



Mallinckrodt Announces Positive Top-line Results from Pivotal Phase 3 Clinical Trial of StrataGraft® Regenerative Tissue in Patients with Deep Partial-thickness Thermal Burns

September 23, 2019

- **Study met both co-primary endpoints with high statistical significance, demonstrating autograft sparing and durable wound closure at three months with StrataGraft -**
- **Company plans to submit Biologics License Application to the U.S. Food and Drug Administration in the first half of 2020 -**

STAINES-UPON-THAMES, United Kingdom, Sept. 23, 2019 /PRNewswire/ -- [Mallinckrodt plc](#) (NYSE: MNK), a global biopharmaceutical company, today announced positive top-line results from its pivotal Phase 3 clinical trial of its investigational StrataGraft® regenerative tissue. The study, which met both primary endpoints, evaluated the efficacy and safety of a single application of StrataGraft in the treatment of deep partial-thickness thermal burns. Each study participant served as his or her own control.



Results showed that a significantly smaller area of burn wounds treated with StrataGraft tissue required autografting by three months compared to the area of burn wounds treated exclusively with autograft ($p < 0.0001$). Additionally, results showed that the proportion of StrataGraft-treated wounds that achieved durable wound closure at three months exceeded the pre-defined threshold for statistical significance.

Based on the positive Phase 3 data, Mallinckrodt plans to submit a Biologics License Application for StrataGraft tissue to the FDA in the first half of 2020. StrataGraft tissue is an investigational product, and its safety and effectiveness have not yet been established by the U.S. Food and Drug Administration (FDA).

"Treatment advances are needed that can help minimize or eliminate the need to harvest skin tissue for autografting, as the second wound created by removing healthy skin can be associated with complications and can be even more painful than the burn wound itself," said **Dr. James H. Holmes IV, study co-lead investigator and Director of Wake Forest Baptist Medical Center's Burn Center**. "The positive top-line results of the Phase 3 trial suggest that this investigational regenerative tissue, if approved, could provide burn surgeons with an alternative treatment option for deep partial-thickness burns."

Autograft is considered to be a standard of care by many for deep partial-thickness thermal burns. Such burns are complex skin injuries in which the damage extends through the entire epidermis (outermost layer of skin) and into the lower part of the dermis (innermost layer of skin). As autograft involves the surgical harvesting of healthy skin from an uninjured site on the patient and transplanting the skin graft to the injury, patients are left with two wounds requiring care. Patients who receive an autograft may experience pain, itching, scarring and impaired function at the donor site.

"Achieving the co-primary endpoints in our pivotal Phase 3 trial and exceeding statistical thresholds for both endpoints represents an important development milestone for StrataGraft tissue, which has the potential to help patients suffering from deep partial-thickness thermal burns. Coupled with the recently announced positive Phase 3 results for terlipressin in hepatorenal syndrome, or HRS, type 1, these Phase 3 results demonstrate our ability to design and execute successful development programs targeting complicated, serious conditions," said **Steven Romano, M.D., Executive Vice President and Chief Scientific Officer at Mallinckrodt**. "We are committed to providing StrataGraft to patients in need as a potential paradigm-changing treatment and alternative to autograft, if approved. We would like to thank the study participants and investigators in the Phase 3 clinical trial and all of the others who have helped us advance the clinical development program for this investigational product."

Design and Results of Phase 3 Study (STRATA2016)

The pivotal open-label, controlled, randomized, multicenter Phase 3 trial in adults evaluated the efficacy and safety of a single application of StrataGraft tissue in the treatment of deep partial-thickness thermal burns. The study enrolled 71 study participants across 12 clinical sites in the United States. Study participants were age 18 years and older and had 3-49% total body surface area complex skin defects caused by thermal burns that contained intact dermal elements for which surgical excision and autografts were clinically indicated. The study design used an intra-patient control, in which two similar areas of burn injury on the same study participant were randomly assigned to either standard of care (autograft) or StrataGraft treatment.

The co-primary endpoints included autograft sparing (the difference in the percent area of thermal burn wounds treated with StrataGraft tissue that required autografting compared with the control autograft treatment sites by three months), and durable wound closure (the proportion of study participants achieving durable wound closure of the StrataGraft-treated site at three months without autograft placement).

Key co-primary endpoints findings included the following:

- On average, 4% of the area of StrataGraft-treated sites required autografting by three months. By design, 100% of the area of control-treated sites was autografted and an additional 2% of the area required subsequent autografting by three months. This resulted in a 98% reduction in the area requiring autograft in the StrataGraft-treated sites compared to the control-treated sites ($p < 0.0001$).
- 83% of burn wounds treated with StrataGraft tissue alone achieved durable wound closure at the treatment site at three months post-placement (95% confidence interval: 74.4-91.8%, meeting the pre-defined threshold of statistical significance). As a reference, 86% of the burn wounds treated with a single application of autograft achieved durable wound closure at three months post-placement (95% confidence interval: 77.8-94.0%).

The safety profile of StrataGraft tissue was comparable to that of autograft. Pruritus was the most commonly reported treatment-emergent adverse event (TEAE), occurring in 25 of 71 (35%) study participants treated with StrataGraft tissue (of which 11 of the 25 were possibly related to study treatment). All study treatment-related TEAEs were mild or moderate in severity. No local infections were related to StrataGraft treatment.

For more information about the design of the Phase 3 clinical trial, visit www.clinicaltrials.gov. ([NCT03005106](https://clinicaltrials.gov/ct2/show/study/NCT03005106)).

About StrataGraft Regenerative Tissue

StrataGraft regenerative tissue is an investigational treatment being developed to reduce or eliminate autograft in patients with severe thermal burns. An engineered, bilayer tissue, StrataGraft is designed to mimic natural human skin with both inner dermis-like and outer epidermis-like layers. StrataGraft can be sutured, stapled or secured with an adhesive. StrataGraft tissue is cryopreserved in order to deliver viable cells upon application.

Mallinckrodt is currently evaluating StrataGraft tissue in an ongoing Phase 2 trial for the treatment of adults with full-thickness burns (also referred to as third-degree burns). Mallinckrodt also plans to study StrataGraft tissue in pediatric populations, and to initiate a continued access clinical trial under an Expanded Access Program (EAP) in the fall of 2019. The trial sites involved in the pivotal Phase 3 trial (STRATA2016) will have the opportunity to participate in that trial.

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The FDA has granted StrataGraft tissue orphan drug status, and it was among the first products designated by the Agency as a Regenerative Medicine Advanced Therapy (RMAT) under the provisions of the 21st Century Cures Act.

Funding and technical support for the continued development of StrataGraft regenerative tissue, including the pivotal Phase 3 clinical study (STRATA2016) and the marketing approval registration process for StrataGraft tissue in the United States, is being provided by the Biomedical Advanced Research and Development Authority (BARDA), under the Assistant Secretary for Preparedness and Response, within the U.S. Department of Health and Human Services, under Project BioShield Contract No. HHSO100201500027C. The BARDA contract supports additional projects, including clinical trials for use in pediatric populations. These efforts are part of BARDA's strategy to build emergency preparedness in response to mass casualty events involving trauma and thermal burns by developing novel medical countermeasures for adult and pediatric populations. In the case of a mass casualty thermal burn event, the Government Accountability Office estimates that more than 10,000 patients might require thermal burn care.¹ The limited number of specialized burn centers and related medical infrastructure in the United States creates a public health need for therapies that could be deployed quickly for use in these and other care sites.

About Deep Partial-thickness Thermal Burns

Deep partial-thickness thermal burns are complex skin injuries in which the damage extends through the entire epidermis (outermost layer of skin) and into the lower part of the dermis (innermost layer of skin).

Autograft is considered to be a standard of care by many for deep partial-thickness thermal burns. It involves the surgical harvesting of healthy skin tissue from an uninjured site on the patient and transplanting the skin graft to the injury. While this process can be effective in providing closure of the original wound, it has significant limitations related to the donor site wounds created during surgical removal of the skin tissue for grafting. Donor site wounds are extremely painful and can create risks of additional scarring and infection. In addition, the amount of healthy skin available for harvesting is frequently limited in those patients with large burns, necessitating sequential re-harvesting of available donor sites. As a result, there is an urgent need for alternatives to donor site harvesting for the treatment of severe burns.

ABOUT MALLINCKRODT

Mallinckrodt is a global business consisting of multiple wholly owned subsidiaries that develop, manufacture, market and distribute specialty pharmaceutical products and therapies. The company's Specialty Brands reportable segment's areas of focus include autoimmune and rare diseases in specialty areas like neurology, rheumatology, nephrology, pulmonology and ophthalmology; immunotherapy and neonatal respiratory critical care therapies; analgesics and gastrointestinal products. Its Specialty Generics reportable segment includes specialty generic drugs and active pharmaceutical ingredients. To learn more about Mallinckrodt, visit www.mallinckrodt.com.

Mallinckrodt uses its website as a channel of distribution of important company information, such as press releases, investor presentations and other financial information. It also uses its website to expedite public access to time-critical information regarding the company in advance of or in lieu of distributing a press release or a filing with the U.S. Securities and Exchange Commission (SEC) disclosing the same information. Therefore, investors should look to the Investor Relations page of the website for important and time-critical information. Visitors to the website can also register to receive automatic e-mail and other notifications alerting them when new information is made available on the Investor Relations page of the website.

CAUTIONARY STATEMENTS RELATED TO FORWARD-LOOKING STATEMENTS

This release includes forward-looking statements with regard to StrataGraft regenerative tissue, including expectations with regard to clinical data and regulatory filings, future research, its potential impact on patients, and anticipated benefits associated with its use. The statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those in the forward-looking statements: clinical trial results; satisfaction of regulatory and other requirements; actions of regulatory bodies and other governmental authorities; changes in laws and regulations; issues with product quality, manufacturing or supply, or patient safety issues; and other risks identified and described in more detail in the "Risk Factors" section of Mallinckrodt's most recent Annual Report on Form 10-K and other filings with the SEC, all of which are available on its website. The forward-looking statements made herein speak only as of the date hereof and Mallinckrodt does not assume any obligation to update or revise any forward-looking statement, whether as a result of new information, future events and developments or otherwise, except as required by law.

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¹ <https://www.gao.gov/assets/590/588738.pdf>. Accessed April 23, 2019.

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