Endo Presents New XIAFLEX® (collagenase clostridium histolyticum) Data Analysis at Sexual Medicine Society of North America (SMSNA) Annual Meeting

October 22, 2021

DUBLIN, Oct. 22, 2021 /PRNewswire/ -- Endo International plc (NASDAQ: ENDP) announced today that new post-hoc data from two Phase 3 studies of XIAFLEX® (collagenase clostridium histolyticum, or CCH) in treating men with Peyronie's disease (PD) will be presented today in an oral presentation during the Sexual Medicine Society of North America (SMSNA) annual meeting.

"The data analysis discusses the importance of patient adherence when treating PD with XIAFLEX," said Dr. Matthew J. Ziegelmann, urologist and the presenting author.

"Collagenase Clostridium Histolyticum Treatment for Peyronie's Disease: Analysis of Outcomes and Cumulative Benefits After Each Injection Cycle" was submitted by authors Matthew Ziegelmann, M.D.; Genzhou Liu, Ph.D.; Michael P. McLane, Ph.D.; Yiqun Hu, M.D., Ph.D.; and Landon Trost, M.D.

The SMSNA Annual Fall Scientific Meeting is taking place in Scottsdale, Arizona, October 21-24, 2021.

About the Data
A post-hoc analysis of pooled data from two randomized, double-blind, placebo-controlled studies Phase 3 trials was conducted to evaluate incremental changes in penile curvature over the course of CCH treatment in men with PD. The analysis included men who received at least one injection of study medication.[1] XIAFLEX is an FDA-approved treatment for adult men with Peyronie's disease with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy.

Changes from baseline and from the previous penile curvature measurement were calculated after each of the four treatment cycles (weeks 6, 12, 18 and 24). CCH injections were administered in up to four treatment cycles at 6-week intervals; each cycle included two injections 1-3 days apart. For all patients, treatment included penile plaque modeling.[1]

Data support that incremental benefits were obtained from each of the four CCH treatment cycles administered to men with PD. Results may suggest incremental benefits with performing a full series of four CCH injections and penile modeling, even among men who were initially considered non-responders (achieved <20% reduction in penile curvature after two cycles of injections).

XIAFLEX is contraindicated in the treatment of Peyronie's plaques that involve the penile urethra due to potential risk to this structure and in patients with a history of hypersensitivity to XIAFLEX or to collagenase used in any other therapeutic application or application method.

About Peyronie's Disease
Peyronie's disease (PD) is a condition in which a buildup of fibrous scar tissue causes a pronounced curvature of the penis. This curvature can be painful during arousal and intimacy. It is estimated that PD can affect as many as 1 in 10 men in the U.S.

About XIAFLEX
XIAFLEX is composed of two purified collagenases (AUX-I and AUX-II) that hydrolyze collagen under physiologic conditions, resulting in lysis of collagen deposits.[2]

XIAFLEX is the only nonsurgical treatment option for appropriate adult men with Peyronie's disease approved by the Food and Drug Administration (FDA).

XIAFLEX® Indication and Important Safety Information

INDICATION
XIAFLEX® is indicated for the treatment of adult men with Peyronie's disease with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy.

IMPORTANT SAFETY INFORMATION FOR XIAFLEX

WARNING: CORPORAL RUPTURE (PENILE FRACTURE) OR OTHER SERIOUS PENILE INJURY IN THE TREATMENT OF PEYRONIE'S DISEASE

Corporal rupture (penile fracture) was reported as an adverse reaction in 5 of 1044 (0.5%) XIAFLEX-treated patients in clinical studies. In other XIAFLEX-treated patients (9 of 1044; 0.9%), a combination of penile ecchymoses or hematoma, sudden penile detumescence, and/or a penile "popping" sound or sensation was reported, and in these cases, a diagnosis of corporal rupture cannot be excluded. Severe penile hematoma was also reported as an adverse reaction in 39 of 1044 (3.7%) XIAFLEX-treated patients.

Signs or symptoms that may reflect serious penile injury should be promptly evaluated to assess for corporal rupture or severe penile hematoma which may require surgical intervention.

Because of the risks of corporal rupture or other serious penile injury, XIAFLEX is available for the treatment of Peyronie's disease only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the XIAFLEX REMS Program.

- **Contraindications:** XIAFLEX is contraindicated in the treatment of Peyronie's plaques that involve the penile urethra due to potential risk to this structure and in patients with a history of hypersensitivity to XIAFLEX or to collagenase used in any other therapeutic application or application method
- **Corporal Rupture or Other Serious Injury to the Penis:** Injection of XIAFLEX into collagen-containing structures such as the corpora cavernosa of the penis may result in damage to those structures and possible injury such as corporal rupture (penile fracture). Therefore, XIAFLEX should be injected only into the Peyronie's plaque and care should be taken to avoid injecting into the urethra, nerves, blood vessels, corpora cavernosa or other collagen-containing structures of the penis. Cases of localized skin and soft tissue necrosis occurring as sequelae of penile hematoma, some requiring surgical intervention, have been reported post-marketing
- **Hypersensitivity Reactions, Including Anaphylaxis:** In the double-blind, placebo-controlled portions of the clinical trials in Peyronie's disease, a greater proportion of XIAFLEX-treated patients (4%) compared to placebo-treated patients (1%) had localized pruritus after up to 4 treatment cycles (involving up to 8 XIAFLEX injection procedures). The incidence of XIAFLEX- associated pruritus was similar after each injection regardless of the number of injections administered
    - Because XIAFLEX contains foreign proteins, severe allergic reactions to XIAFLEX can occur. Anaphylaxis was reported in a post-marketing clinical trial in one patient who had previous exposure to XIAFLEX for the treatment of Dupuytren's contracture. Healthcare providers should be prepared to address severe allergic reactions following XIAFLEX injections. The safety of more than one treatment course of XIAFLEX is not known
- **Risk of Bleeding in Patients with Abnormal Coagulation:** In the XIAFLEX controlled trials in Peyronie's disease, 65.5% of XIAFLEX-treated patients developed penile hematoma, and 14.5% developed penile ecchymosis. Patients with abnormal coagulation (except for patients taking low-dose aspirin, eg, up to 150 mg per day) were excluded from participating in these studies. Therefore, the efficacy and safety of XIAFLEX in patients receiving anticoagulant medications (other than low-dose aspirin, eg, up to 150 mg per day) within 7 days prior to XIAFLEX administration is not known. In addition, it is recommended to avoid use of XIAFLEX in patients with coagulation disorders, including patients receiving concomitant anticoagulants (except for low-dose aspirin)
- **Acute Post-Injection Back Pain Reactions:** Post approval reports of acute lower back pain reactions, sometimes accompanied by radiation to the lower extremities, chest and arms, muscle spasms, chest pain, paresthesias, headache, and dyspnea, have been received by patients treated with XIAFLEX for Peyronie's disease. These events can be mild to severe in intensity. The events typically lasted for 15 minutes and typically did not require intervention. Administer the smallest number of treatment cycles necessary to treat the patient's curvature

Adverse Reactions: Clinical trials – In the XIAFLEX clinical trials for Peyronie's disease, the most frequently reported adverse drug reactions (≥25%) and at an incidence greater than placebo included: penile hematoma, penile swelling, and penile pain. Post-marketing experience – Acute post-injection lower back pain reactions; and cases of localized skin and soft tissue necrosis events as sequelae of penile hematoma, some of which required surgical intervention

Click for full Prescribing Information, including Boxed Warning and Medication Guide.

About Endo International plc
Endo (NASDAQ: ENDP) is a specialty pharmaceutical company committed to helping everyone we serve live their best life through the delivery of quality, life-enhancing therapies. Our decades of proven success come from passionate team members around the globe collaborating to bring the best treatments forward. Together, we boldly transform insights into treatments benefiting those who need them, when they need them. Learn more at www.endo.com or connect with us on LinkedIn.

Forward-Looking Statements
Certain information in this press release may be considered "forward-looking statements," within the meaning of the Private Securities Litigation Reform Act of 1995 and any applicable Canadian securities legislation including, but not limited to, the statements by Dr. Ziegelmann and any statements relating to the potential progress, timing or results of clinical studies or trials, research and development outcomes, market potential or product potential, safety, efficacy, effectiveness or availability. All forward-looking statements in this press release reflect Endo's current expectations of future events based on information available to Endo as of the date of this press release. If underlying assumptions prove inaccurate or unknown risks or uncertainties materialize, actual results could vary materially from Endo's expectations and projections, including with respect to the impact of any litigation, investigation or settlement proceeding on our financial statements, including our cash flows from operations; our ability to adjust to

changing market conditions; our ability to attract and retain key personnel; our ability to maintain compliance with our financial obligations under certain of our outstanding debt obligations, causing a downgrade of our debt and long-term corporate ratings (which could increase our cost of capital) and exposing us to potential events of default (if not cured or waived) under financial and operating covenants contained in our or our subsidiaries' outstanding indebtedness; our ability to incur additional borrowings under the covenants in our then-existing facilities or to obtain additional debt or equity financing for working capital, capital expenditures, business development, debt service requirements, acquisitions or general corporate or other purposes, or to refinance our indebtedness; and/or a significant reduction in our short-term and long-term revenues and/or otherwise cause us to be unable to fund our operations and liquidity needs, such as future capital expenditures and payment of our indebtedness. The occurrence or possibility of any such result may cause us to pursue one or more significant corporate transactions or remedial measures, including on a preventative or proactive basis. Actions that may be evaluated or pursued could include reorganization or restructuring activities of all or a portion of our business, asset sales or other divestitures, cost-saving initiatives or other corporate realignments, seeking strategic partnerships and exiting certain product or geographic markets. Some of these measures could take significant time to implement and others may require judicial or other third party approval. Any such actions may be complex, could entail significant costs and charges or could otherwise negatively impact shareholder value, and there can be no assurance that we will be able to accomplish any of these alternatives on terms acceptable to us, or at all, or that they will result in their intended benefits. Other risks and uncertainties include general industry and market conditions; technological advances and patents attained by competitors; challenges inherent in the research and development and regulatory processes, including regulatory decisions, product recalls, withdrawals and other unusual items; challenges related to product marketing, such as the unpredictability of market acceptance for new products and/or the acceptance of new indications for such products; inconsistency of treatment results among patients; potential difficulties in manufacturing; general economic conditions; 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 risk factors can be found in Endo's periodic reports filed with the U.S. Securities and Exchange Commission and in Canada on the System for Electronic Data Analysis and Retrieval, including current reports on Form 8-K, quarterly reports on Form 10-Q and annual reports on Form 10-K.

References:

1. Gelbard M, et al. *J Urol.* 2013;190(1):199-207.
2. XIAFLEX® (collagenase clostridium histolyticum) for injection, for intralesional use [package insert]. Malvern, PA: Endo Pharmaceuticals Inc.

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