



Endo Announces Initiation of Phase 2B Clinical Trial of Collagenase Clostridium Histolyticum in Cellulite

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DUBLIN, Feb. 17, 2016 /PRNewswire/ -- Endo International plc (NASDAQ: ENDP) (TSX: ENL) today announced the initiation of its Phase 2b study of collagenase clostridium histolyticum (or "CCH") for the treatment of edematous fibrosclerotic panniculopathy ("EFP"), commonly known as cellulite. CCH is known in its currently approved indications in the U.S. as XIAFLEX®.

"Cellulite affects millions of U.S. women, dimpling their skin, impacting their appearance and causing bother and self-consciousness for many," said Dr. Susan Hall, Executive Vice President, Chief Scientific Officer and Global Head of R&D and Quality at Endo. "There are no FDA-approved pharmacological options for cellulite and many currently available treatment options have not demonstrated a scientific benefit. We believe that if CCH is successful in clinical trials and if approved by the FDA, it could become the first office-based biological treatment option for cellulite that is supported by scientific results. Endo is looking forward to expanding the understanding of using CCH for this aesthetic indication."

The Phase 2b trial is expected to enroll 350 women aged 18 years or older in the United States. Each subject will receive up to three treatment sessions of CCH (0.84 mg / session) or placebo with each treatment session occurring approximately 21 days apart. Twelve injections will be administered into cellulite dimples during each session across an entire treatment quadrant – left or right buttock or left or right posterior thigh. At both the outset and conclusion of treatment, cellulite severity will be assessed by each patient and clinician using two photonumeric cellulite severity scales developed by Endo and third-party experts and reviewed by the U.S. Food and Drug Administration (FDA). The scales – the Photonumeric Cellulite Severity Scale (PCSS) – are 5-point scales ranging from 0 (no cellulite) to 4 (severe cellulite) that measure improvement in the appearance of cellulite. In addition to the patient and physician assessments, an independent, blinded five-member panel of trained aesthetic clinicians will evaluate pre-treatment and end-of-study photo images of patients using the PCSS.

The Phase 2b trial's primary endpoint is the proportion of composite responders at Day 71 defined as subjects with a 2-point improvement in severity from baseline in the clinician-rated PCSS and a 2-point improvement in the patient-rated PCSS. Additional endpoints include assessment of patient and clinician satisfaction using the Global Aesthetic Improvement Scale (GAIS) and change in the Hexsel cellulite severity scale.

Results for an earlier Phase 2a trial of CCH for the treatment of cellulite demonstrated that three doses of CCH (low (0.06mg), mid (0.48mg) and high (0.84mg)) showed an improvement in the appearance of cellulite as measured by the trial endpoints of an investigator and a patient score on the GAIS, which was adapted for use in cellulite. The mid and high dose groups demonstrated a statistically significant improvement in the appearance of cellulite, as measured by GAIS scores, with a p-value of <0.05 compared to placebo for both endpoints. In the mid and high dose groups, 68 percent of patients reported being "Satisfied" or "Very Satisfied" with the results of their treatment, compared to only 34 percent of patients randomized to placebo. CCH was well-tolerated by all dose groups with most adverse events (AEs) being mild to moderate and primarily limited to the local injection area.

About Cellulite

Cellulite is a localized metabolic disorder of tissue under the skin that has been reported in 85 to 98 percent of post-pubertal females and affects women of all races and ethnicities[i] [ii]. The condition can involve the loss of elasticity or shrinking of collagen cords, called "septae," that attach the skin to the muscle layers below. When fat in cellulite prone areas swells and expands, the septae tether the skin, which causes the surface dimpling characteristic of cellulite[iii]. CCH is intended to target and lyse, or break, those collagen tethers with the goal of releasing the skin dimpling and potentially resulting in smoothing of the skin. Despite multiple therapeutic approaches for the attempted treatment of cellulite, there are no FDA-approved pharmacological treatments and little scientific evidence that any current treatments are beneficial[iv].

About XIAFLEX

XIAFLEX® (collagenase clostridium histolyticum, or CCH) is a biologic approved in the U.S., EU, Canada, Australia and Japan for the treatment of adult Dupuytren's contracture (DC) patients with a palpable cord and in the U.S. and EU 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 subtypes are thought to work synergistically to break the bonds of the collagen structure. XIAFLEX® has been granted Orphan status in the U.S. by the FDA for DC and PD and is currently in Phase 2 development for adhesive capsulitis. XIAFLEX® is also expected to enter a registration trial for Dupuytren's nodules in mid-2016 and studies in plantar fibromatosis and lateral hip fat later this year.

About Endo International plc

Endo International plc (NASDAQ: ENDP) (TSX: ENL) is a global specialty pharmaceutical company focused on improving patients' lives while creating shareholder value. Endo develops, manufactures, markets and distributes quality branded 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.

Forward Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and Canadian securities legislation, including the statements by Dr. Hall, and other statements regarding research and development outcomes, efficacy, adverse reactions, market and product potential and product availability. Statements including words such as "believes," "expects," "anticipates," "intends," "estimates," "plan," "will," "may," "look forward," "intend," "guidance," "future" or similar expressions are forward-looking statements. Because these statements reflect Endo's current views, expectations and beliefs concerning future events, they involve risks and uncertainties. Although Endo believes that these forward-looking statements and information are based upon reasonable assumptions and expectations, readers should not place undue reliance on them, or any other forward-looking statements or information in this news release. Investors should note that many factors, as more fully described in the documents filed by Endo with the Securities and Exchange Commission ("SEC") and with securities regulators in Canada on the System for Electronic Document Analysis and Retrieval ("SEDAR"), including under the caption "Risk Factors" in Endo's Form 10-K, Form 10-Q and Form 8-K filings, and as otherwise enumerated herein or therein, could affect Endo's future financial results and could cause Endo's actual results to differ materially from those expressed in forward-looking statements contained in this communication. The forward-looking statements in this press release are qualified by these risk factors. Endo assumes no obligation to publicly update any forward-looking statements, whether as a result of new information, future developments or otherwise, except as may be required under applicable securities laws.

[i] Avram, Cellulite: a review of its physiology and treatment, *Journal of Cosmetic Laser Therapy* 2004; 6: 181–185.

[ii] Khan MH et al. Treatment of cellulite: Part I. Pathophysiology. *J Am Acad Dermatol.* 2010 Mar;62(3):361-70.

[iii] Querleux, Anatomy and physiology of subcutaneous adipose tissue by in vivo MRI and spectroscopy: Relationship with sex and presence of cellulite, *Skin Research and Technology*; 8: 118-124.

[iv] Wanner M et al. An evidence-based assessment of treatments for cellulite. *J Drugs Dermatol.* 2008 Apr;7(4):341-5.

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Investors/Media: Keri P. Mattox, (484) 216-7912; Media: Heather Zoumas-Lubeski, (484) 216-6829