Endo Presents New Investigational Collagenase Clostridium Histolyticum (CCH) Survey Data at American Society for Surgery of the Hand (ASSH) Annual Meeting

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DUBLIN, Sept. 30, 2021 /PRNewswire/ --

- *Survey data indicated a high level of consensus among expert hand surgeons for using CCH for the treatment of metacarpophalangeal (MP) and/or joint contractures of varying severity and MP and/or interphalangeal thumb contractures; data also achieved consensus for using CCH for treating proximal interphalangeal (PIP) joint contractures of varying severities*
- *Consensus-based findings among expert hand surgeons point to wide-ranging application of CCH for the treatment of DD for patients with varying degrees of disease severity and functional impairment*

Endo International plc (NASDAQ: ENDP) today announced results from the first two rounds of Delphi research exploring the expert positions of hand surgeons on the appropriate treatment of Dupuytren's disease (DD) with collagenase clostridium histolyticum (CCH) in patients with varying degrees of disease severity and functional impairment. The data are being presented on an e-poster at the American Society for Surgery of the Hand (ASSH) Annual Meeting in San Francisco, September 30–October 2. The poster is viewable here.

Dupuytren's disease is a heterogenous fibroproliferative condition of the palmar fascia characterized by the development of fascial nodules and cords that may result in digital contracture affecting hand function.[1,2] XIAFLEX® (collagenase clostridium histolyticum) is a nonsurgical treatment option composed of two purified collagenases that work to break down collagen when injected into fibrous tissue.[3]

"There are multiple nonsurgical and surgical options available to hand surgeons to effectively treat Dupuytren's disease, but right now, we don't have guidelines to support shared decision-making," said Gary M. Pess, MD, presenting author and a hand and upper extremity surgeon practicing in New Jersey. "These results demonstrate agreement among participating experienced hand surgeons that CCH may be an appropriate choice for patients with varying degrees of Dupuytren's contracture."

About the Report
Researchers used a modified Delphi method employing three successive online survey rounds to capture the clinical expertise of panelists and determine if consensus could be reached regarding the use of CCH for the treatment of DD.

In Round 1, 22 real-world case scenarios were used to determine the panelists' recommendations for using CCH to treat metacarpophalangeal (MP) and/or proximal interphalangeal (PIP) joint contractures involving a single finger or 2 fingers, with varying degrees of contracture and clinical severity. Each scenario presented a distinct contracture(s) with a series of statements to evaluate the impact of patient- or disease-related features (ie, age, recurrence, risk of anesthesia, diathesis, poor-quality skin, post-fasciectomy scarring) on the clinical decision to use CCH. Appropriate use of CCH for the treatment of thumb contractures and in patients who are on blood thinners other than aspirin also were explored.

Researchers captured responses using a 5-point Likert scale ("strongly agree," "agree," "deficient information," "disagree," and "strongly disagree"). Level of agreement for each statement was determined, with a consensus threshold of ≥66.7% for agreement ("strongly agree" and "agree") or disagreement ("strongly disagree" and "disagree").

Of the 33 hand surgeons who were invited based on their expertise in DD, 22 agreed to participate in the survey, 20 of whom completed Round 1 of the survey; 19 completed Round 2. Overall, 80% had practiced medicine for at least 15 years and all had completed a fellowship in hand surgery. Ninety percent were added qualification [CAQ]-certified hand surgeons.

Consensus data from Rounds 1 and 2 indicated a high level of consensus for using CCH for the treatment of MP joint contractures of varying severity and in patients with MP and/or interphalangeal thumb contractures. Additional contextual data in Round 2 helped achieve consensus for using CCH

for treating PIP joint contractures of varying severities. Statements not achieving consensus are being explored in Round 3. Consensus-based findings among expert hand surgeons point to wide-ranging application of CCH for the treatment of DD for patients with varying degrees of disease severity and functional impairment.

IMPORTANT SAFETY INFORMATION FOR XIAFLEX®

- XIAFLEX is contraindicated in patients with a history of hypersensitivity to XIAFLEX or to collagenase used in any other therapeutic application or application method
- In the controlled and uncontrolled portions of clinical trials in Dupuytren's contracture, flexor tendon ruptures occurred after XIAFLEX injection. Injection of XIAFLEX into collagen-containing structures such as tendons or ligaments of the hand may result in damage to those structures and possible permanent injury such as tendon rupture or ligament damage. Therefore, XIAFLEX should be injected only into the collagen cord with a metacarpophalangeal (MP) or proximal interphalangeal (PIP) joint contracture, and care should be taken to avoid injecting into tendons, nerves, blood vessels, or other collagen-containing structures of the hand. When injecting a cord affecting a PIP joint of the fifth finger, the needle insertion should not be more than 2 to 3 mm in depth and avoid injecting more than 4 mm distal to the palmar digital crease
- Other XIAFLEX-associated serious local adverse reactions in the controlled and uncontrolled portions of the clinical studies included pulley rupture, ligament injury, complex regional pain syndrome (CRPS), sensory abnormality of the hand, and skin laceration (tear). In a historically controlled post-marketing trial, the incidence of skin laceration (22%) was higher for subjects treated with two concurrent injections of XIAFLEX compared with subjects treated with up to three single injections in the placebo-controlled premarketing trials (9%). Postmarketing cases of skin laceration requiring skin graft after finger extension procedures and local skin and soft-tissue necrosis, some requiring skin grafting, or other surgical interventions including finger amputation have been reported. Signs or symptoms that may reflect serious injury to the injected finger/hand should be promptly evaluated because surgical intervention may be required
- In the controlled portions of the clinical trials in Dupuytren's contracture, a greater proportion of XIAFLEX-treated patients (15%) compared to placebo-treated patients (1%) had mild allergic reactions (pruritus) after up to 3 injections. The incidence of XIAFLEX-associated pruritus increased after more XIAFLEX injections in patients with Dupuytren's contracture
- 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
- In the XIAFLEX trials in Dupuytren's contracture, 70% and 38% of XIAFLEX-treated patients developed an ecchymosis/contusion or an injection site hemorrhage, respectively. 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)
- In the XIAFLEX clinical trials for Dupuytren's contracture, the most common adverse reactions reported in ≥25% of patients treated with XIAFLEX and at an incidence greater than placebo were edema peripheral (eg, swelling of the injected hand), contusion, injection site hemorrhage, injection site reaction, and pain in the injected extremity

About CCH

XIAFLEX® (collagenase clostridium histolyticum, or CCH) is composed of 2 purified collagenases (AUX-I and AUX-II) that hydrolyze collagen under physiologic conditions, in lysis of collagen deposits.[3]

XIAFLEX® is approved by the Food and Drug Administration (FDA) for the treatment of adults with Dupuytren's contracture with a palpable cord.

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 a global team of passionate team members 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 Statement

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. Pess 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. Warwick D, et al. *Int. J Clin Rheumatol*. 2012;7(3):309-323.
2. Warwick D. *J Hand Surg Eur* Vol. 2017;42(7):665-672.
3. XIAFLEX® (collagenase clostridium histolyticum) for injection, for intralesional use [package insert]. Malvern, PA: Endo Pharmaceuticals Inc.

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