Apligraf® is First Wound Healing Therapy to Demonstrate Significant Change in Chronic Wound's Genomic Profile

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- New Research Evaluating Apligraf's ® Role in Converting Chronic Wound Environment into Acute Healing Profile Published in *Science Translational Medicine* -

CANTON, Mass. - January 4, 2017 – Apligraf® – an FDA-approved, bioengineered living-cell therapy from Organogenesis Inc. – has become the first wound-healing therapy to demonstrate a significant change in the genomic profile of a treated non-healing wound, according to new research published in the peer-reviewed journal *Science Translational Medicine*. The analysis from a multidisciplinary research team at the University of Miami, titled "A bioengineered living cell construct activates an acute wound healing response in venous leg ulcers," provides new insight on what happens to a wound's genomic profile when Apligraf is applied to a chronic venous leg ulcer (VLU), when compared to standard care with compression therapy alone. The analysis found that the application of Apligraf in conjunction with compression therapy altered specific molecular and cellular responses in the wound environment, converting the chronic wound profile to resemble an acute, healing wound profile.

"This is the first time this type of detailed gene expression analysis has been conducted to evaluate the response to a wound healing modality," said Marjana Tomic-Canic, PhD, Director of the Wound Healing and Regenerative Medicine Research Program at the University of Miami. "Our findings show that Apligraf can shift the gene expression profile of a chronic, non-healing ulcer to resemble a profile similar to that of an acute, healing wound. This is important as we now can use this as a guiding tool to understand healing of a chronic wound and mechanisms by which therapies can work."

The research consisted of a prospective, randomized, controlled clinical trial that analyzed VLUs with less than 40 percent area reduction after four weeks of treatment with standard care with compression therapy. Biopsies were performed at the edge of the wound to define the profile of the non-healing VLUs. Patients were then randomized into: a) a group receiving treatment with standard of care therapy alone; and b) a group receiving treatment with Apligraf and standard of care therapy. At Day 7 after Apligraf was applied, biopsies were performed again to assess changes in the ulcer profile. Results of the biopsies from this study were compared to the existing data set for biopsies taken from acute, healing wounds.

The study concluded that, for the group treated with both Apligraf and standard of care therapy, Apligraf modulated inflammatory and growth factor signaling and activated keratinocytes at the wound edge; thus successfully shifting the wound environment from a chronic, non-healing ulcer microenvironment to a distinctive healing milieu resembling that of an acute, healing wound.

"The acceptance of this groundbreaking research into the prestigious *Science Translational Medicine* journal underscores our company's commitment to developing safe, effective, and

evidence-based advanced wound care products for clinicians," said Gary S. Gillheeney, Sr., President & CEO of Organogenesis. "This study provides valuable information to researchers and clinicians working to promote healing in chronic wounds."

According to a new report from THE SAGE GROUP, more than three million U.S. adults suffer from venous ulcers. The cost of venous disease represents a significant burden on patients and the U.S. economy, with venous ulcers alone costing at least $21 billion annually.

The journal *Science Translational Medicine* publishes original, peer-reviewed, science-based research articles that report successful advances toward the goal of improving patients' lives. Published articles meet the high standards set by the journal's editors and an international advisory group of scientists and clinician-scientists.

Apligraf is FDA-approved for the treatment of venous leg ulcers and diabetic foot ulcers lasting longer than one month that have not adequately responded to conventional therapy. Apligraf contains two layers of human living cells: a layer of differentiated keratinocytes and a layer of fibroblasts in a collagen matrix. When placed on a wound previously unresponsive to treatment, Apligraf provides cells, collagen matrix and other proteins and has been demonstrated to promote healing. In controlled clinical studies, Apligraf has been shown to be an effective and safe wound care treatment, superior to conventional treatments alone.

About Organogenesis

Massachusetts-based Organogenesis Inc. is a global leader in advanced wound care innovation and technologies, including bio-active wound healing and tissue regeneration. The company's mission is to bring safe and effective wound care products to patients and to standardize their use in everyday medical care. Among Organogenesis' suite of products are FDA-approved Apligraf ® and Dermagraft®, the best-in-class products for bio-active wound healing, and recently introduced FDA-cleared PuraPly Antimicrobial™, which advances wound management for a wide variety of wound types. For more information, please visit www.organogenesis.com.