Mallinckrodt Announces U.S. FDA Approval of StrataGraft® (allogeneic cultured keratinocytes and dermal fibroblasts in murine collagen - dsat)

June 15, 2021

-- First approved donor site-free alternative to autograft for deep partial-thickness burns designed to handle like an autograft and support body's own ability to heal --

-- Clinical trials of StrataGraft demonstrated autograft sparing and durable wound closure by 3 months in adults with deep partial-thickness burns, providing burn surgeons with a new treatment option to reduce or eliminate autografting --

DUBLIN, June 15, 2021 /PRNewswire/ -- Mallinckrodt plc (OTCMKTS: MNKKQ), a global biopharmaceutical company, today announced that the U.S. Food and Drug Administration (FDA) has approved StrataGraft® (allogeneic cultured keratinocytes and dermal fibroblasts in murine collagen – dsat) for the treatment of adults with thermal burns containing intact dermal elements for which surgical intervention is clinically indicated (deep partial-thickness burns). Please see Important Safety Information for StrataGraft below.

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This project was funded in part with $86 million from 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), under contract HHSO100201500027 for Stratatech Corporation, a Mallinckrodt company, to develop StrataGraft.

The FDA approval is supported by data from the pivotal Phase 3 STRATA2016 clinical trial of a single application of StrataGraft in patients with acute thermal burns containing intact dermal elements (deep partial-thickness burns) involving 3%-37% total body surface area, which was conducted at U.S. burn centers. Results, which were recently published in *Burns*, showed a significantly smaller area of burn wounds treated with StrataGraft required autografting by 3 months compared to the area of burn wounds treated exclusively with autograft ($p<0.0001$).

"While autografting is effective in providing closure of the original wound in patients with deep partial-thickness burns, it can lead to donor site complications, including pain, itching, increased risk of infection and scarring," said **Tracee Short, M.D., burn surgeon and burn unit medical director at the Regional Burn Center at Baton Rouge General**. "The approval of StrataGraft represents an important advancement in the treatment of patients with deep partial-thickness burns. Burn surgeons will now have a new biologic treatment to eliminate or reduce the need for autografting."

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.

"Today's FDA approval of StrataGraft marks a significant milestone for the burn care community and underscores our unwavering commitment and ability to bring paradigm-changing treatment options to patients with severe and critical conditions," said **Steven Romano, M.D., Executive Vice President and Chief Scientific Officer at Mallinckrodt**. "We are deeply appreciative of the patients who participated in the StrataGraft clinical trials, the physicians and study investigators involved in the clinical development program, and our employees, who have worked tirelessly over the last 20 years to help us bring StrataGraft to burn surgeons and the patients they treat."

In the pivotal Phase 3 clinical trial, 96% (68 of 71) of the StrataGraft-treated burn sites across all participants did not require autografting. The difference in the percent area of StrataGraft and control autograft treatment sites that required autografting by 3 months was 98% ($p<0.0001$). The proportion of patients achieving durable closure of the StrataGraft treatment site at 3 months without autograft placement was 83% (95% CI: 74, 92). The proportion of patients achieving durable closure of the autograft control treatment site at 3 months without additional autograft placement was 86% (95% CI: 78, 94).

"Multiple health security threats can result in severe burn wounds, and, to save lives in a public health emergency, healthcare providers need products that are effective and easy to use," said **BARDA Director Gary Disbrow, Ph.D.** "Having new products available on the commercial market to improve routine care for burn patients gives healthcare providers a level of familiarity and comfort in using the products. This improves our healthcare response during a national emergency and reduces the long-term cost of national preparedness."

Clinical trials demonstrated that the safety profile of StrataGraft with regard to wound-related events, including erythema, swelling, local warmth and wound site infections, was comparable to that of autografting in clinical studies. The most common (>2%) adverse reactions were pruritus (itching), blisters, hypertrophic scar and impaired healing. There were no reports of rejection to

StrataGraft in the clinical studies, and no patients discontinued study participation due to adverse reactions.

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

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 anticipated launch timing, 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 May 15, 2020.

[2] United States Government Accountability Office. National Preparedness: Countermeasures for Thermal Burns. https://www.gao.gov/assets/590/588738.pdf. Accessed February 12, 2020.

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