvature and other physical symptoms of the condition, but not as much on the psychosocial impact on men and their partners," said Larry I. Lipshultz, M.D., Professor of Urology and Chief of the Division of Male Reproductive Medicine and Surgery at the Baylor College of Medicine in Houston. "These data support that patient-reported bother associated with Peyronie's Disease is a clinically important measure in understanding and treating this condition, and underscore the need for adopting a holistic approach that assesses and addresses the overall well-being of PD patients and their partners."

- ***PD treatment: Impact on men and their female partners***: In a 24-week, Phase 3, open-label study, men with PD who had previously received placebo in the IMPRESS trials received up to eight injections of XIAFLEX® for 24 weeks. Their female sexual partners (FSPs), who chose to participate in the study, completed the female sexual function index (FSFI) and the PD questionnaire for FSPs (PDQ-FSP) – a 12-item, investigational questionnaire adapted from the men's PDQ. From treatment initiation to Week 52, men treated with XIAFLEX® experienced improvements in penile curvature and in PD bother (as measured by PDQ bother score). The most common AEs reported were penile hematoma, penile pain and penile swelling. There were no serious treatment-related AEs.

The 30 FSPs who participated in the open-label study reported improvements in the PDQ-FSP following XIAFLEX® treatment in their male partners with PD. Based on 95% confidence intervals for the change from baseline, statistically significant improvements were observed for the FSFI scales of arousal, lubrication, orgasm, satisfaction and pain, as well as the full scale total scores. The proportion of women reporting sexual dysfunction (FSFI total score of <26.55) also decreased after their partner received treatment.

About Peyronie's Disease

Peyronie's Disease (PD) is a condition that involves the development of collagen plaque, or scar tissue, on the shaft of the penis. The scar tissue, known as a Peyronie's plaque, may harden and reduce flexibility, which may cause bending or arching of the penis during erection. PD can result in varying degrees of penile curvature deformity and disease "bother" (encompassing concern about erection appearance, erection pain and the impact of PD on intercourse and on frequency of intercourse). PD is a disease with an initial inflammatory component. This inflammatory phase is poorly understood with a somewhat variable disease course and spontaneous resolution occurring in less than 13 percent of cases. After approximately 12 months of disease, the disease is reported to often develop into a more chronic, stable phase. The incidence of PD is estimated between 3 and 9 percent; however the disease is thought to be underdiagnosed and undertreated.

About XIAFLEX®

XIAFLEX® (collagenase clostridium histolyticum, or CCH) is a biologic approved in the U.S., EU, Canada and Australia for the treatment of adult Dupuytren's contracture (DC) patients with a palpable cord, and approved in the U.S. for the treatment of adult men with Peyronie's disease (PD) with a palpable plaque and penile curvature deformity of at least 30 degrees at the start of therapy. XIAFLEX® consists of a combination of two subtypes of collagenase, derived from Clostridium histolyticum. Together, the collagenase sub-types are thought to work synergistically to break the bonds of the triple helix collagen structure. XIAFLEX® has been granted Orphan status in the U.S. by the FDA for DC and PD.

IMPORTANT SAFETY INFORMATION

What is XIAFLEX®?

XIAFLEX® is approved for two uses: Dupuytren's contracture and Peyronie's disease.

XIAFLEX® is a prescription medicine used to treat adults with Dupuytren's contracture when a "cord" can be felt.

XIAFLEX® is a prescription medicine used to treat adult men with Peyronie's disease who have a "plaque" that can be felt and a curve in their penis greater than 30 degrees when treatment is started.

It is not known if XIAFLEX® is safe and effective in children under the age of 18.

Who should not receive XIAFLEX®?

Do not receive XIAFLEX® if you:

- Have been told by your healthcare provider that the Peyronie's plaque to be treated involves the "tube" that your urine passes through (urethra).
- Have had an allergic reaction to collagenase clostridium histolyticum or any of the ingredients in XIAFLEX®, or to any other collagenase product. See the end of the Medication Guide for a complete list of ingredients in XIAFLEX®.

What is the most important information I should know about XIAFLEX® for the treatment of Dupuytren's contracture?

XIAFLEX® can cause serious side effects, including:

- **Tendon rupture or ligament damage.** Receiving an injection of XIAFLEX® may cause damage to a tendon or ligament in your hand and cause it to break or weaken. This could require surgery to fix the damaged tendon or ligament. Call your healthcare provider right away if you have trouble bending your injected finger (towards the wrist) after the swelling goes down or you have problems using your treated hand after your follow-up visit.
- **Nerve injury or other serious injury of the hand. Call your healthcare provider right away** if you get numbness, tingling, or increased pain in your treated finger or hand after your injection or after your follow-up visit.
- **Allergic reactions.** Severe allergic reactions can happen in people who receive XIAFLEX®, because it contains foreign proteins.

Call your healthcare provider right away if you have any of these symptoms of an allergic reaction after an injection of XIAFLEX®:

- Hives
- Swollen face
- Breathing trouble
- Chest pain

What is the most important information I should know about XIAFLEX® for the treatment of Peyronie's disease?

XIAFLEX® can cause serious side effects, including:

1. **Penile fracture (corporal rupture) or other serious injury to the penis.** Receiving an injection of XIAFLEX® may cause damage to the tubes in your penis called the corpora. After treatment with XIAFLEX®, one of these tubes may break during an erection. This is called a corporal rupture or penile fracture. This could require surgery to fix the damaged area. Damage to your penis might not get better after a corporal rupture.

- After treatment with XIAFLEX®, blood vessels in your penis may also break, causing blood to collect under the skin (hematoma). This could require a procedure to drain the blood from under the skin.
  Symptoms of corporal rupture or other serious injury to your penis may include:
  - a popping sound or sensation in an erect penis
  - sudden loss of the ability to maintain an erection
  - pain in your penis
  - purple bruising and swelling of your penis
  - difficulty urinating or blood in the urine

Call your healthcare provider right away if you have any of the symptoms of corporal rupture or serious injury to the penis listed above.
Do not have sex or have any other sexual activity for at least 2 weeks after the second injection of a treatment cycle with XIAFLEX® and after any pain and swelling has gone away.

XIAFLEX® for the treatment of Peyronie's disease is only available through a restricted program called the XIAFLEX® Risk Evaluation and Mitigation Strategy (REMS) Program. For more information about the XIAFLEX® REMS Program go to www.XIAFLEXREMS.com or call 1-877-942-3539.

2. **Allergic reactions.** Severe allergic reactions can happen in people who receive XIAFLEX®, because it contains foreign proteins.
Call your healthcare provider right away if you have any of these symptoms of an allergic reaction after an injection of XIAFLEX®:

- Hives
- Swollen face
- Breathing trouble
- Chest pain

XIAFLEX® when used for either Dupuytren's contracture or Peyronie's disease can cause serious side effects, including:

- **Increased chance of bleeding.** Bleeding or bruising at the injection site can happen in people who receive XIAFLEX®. Talk to your healthcare provider if you have a problem with your blood clotting. XIAFLEX® may not be right for you.

The most common side effects with XIAFLEX® for the treatment of Dupuytren's contracture include:

- Swelling of the injection site or the hand
- Bruising or bleeding at the injection site
- Pain or tenderness of the injection site or the hand
- Swelling of the lymph nodes (glands) in the elbow or armpit (axilla)
- Itching
- Breaks in the skin
- Redness or warmth of the skin
- Pain in the armpit

The most common side effects with XIAFLEX® for the treatment of Peyronie's disease include:

- A small collection of blood under the skin at the injection site (hematoma)
- Swelling at the injection site or along your penis
- Pain or tenderness at the injection site, along your penis and above your penis
- Penis bruising
- Itching of your penis or scrotum (genitals)
- Painful erection
- Erection problems (erectile dysfunction)
- Changes in the color of the skin of your penis
- Blisters at the injection site
- Pain with sex
- A lump at the injection site (nodule)

Tell your healthcare provider if you have any side effect that bothers you or does not go away.
These are not all of the possible side effects with XIAFLEX®. For more information, ask your healthcare provider or pharmacist.

Please see the full Prescribing Information and Medication Guide available at www.XIAFLEX.com.

About Endo International plc
Endo International plc is a global specialty pharmaceutical company focused on improving patients' lives while creating shareholder value. Endo develops, manufactures, markets and distributes quality branded pharmaceutical and generic pharmaceutical products as well as over-the-counter medications through its operating companies. Endo has global headquarters in Dublin, Ireland, and U.S. headquarters in Malvern, PA. Learn more at www.endo.com.

About Endo Pharmaceuticals Inc.
Endo Pharmaceuticals Inc. is focused on developing and delivering high-value branded pharmaceutical products that meet the unmet needs of patients. Endo Pharmaceuticals is an operating company of Endo International plc (NASDAQ: ENDP) (TSX: ENL), a global specialty pharmaceutical company focused on improving patients' lives while creating shareholder value. Learn more at www.endo.com or www.endopharma.com.

Cautionary Note Regarding Forward-Looking Statements
This press release contains "forward-looking statements," including but not limited to the statements by Dr. Hall and Dr. Lipshultz, as well as statements regarding the safety, efficacy, market and product potential, and other statements regarding XIAFLEX®. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or unknown risks or uncertainties materialize, actual results could

vary materially from Endo's expectations and projections. Risks and uncertainties include, among other things, general industry and pharmaceutical market conditions; technological advances and patents attained by competitors; challenges inherent in the research and development process; challenges related to new product marketing, such as the unpredictability or market acceptance for new pharmaceutical products and new indications for such products; and governmental laws and regulations affecting domestic and foreign operations. Endo expressly disclaims any intent or obligation to update these forward-looking statements except as required by law. Additional information concerning these and other risks can be found in press releases issued by Endo, as well as in Endo's public filings with the U.S. Securities and Exchange Commission and Canadian securities regulators, including the discussion under the heading "Risk Factors" in Endo's Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q. Copies of Endo's press releases and additional information about Endo are available at www.endo.com.

XIAFLEX is a registered trademark of Endo Global Ventures.

**Abstracts #PD48-06 (L. Levine), #PD48-07 (I. Goldstein), #PD48-12 (E. Serefoglu) presented on May 18, 2015 3:30 – 5:30 PM CT*

To view the original version on PR Newswire, visit:http://www.prnewswire.com/news-releases/first-ever-peyronies-disease-pd-treatment-guidelines-support-use-of-xiaflex-in-appropriate-patients-300085384.html

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