



Endo Provides Top-Line Results from Phase 2 Study of Collagenase Clostridium Histolyticum (CCH) in Participants with Adhesive Capsulitis of the Shoulder

July 1, 2022

DUBLIN, July 1, 2022 /PRNewswire/ -- Endo International plc (NASDAQ: ENDP) today announced top-line results from its Phase 2 study of Collagenase Clostridium Histolyticum (or "CCH") in participants with adhesive capsulitis (AC) of the shoulder, commonly known as "frozen shoulder." While Phase 2 study participants receiving up to three doses of CCH showed some improvement in the change from baseline in the adapted American Shoulder and Elbow Surgeons (ASES) Standardized Shoulder Form composite score for the affected shoulder at the Day 95 visit, the difference compared to those study participants receiving placebo was not statistically significant. The safety profile of CCH in the Phase 2 study was consistent with the known safety profile from other studies. Most treatment-emergent adverse events were of mild to moderate severity with the most common events following treatment with CCH being injection site bruising, arthralgia, injection site pain, injection site swelling and contusion.



"We are disappointed in the study outcome, and based on these data, we will be reevaluating our path forward for CCH for the treatment of adhesive capsulitis of the shoulder. We will continue focusing on our pipeline, including with respect to other potential CCH indications," said James P. Tursi, M.D., Executive Vice President, Global Research & Development at Endo. "We are committed to advancing our strategic priority of expanding and enhancing our portfolio for growth."

The Phase 2 trial enrolled 198 participants with unilateral idiopathic AC of the shoulder with restricted range of motion (ROM) and function in the affected shoulder. Participants were randomized 1:1 to receive CCH or placebo administered by ultrasound-guided injection. Participants received up to 3 injections separated by a minimum of 21 days. Participants completed standard home exercises and received physical therapy at designated time points during the study.

The Phase 2 trial's primary endpoint was the change from baseline in the adapted American Shoulder and Elbow Surgeons (ASES) Standardized Shoulder Form composite score for the affected shoulder at the Day 95 visit. This adapted scale measures pain and function parameters of the shoulder. Secondary endpoints included measures of passive and active range of motion improvement (PROM and AROM respectively).

About Adhesive Capsulitis

Adhesive capsulitis (AC) is characterized by a painful and gradual loss of active and passive shoulder motion resulting from fibrosis and contracture of the joint capsule. It is a specific pathologic entity in which chronic inflammation of the joint capsule produces thickening and fibrosis. Patients typically present with pain of insidious onset of several months' duration.¹ AC is believed to affect from 3% to 5% of the U.S. general population with an incidence of up to 20% in those with diabetes.²

Treatment options include a range of conservative and potentially even surgical measures. Oral and intra-articular corticosteroids have been shown to have a limited benefit in reducing pain and increasing ROM in AC. Physical therapy (PT) to the limit of pain is widely accepted as part of the management of AC, commonly in the early stages of the disease.³ More invasive management options include nerve blocks, a variety of injection options with varying degrees of efficacy demonstrated and ultimately, hydrodilatation or manipulation under anesthesia (MUA) may be required. Arthroscopic capsular release has also been used to treat AC often as a last resort, with the associated risks of postoperative pain, recurrent postoperative AC, and axillary nerve damage, as well as the risks associated with general anesthesia.³

About Endo

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](https://www.linkedin.com/company/endo).

Cautionary Note Regarding 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. Tursi and any statements

relating to clinical trials or studies, potential treatments or indications, future research, portfolio growth, timelines or expectations. Statements including words or phrases such as "believe," "expect," "anticipate," "intend," "estimate," "plan," "will," "may," "look forward," "intend," "future," "potential" or similar expressions are forward-looking statements. All forward-looking statements in this press release reflect Endo's current expectations of future events based on existing trends and information and represent Endo's judgment only as of the date of this press release. Actual results may differ materially and adversely from current expectations based on a number of factors affecting Endo's businesses, including, among other things, the following: the outcome of our strategic review, contingency planning and any potential restructuring; the timing, impact or results of any pending or future litigation, investigations, proceedings or claims, including opioid, tax and antitrust matters; actual or contingent liabilities; settlement discussions or negotiations; the impact of competition including loss of exclusivity and generic competition; our ability to satisfy judgments or settlements or to pursue appeals including bonding requirements; our ability to adjust to changing market conditions; our inability to maintain compliance with financial covenants and operating obligations which would expose us to potential events of default under our outstanding indebtedness; our ability to incur additional debt or refinance our outstanding indebtedness; a significant reduction in our short-term or long-term revenues which could cause us to be unable to fund our operations and liquidity needs; the performance of and consumer and physician acceptance of our products; the impact that known and unknown side effects may have on market perception and consumer preference; the effectiveness of advertising and other promotional campaigns; and our ability to develop products and our pipeline of products. The occurrence or possibility of any such result has caused us to engage and may result in further engagement in strategic reviews that ultimately may result in our pursuing one or more significant corporate transactions or other remedial measures, including on a preventative or proactive basis. Those remedial measures could include a potential corporate reorganization, restructuring or bankruptcy filing involving all or a portion of our business, asset sales or other divestitures, cost-saving initiatives, corporate realignments or strategic partnerships. 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. Therefore, the reader is cautioned not to rely on these forward-looking statements. Endo expressly disclaims any intent or obligation to update these forward-looking statements, except as required to do so by law. Additional information concerning risk factors, including those referenced above, can be found in press releases issued by Endo, as well as Endo's public periodic filings with the U.S. Securities and Exchange Commission and with securities regulators in Canada, including the discussion under the heading "Risk Factors" in Endo's most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or other filings with the U.S. Securities and Exchange Commission.

References:

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2. Le HV, Lee SJ, Nazarian A, et al. Adhesive capsulitis of the shoulder: Review of pathophysiology and current clinical treatments. *Shoulder & Elbow* 2017;9(2):75-84.
3. Cho C-H, Bae K-C, Kim D-H. Treatment strategy for frozen shoulder. *Clin Orthoped Surg* 2019;11:249-257.

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