Two New Studies Demonstrate in vitro Bioactivity Potential of Micronized Dehydrated Human Amnion Chorion Membrane (mdHACM) to Prevent Pathological Processes Underlying Osteoarthritis (OA) and Tendinopathy

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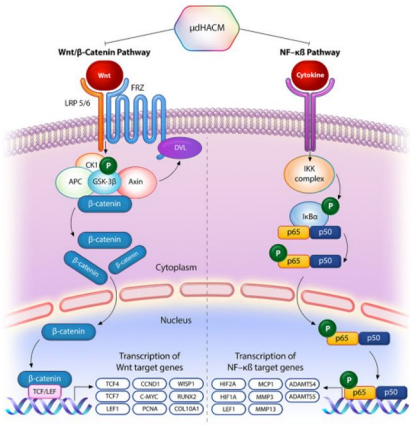
Data Show mdHACM Mitigates Effects of Inflammatory-Induced Degeneration in Chondrocytes, the Primary Cell Type in Cartilage; May Mitigate Vessel Formation and Repair

MARIETTA, Ga., Nov. 01, 2021 (GLOBE NEWSWIRE) -- MiMedx Group, Inc. (Nasdaq: MDXG) ("MIMEDX" or the "Company"), an industry leader in utilizing amniotic tissue as a platform for regenerative medicine, announced two peer-reviewed studies investigating the use of micronized dehydrated human amnion chorion membrane (mdHACM) for the treatment of debilitating conditions involving degeneration of connective tissue: osteoarthritis (OA) and tendinopathy.

The first study, published in *Osteoarthritis and Cartilage Open*, identified a novel mechanism of action by which PURION® Processed mdHACM regulates degradative processes in human articular chondrocytes, the primary cell type comprising articular cartilage. These results further support mdHACM as an investigational new drug (IND) candidate for the treatment of OA and highlight potential disease modifying activities.

The second study, published in the *Journal of Biomedical Materials Research, Part B,* examined chronicity and poor outcomes following tendon injury attributable to prolonged inflammation and hypervascularity. These complications were modeled *in vitro* for the purposes of evaluating mdHACM as a treatment for tendinopathy, which led to the identification of specific mechanisms responsible for counteracting these disease processes.

Figure 1



Micronized dHACM regulation of Wnt and NF-κβ signaling

"These studies reaffirm our commitment to advancing the science of amniotic tissue," said Timothy R. Wright, MIMEDX Chief Executive Officer. "Through our continued investment in research and clinical development, we aim to demonstrate the utility of PURION® Processed mdHACM as a platform for regenerative medicine. With each new study, we broaden our understanding of the product's mechanism of action and further our potential for applying these scientific findings to advance meaningful medicines in areas of unmet clinical need."

About the Osteoarthritis (OA) Study *(Osteoarthritis & Cartilage Open Journal)*

With more than 300 million global cases of hip and knee OA and the current treatment paradigm focusing primarily on symptomatic relief (Non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroid injections) followed by prosthetic joint replacement when needed, developing a regenerative therapy that addresses the underlying structural damage is becoming increasingly more important.

Micronized dHACM is hypothesized to target specific OA-related pathways to re-establish homeostasis, and thereby mitigate the physical effects of OA. To test this theory, an *in vitro* system was developed to recapitulate the disease state. OA was modeled using an established *in vitro* platform consisting of a 3D pellet culture of human articular chondrocytes and a cartilaginous extracellular matrix (ECM). The addition of inflammatory stimuli induced OA-like changes and elevated two key signaling pathways associated with disease progression, NF-κβ (Nuclear Factor kappa-light-chain-enhancer of activated B cells) and canonical Wnt signaling.

Introduction of mdHACM treatment specifically inhibited these pathways (Figure 1), effectively reversing the effects of the inflammatory stimuli and diminishing the expression and activity of key enzymes responsible for cartilage matrix degradation.

While the onset of OA is likely multifactorial, this study indicates mdHACM regulation of both NF-κβ and canonical Wnt signaling is one such mechanism by which this treatment elicits a chondroprotective effect and attenuates degeneration *in vitro*. This study substantiates previous clinical and preclinical evidence suggesting mdHACM treatment improves the outcomes associated with OA.

About the Tendinopathy Study *(Journal of Biomedical Materials Research, Part B)*

Tendon injuries are among the most common ailments of the musculoskeletal system. Chronicity is linked to overuse, age and disease-related changes resulting in prolonged inflammation and hypervascularity. Excessive scar tissue replaces the damaged tendon tissue, disrupting the native structural and biomechanical properties and ultimately, impairing functionality. This study evaluated the effects of micronized dehydrated human amnion chorion membrane (mdHACM) on the inflammatory environment and hypervascularity associated with chronic tendon injury.

In this study, human tenocytes were treated with interleukin-1 beta (IL-1β) to induce a phenotypic shift mimicking a tendon injury *in vitro,* as evident by the increased expression of inflammatory and catabolic markers. Introduction of mdHACM diminished the effects of IL-1β, including downregulation of interleukin-6 (IL-6), Monocyte Chemotactic Protein-1 (MCP-1), Matrix Metalloproteinase-1 (MMP-1), and Matrix Metalloproteinase-3 (MMP-3), demonstrating the role of mdHACM in regulating the inflammatory environment and matrix degradation. Furthermore, mdHACM reversed the

pro-inflammatory-induced expression of type III collagen. Type III collagen is indicative of immature matrix formation, and persistence of this rudimentary matrix is often associated with a compromised repair and weakened mechanical properties. Regulation of extracellular matrix components alludes to a potential role for mdHACM in the direct repair of the damaged tissue.

The inflammation triggered by chronic tendon injury drives vessel formation in a typically avascular tissue. The persistence of vasculature perpetuates the inflammatory signals and disrupts the normal tendon architecture. The role of mdHACM in regulating vessel formation in a tendon-like culture was evaluated in an *in vitro* culture system comprised of human endothelial cells grown atop a monolayer of human tenocytes. Micronized dHACM contains known proangiogenic factors within its complex milieu of signaling proteins; however, when introducing mdHACM into a culture with elevated proangiogenic factors or an already established vascular network, mdHACM resulted in network inhibition and network disruption, respectively. This dynamic response is the first documentation of mdHACM stimulating differential outcomes based upon the environment in which it is placed.

The results of this study are promising for the use of mdHACM in the treatment of tendinopathy. Furthermore, this marks the first study highlighting the dynamic nature of mdHACM and its ability to elicit multiple biological changes required to effectively achieve tissue homeostasis and promote more effective healing.

About MIMEDX

MIMEDX is an industry leader in utilizing amniotic tissue as a platform for regenerative medicine, developing and distributing placental tissue allografts with patent-protected, proprietary processes for multiple sectors of healthcare. As a pioneer in placental biologics, we have both a base business, focused on addressing the needs of patients with acute and chronic non-healing wounds, and a promising late-stage pipeline targeted at decreasing pain and improving function for patients with degenerative musculoskeletal conditions. We derive our products from human placental tissues and process these tissues using our proprietary methods, including the PURION® process. We employ Current Good Tissue Practices, Current Good Manufacturing Practices, and terminal sterilization to produce our allografts. MIMEDX has supplied over two million allografts, through both direct and consignment shipments. For additional information, please visit www.mimedx.com.

A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/0c074397-9081-48a6-8cd2-6042903327a8

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