Mallinckrodt Announces Publication of Phase 3 STRATA2016 Study in Burns

July 7, 2021

- First publication of full data set shows use of StrataGraft® (allogeneic cultured keratinocytes and dermal fibroblasts in murine collagen - dsat) eliminated autografting in 96% of burn sites treated with StrataGraft, and 83.1% of patients achieved durable wound closure of the StrataGraft treatment site without autograft by three months -

- Secondary endpoint data showed cosmesis at the StrataGraft and autograft treatment sites was clinically similar at 12 months -

DUBLIN, July 7, 2021 /PRNewswire/ -- Mallinckrodt plc (OTCMKTS: MNKKQ), a global biopharmaceutical company, today announced publication of results from the pivotal Phase 3 STRATA2016 clinical trial of StrataGraft® (allogeneic cultured keratinocytes and dermal fibroblasts in murine collagen – dsat), which is approved for the treatment of adults with thermal burns containing intact dermal elements for which surgical intervention is clinically indicated (deep partial-thickness burns). The data were published in *Burns*, a peer-reviewed journal of the International Society for Burn Injuries. The trial, which evaluated the efficacy and safety of a single application of StrataGraft in adult patients with deep partial-thickness thermal burns, achieved both co-primary efficacy endpoints. Please see Important Safety Information for StrataGraft below.

The Phase 3 clinical trial was supported by the Biomedical Advanced Research and Development Authority (BARDA), part of the Office of the Assistant Secretary for Preparedness and Response at the U.S. Department of Health and Human Services (HHS). BARDA is providing funding and technical support for the continued development of StrataGraft under Project BioShield Contract No. HHSO100201500027C.

The published data showed that 96% of the burn sites treated with StrataGraft did not require autografting, and 83.1% of patients achieved durable wound closure of the StrataGraft treatment site without autografting by three months. As a reference, 86% of patients achieved durable wound closure of the autograft control sites. The significant reduction in use of autograft in patients treated with StrataGraft resulted in favorable outcomes in the secondary efficacy endpoints of donor site pain and donor site cosmesis (preservation or restoration of physical appearance). Additionally, cosmesis at the StrataGraft and autograft treatment sites was clinically similar at 12 months.

Safety results showed the most common treatment-emergent adverse event (TEAE) was pruritus (itching) at the treatment site, which occurred in 36.6% (26 of 71) of patients and was causally related to StrataGraft treatment in 11 patients. All TEAEs related to StrataGraft treatment were mild to moderate in severity. Hypertrophic scarring (HTS) occurred at the StrataGraft treatment site in 12.7% (9 of 71) of patients, and 4.2% (3 of 71) of patients had HTS determined by the investigator to be causally related to StrataGraft treatment.

"Surgical advances have improved survival rates in patients with severe burns. However, new treatments are needed that can help reduce or eliminate autografting, as the need to harvest healthy skin tissue can lead to pain, itching, scarring and impaired function at the donor site," said **James H. Holmes, IV, M.D., Co-Lead Investigator of STRATA2016 and Professor, Trauma Surgery, Wake Forest School of Medicine**. "We were encouraged to see in the Phase 3 trial that treatment with StrataGraft eliminated donor tissue harvest in all but three of the 71 study participants. Now that StrataGraft is approved, burn surgeons have an alternative biologic treatment option for patients with deep partial-thickness burns."

Each year, approximately 40,000 patients in the United States require hospitalization for the treatment of severe burns.[1] Autograft is the current standard of care for deep partial-thickness burns – 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 involves the surgical harvesting of healthy skin from an uninjured site on the patient and transplanting the skin graft to the injury, creating a donor site wound and leaving the patient with more wounded areas requiring care.

"This marks the first publication of the full data set from the pivotal Phase 3 StrataGraft clinical trial, and we are pleased to be able to share these important clinical findings with the burn care community," said **Steven Romano, M.D., Executive Vice President and Chief Scientific Officer at Mallinckrodt**. "With StrataGraft having received regulatory approval in the U.S. for the treatment of deep partial-thickness burns, we look forward to bringing it to healthcare providers and patients who could benefit."

Data from the Phase 3 trial supported the U.S. Food and Drug Administration approval of StrataGraft on June 15, 2021.

Design of STRATA2016

The open-label, controlled, randomized, multicenter Phase 3 clinical trial evaluated the efficacy and safety of a single application of StrataGraft in the treatment of deep partial-thickness thermal burns. The trial enrolled 71 patients (55 males and 16 females; 78% white and 20% African American) at 12 burn centers across the United States. Eligible patients were age 18 years and older and had thermal burns comprising 3% to 49% total body

surface area involving the torso or upper or lower extremities for which surgical excision and autografting were clinically indicated. The study design used an intra-patient comparator, in which two similar areas of burn injury on the same patient were randomly assigned to either StrataGraft treatment or autograft.

The co-primary endpoints were the difference in the percent area of the StrataGraft treatment site and the control autograft treatment site that was autografted by three months and the proportion of patients achieving durable wound closure of the StrataGraft treatment site without autograft placement at three months. Secondary endpoints assessed donor site pain, donor site cosmesis and treatment site cosmesis.

Full Results of STRATA2016
Results published in *Burns* showed the study met its co-primary efficacy endpoints of autograft sparing and durable wound closure by three months. A significantly smaller area of burn wounds treated with StrataGraft required autografting by three months compared to the area of burn wounds treated exclusively with autograft ($p<0.0001$). Additionally, 96% (68 of 71) of the burn sites treated with StrataGraft did not require autografting. By three months, 83.1% of patients achieved durable wound closure of the StrataGraft treatment site without autografting (95% CI: 74.4, 91.8), which was clinically similar to that of the autograft control site (86% [95% CI: 77.8, 94.0%]).

Secondary efficacy endpoint data also showed favorable outcomes with StrataGraft. In all but three patients, the StrataGraft treatment site did not need to be autografted, and the donor sites were therefore not harvested. As a result, significantly lower mean donor site pain intensity was observed through Day 14 at StrataGraft donor sites compared with autograft donor sites, as measured by the Wong-Baker FACES pain rating scale ($p<0.0001$). At three months, cosmesis data showed the mean donor site Patient and Observer Scar Assessment Scale (POSAS) observer total score was significantly lower (more like normal skin) for StrataGraft donor sites compared with autograft donor sites ($p<0.0001$). At 12 months, cosmesis at the StrataGraft and autograft treatment sites was clinically similar, as measured by POSAS total scores by observer.

A molecular analysis of patient biopsies at the StrataGraft treatment site at three months demonstrated that DNA from cells of StrataGraft was not detectable in any patients evaluated, which is consistent with wound healing by the patients' own cells.

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About StrataGraft
StrataGraft is a viable, bioengineered, allogeneic, cellularized scaffold product derived from keratinocytes grown on gelled collagen containing dermal fibroblasts. StrataGraft is designed to deliver viable cells to support the body's own ability to heal. StrataGraft contains metabolically active cells that produce and secrete a variety of growth factors and cytokines. Growth factors and cytokines are known to be involved in wound repair and regeneration. The product is designed with both dermal and epidermal layers composed of well-characterized human cells. StrataGraft is intended to be applied in appropriate aseptic conditions, such as the operating room, and can be sutured, stapled or secured with a tissue adhesive.

The FDA granted StrataGraft orphan drug designation, 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. At the time of approval, the FDA awarded Stratatech Corporation, a Mallinckrodt company, a Priority Review Voucher (PRV).

Mallinckrodt is currently conducting a StrataGraft continued access clinical trial (StrataCAT, NCT04123548) under an Expanded Access Program (EAP). The trial sites involved in the pivotal Phase 3 trial (STRATA2016, NCT03005106) have the opportunity to participate in this multicenter, open-label study. The company is planning to evaluate StrataGraft for the treatment of adults with full-thickness burns (also referred to as third-degree burns). Additionally, Mallinckrodt plans to conduct a study evaluating StrataGraft in the treatment of pediatric populations.

BARDA expressed interest in StrataGraft as a medical countermeasure in response to large-scale burn incidents, and provided funding and technical support for the continued development of StrataGraft. 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 at-risk 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.[2] 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.

IMPORTANT SAFETY INFORMATION

INDICATION
StrataGraft® is an allogeneic cellularized scaffold product indicated for the treatment of adults with thermal burns containing intact dermal elements for which surgical intervention is clinically indicated (deep partial-thickness burns).

IMPORTANT SAFETY INFORMATION
Contraindications

- Do not use in patients with known allergies to murine collagen or products containing ingredients of bovine or porcine origin.

Warnings and Precautions

- StrataGraft contains glycerin. Avoid glycerin in patients with known sensitivity (irritant reaction) to glycerin.
- Severe hypersensitivity reactions may occur. Monitor for both early and late symptoms and signs of hypersensitivity reaction following StrataGraft application, and treat according to standard medical practice.

- StrataGraft contains cells from human donors and may transmit infectious diseases or infectious agents, eg, viruses, bacteria, or other pathogens, including the agent that causes transmissible spongiform encephalopathy (TSE, also known as Creutzfeldt-Jakob disease [CJD or variant CJD]).

  StrataGraft is a xenotransplantation product because of an historic exposure of the keratinocyte cells to well-characterized murine cells. The cell banks have been tested and found to be free of detectable adventitious agents, and mouse cells are not used in the manufacture of StrataGraft; however, these measures do not entirely eliminate the risk of transmitting infectious diseases and disease agents.

  Transmission of infectious diseases or agents by StrataGraft has not been reported.

- Because StrataGraft is a xenotransplantation product, StrataGraft recipients should not donate whole blood, blood components, plasma, leukocytes, tissues, breast milk, ova, sperm, or other body parts for use in humans.

Adverse Reactions

- The most common adverse reactions (incidence ≥2%) were itching (pruritus), blisters, hypertrophic scar, and impaired healing. Other adverse events reported are included in the full Prescribing Information.

Pediatric Use

- The safety and effectiveness of StrataGraft in pediatric patients (<18 years) have not been established.

Please see full Prescribing Information.

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 concerning StrataGraft, including future plans for its launch, its potential impact on patients and anticipated benefits associated with its use, and future clinical trial plans. 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: 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] American Burn Association. Burn Incidence Fact Sheet. http://ameriburn.org/who-we-are/media/burn-incidence-fact-sheet/. Accessed March 22, 2021.

[2] United States Government Accountability Office. National Preparedness: Countermeasures for Thermal Burns. https://www.gao.gov/assets/590/588738.pdf. Accessed March 22, 2021.

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