Zimmer Biomet Announces Publication of Positive Results from PROGRESS II Trial of Autologous Protein Solution Prepared with nSTRIDE® APS Kit in Treating Osteoarthritis of the Knee

Dec 22, 2017

Pilot Study Data Shows nSTRIDE APS Kit Provides Significantly Better Improvement in Pain from Baseline and Comparable Safety to Saline Control

WARSAW, Ind., Dec. 22, 2017 /PRNewswire/ -- Zimmer Biomet Holdings, Inc. (NYSE and SIX: ZBH), a global leader in musculoskeletal healthcare, today announced the publication of positive results from a pilot study demonstrating the safety and promising efficacy of the nSTRIDE® Autologous Protein Solution (APS) Kit for the treatment of knee osteoarthritis (OA). In the trial, known as PROGRESS II, investigators prepared APS by using Zimmer Biomet's nSTRIDE APS Kit, which concentrates anti-inflammatory cytokines and growth factors from a sample of the patient's own blood, for delivery via a single intra-articular injection into the knee joint. The results, which appeared in The American Journal of Sports Medicine[1], show significant improvement in the percentage change from baseline in pain scores measured by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), as well as comparable safety to saline.

OA, the most common type of arthritis, is a progressive disease of the joints. Often referred to as "wear and tear" arthritis, OA occurs when the top layer of cartilage, the slippery tissue that covers the ends of bones in a joint and helps absorb the shock of movement, breaks down and wears away. The bones under the cartilage then rub together, causing pain, swelling and loss of motion in that joint. Eventually, the joint may lose its normal shape and/or develop bone spurs around its edges.

"Inflammation is a critical factor in the pain and cartilage breakdown associated with knee osteoarthritis, and research has established that APS derived from the patient's whole blood contains a host of powerful anti-inflammatory and anabolic proteins," said Elizaveta Kon, MD, Associate Professor, Humanitas University, Milan, Italy, and lead investigator of the PROGRESS II trial. "After nearly a decade of preclinical and clinical research into the use of autologous anti-inflammatory cytokines and growth factors to treat osteoarthritis pain, we were pleased to demonstrate that APS, prepared with the nSTRIDE APS Kit, may be a promising, safe and viable new treatment for patients living with osteoarthritis of the knee."

The PROGRESS II trial was a prospective, randomized, double-blind, saline-controlled pilot study that enrolled 46 patients with unilateral, mild-to-moderate, symptomatic knee OA pain from the four trial sites across Europe. Patients were randomized to receive either a single injection of APS prepared by the nSTRIDE APS Kit (n=31), or a single saline injection (n=15). Patient-reported outcomes and adverse events were assessed at two weeks, and at one, three, six and 12 months post-injection. Clinical effectiveness was measured using the Visual Analog Scale (VAS), the WOMAC, and the Knee Injury and Osteoarthritis Outcome Score (KOOS). X-ray and magnetic resonance imaging (MRI) evaluations were taken at baseline, as well as three and 12 months following treatment.

Top-line results showed that patients treated with APS demonstrated:

- A 65 percent change in WOMAC pain score from baseline to 12 months compared to a 41 percent change in the saline group ($p = 0.02$).
- A 49 percent improvement in VAS pain scores compared to a 13 percent improvement in the saline group ($p = 0.06$).
- No procedure- or device-related serious adverse events, and comparable frequency, severity and relatedness of adverse events as compared to the saline group.

The nSTRIDE APS Kit is not commercially available in the United States but is currently marketed in Europe, via CE Mark, and in Japan, where it is marketed as the APS Kit. Results from the PROGRESS II study formed the basis for two additional confirmatory trials: the PROGRESS IV trial (NCT02905240), which received Investigational Device Exemption (IDE) approval from the U.S. Food and Drug Administration (FDA) in July 2016 and is currently enrolling patients, and the PROGRESS V trial (NCT03182374), which is underway in Europe to support global reimbursement efforts.

"As a global leader in musculoskeletal healthcare, Zimmer Biomet is committed to addressing the needs of patients along the entire continuum of care, from the management of symptoms like pain and stiffness with safe, non-invasive intra-articular injections like APS and Gel-One®, to restoring joint function and mobility with

our extensive portfolio of implant systems to treat advanced orthopaedic disease," said David Nolan, Group President, Biologics, Extremities, Sports Medicine, Surgical, Trauma, Foot and Ankle, Office Based Technologies and Zimmer Biomet Signature Solutions. "The positive results of the PROGRESS II trial not only reinforce the safety and clinical value of the autologous anti-inflammatory protein solution prepared with the nSTRIDE APS Kit, but also lay the groundwork to advance our regulatory efforts in the United States and accelerate our commercial adoption and expansion in Europe and Asia-Pacific."

About nSTRIDE APS

The nSTRIDE APS Kit is currently under clinical evaluation in the United States. It holds a CE Mark in Europe and is approved in Japan as the APS Kit. The device produces an anti-inflammatory-rich cellular solution from a patient's own blood. The output of the nSTRIDE APS Kit contains white blood cells and their corresponding anti-inflammatory cytokines in concentrations much higher than that of whole blood, in addition to anabolic cytokines that may promote cartilage health.[2] These anti-inflammatory cytokines target and inhibit the pro-inflammatory and catabolic cytokines Interleukin-1 (IL-1) and Tumor Necrosis Factor Alpha (TNFα). Zimmer Biomet currently licenses the nSTRIDE APS technology to Owl Manor Veterinary, a privately held medical device company dedicated to joint preservation, tendon and ligament treatment, and advanced wound care treatment of equine and canine companion animals, under the brand name Pro-Stride Injection™. For more information, please visit http://www.omveterinary.com/.

References:

1. Kon E, Engebretsen L, Verdonk P, Nehrer S, Filardo G Clinical outcomes of an autologous protein solution injection for knee osteoarthritis: a 1-year pilot double-blinded randomized controlled trial. Published in The American Journal of Sports Medicine, October 2017 [Epub ahead of print].
2. O'Shaughnessey K, Matuska A, Hoeppner J, et al. Autologous protein solution prepared from the blood of osteoarthritic patients contains an enhanced profile of anti-inflammatory cytokines and anabolic growth factors. J Orthop Res 2014;32(10):1349-55.

About Zimmer Biomet

Founded in 1927 and headquartered in Warsaw, Indiana, Zimmer Biomet is a global leader in musculoskeletal healthcare. We design, manufacture and market orthopaedic reconstructive products; sports medicine, biologics, extremities and trauma products; office based technologies; spine, craniomaxillofacial and thoracic products; dental implants; and related surgical products.

We collaborate with healthcare professionals around the globe to advance the pace of innovation. Our products and solutions help treat patients suffering from disorders of, or injuries to, bones, joints or

supporting soft tissues. Together with healthcare professionals, we help millions of people live better lives.

We have operations in more than 25 countries around the world and sell products in more than 100 countries. For more information, visit www.zimmerbiomet.com, or follow Zimmer Biomet on Twitter at www.twitter.com/zimmerbiomet.

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