Mallinckrodt Announces Publication of Results of Phase 1b Clinical Trial of StrataGraft® Regenerative Tissue in Burns

August 13, 2019
- Study results showed that StrataGraft-treated deep partial-thickness burns did not require surgical harvest of healthy skin by 28 days -
- StrataGraft is currently being evaluated in an ongoing pivotal Phase 3 clinical trial -

STAINES-UPON-THAMES, United Kingdom, Aug. 13, 2019 /PRNewswire/ -- Mallinckrodt plc (NYSE: MNK), a leading global biopharmaceutical company, today announced publication of results of its Phase 1b clinical trial of StrataGraft®, an investigational regenerative tissue, in Burns, the journal of the International Society for Burn Injuries (ISBI). Study data showed that treatment with a single application of StrataGraft tissue resulted in wound closure by three months in 27 of 29 study participants. None of these 27 study participants required the harvest of donor skin (autograft) by 28 days after application. Additionally, the observed characteristics of the wounds treated with StrataGraft were comparable to those treated with autograft at 12 months after treatment. The safety and effectiveness of StrataGraft have not yet been established by the U.S. Food and Drug Administration (FDA).

"In the last two to three decades, survival among burn patients has increased, but there have been few advances in the treatment of severe burn wounds. New approaches are needed to help minimize the challenges associated with autografting, the current standard of care," said Dr. James H. Holmes IV, Director of Wake Forest Baptist Medical Center’s Burn Center. "The results of the Phase 1b study of StrataGraft are encouraging and suggest that this investigational regenerative tissue could potentially reduce or eliminate the need for autografting, which may minimize pain and other risks."

Autograft is considered to be a standard of care by many for deep partial-thickness thermal burns, complex skin injuries in which the burn extends into the lower dermis (skin below the surface of the outer layer of skin), as well as the entire epidermis (outer 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 have two wounds requiring care. Not only do patients experience increased pain, but both the burn injury site and the donor site are at increased risk of infection, scarring and impaired skin function.

"Based on the positive efficacy and safety results of the Phase 1b study, we advanced the clinical development of StrataGraft tissue and recently completed enrollment in a pivotal Phase 3 trial evaluating StrataGraft in adults with deep partial-thickness thermal burns," said Steven Romano, M.D., Executive Vice President and Chief Scientific Officer at Mallinckrodt. "We are appreciative of the patients who have participated in the clinical development program for StrataGraft. If data from the pivotal Phase 3 trial are supportive, we anticipate submitting a Biologics License Application to the FDA in 2020. We believe that StrataGraft, if approved, has the potential to revolutionize the treatment of patients with deep partial-thickness thermal burns, and we are committed to bringing it to patients in need as quickly as possible."

Top-line data from the StrataGraft Phase 3 pivotal trial are expected to be released in the next few months.

Design and Results of StrataGraft Regenerative Tissue Phase 1b Study
The prospective, randomized, controlled, open-label, multicenter, dose-escalation Phase 1b study (STRATA2011) assessed the safety, tolerability and efficacy of a single application of StrataGraft tissue compared with autograft for the treatment of deep partial-thickness thermal burns. A total of 30 study participants ages 18 to 65 years with deep partial-thickness thermal burns of 3-49% total body surface area (TBSA) were treated with StrataGraft in three dose-escalation cohorts of 10 patients each:

- Cohort 1: ≤220 cm² refrigerated StrataGraft tissue
- Cohort 2: ≤440 cm² refrigerated StrataGraft tissue
- Cohort 3: ≤440 cm² of cryopreserved StrataGraft tissue

Two areas of deep partial-thickness burns on the upper or lower extremities or torso of each study participant were randomly assigned 1:1 to receive StrataGraft or autograft control treatment. The coprimary endpoints of the study were the percent area of the StrataGraft treatment site requiring autografting by Day 28, and wound closure (defined as ≥95% re-epithelialization with absence of drainage) of the treatment sites at three months post-treatment. Secondary efficacy endpoints included the proportion of treatment site wounds completely closed, percent wound closure, cosmesis (physical appearance) of treatment and donor sites, and donor site pain.

Key primary and secondary clinical endpoint findings included the following:

- Study participants experienced a reduction in the percent area autografted at the StrataGraft tissue treatment site relative to the autograft treatment site. By Day 28, no StrataGraft-treated sites required autografting.
- By three months post-treatment, 27 of 29 study participants (93%) in the intent-to-treat population achieved wound closure at the burn site treated with StrataGraft.


- Overall, the proportion of treatment site wounds that achieved closure was not statistically different between StrataGraft and autograft treatment (p=0.491).
- Evaluation of scarring using Patient and Observer Scar Assessment Scale (POSAS) scores showed no significant differences between outcomes for StrataGraft and autograft treatment sites at any timepoint as assessed by clinical observers, or at 12 months after treatment as assessed by study participants.
- Wounds treated with StrataGraft did not require harvesting at prospective donor sites, resulting in less reported pain.

The Phase 1b study results showed that safety observations for StrataGraft were comparable to those for autograft. Pruritus (itching) was the most commonly reported adverse event (TAE), occurring in five of 30 study participants (17%); two of the five were possibly related to study treatment. All study treatment-related TAEs were mild or moderate in severity, and all resolved by the end of the study. Local infection was not observed at any of the StrataGraft treatment sites.

For more information about the design of the Phase 1b clinical trial, visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (NCT01437852).

About StrataGraft Regenerative Tissue

StrataGraft is an investigational regenerative tissue in development 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 in an ongoing pivotal Phase 3 clinical trial, which is assessing the efficacy and safety of StrataGraft in the promotion of autologous skin regeneration of complex skin defects due deep partial-thickness burns. Enrollment in the Phase 3 trial is complete. The company is also evaluating StrataGraft 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 in pediatric populations.

StrataGraft regenerative tissue is an investigational product. The safety and effectiveness of StrataGraft have not yet been established by the FDA.

The FDA has granted StrataGraft 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.

The Phase 1b trial was funded by a grant from the Armed Forces Institute of Regenerative Medicine I (contract W81XWH-08-2-0032) to Wake Forest University Health Sciences with a subcontract (WFUHS 40269). Funding and technical support for the continued development of StrataGraft regenerative tissue 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. 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. The limited number of specialized burn centers and related medical infrastructure in the U.S. creates a public health need for therapies that could be deployed quickly for use in these and other care sites.

About Deep Partial-Thickness Burns

Deep partial-thickness burns are complex skin injuries in which the burn extends down into the lower dermis (the skin below the surface of the outer layer of skin) as well as the entire epidermis (outer layer of skin).

Autograft is considered to be a standard of care by many for deep partial-thickness 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 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](http://www.mallinckrodt.com).

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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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