MediWound Announces Positive Topline Results from Phase 3 Pediatric Study (CIDS) of NexoBrid for Eschar Removal of Severe Thermal Burns

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Primary Endpoints Met with Highly Statistically Significant Results Compared with Standard-of-Care

YAVNE, Israel, July 20, 2021 (GLOBE NEWSWIRE) -- MediWound Ltd. (Nasdaq: MDWD), a fully-integrated biopharmaceutical company focused on next-generation bio-therapeutics solutions for tissue repair and regeneration, today announced positive topline results from its pivotal phase 3 pediatric clinical study (CIDS - Children Innovation Debridement Study) with NexoBrid® to treat children with severe thermal burns, evaluating the efficacy and safety compared with standard-of-care (SOC).

The study met its three primary endpoints with a high degree of statistical significance. NexoBrid demonstrated a significant reduction in time to achieve complete eschar removal and significant reduction in wound area requiring surgical excision (surgical need) while demonstrating non-inferiority to SOC in quality of scars. The study also met certain secondary endpoints showing statistically significant reduction in the incidence of surgical excision and reduction in need for autograft in deep partial burns, as well as a favorable trend in reduction of blood loss during the eschar removal process. In addition, the study showed that NexoBrid was safe and well-tolerated.

“We are thrilled to see such robust results across all primary endpoints, which corroborate the positive results of our pivotal phase 3 clinical studies in adult patients, and clearly demonstrate the significant beneficial impact NexoBrid has on the lives of pediatric burn patients,” said Sharon Malka, Chief Executive Officer of MediWound. "It is gratifying to know that NexoBrid, with these highly compelling top-line results, is one step closer to becoming available as a treatment option for pediatric patients with severe burns."

Dr. Lior Rosenberg, MediWound's Chief Medical Technology Officer, added, “This study is one of the most comprehensive randomized controlled studies ever conducted in burn care generally and within the pediatric population specifically. We thank all the Principal Investigators and their teams, as well as the patients and their families, for their work and commitment to advance burn care. We also thank the U.S. Biomedical Advanced Research and Development Authority (BARDA) for their continued support for this project. The current mode of pediatric burn management requires intensive medical therapy, which poses challenges due to the surgical complexities in treating young patients with severe burns. Having NexoBrid as a non-surgical option provides a minimally invasive alternative to the current surgical standard of care for treating severe burns in pediatric patients.”

CIDS Study Design and Objectives

The NexoBrid CIDS study is a multicenter, multinational, randomized, controlled, open label study, performed in children with deep partial thickness (DPT) and full thickness (FT) thermal burns. The study's objectives are to evaluate the efficacy and safety of treatment with NexoBrid compared with standard of care (SOC) in hospitalized children with severe thermal burns of 1 percent to 30 percent Total Body Surface Area (TBSA). The study enrolled 145 pediatric patients, from newborn to eighteen years of age, randomized to either NexoBrid or SOC at a ratio of 1:1, across 36 burn centers worldwide. Topline results include acute phase and twelve-month follow-up data analysis. The long-term follow-up for cosmesis and function, quality of life and safety measurements is ongoing, and data is expected in the first half of 2023.

The European Medicines Agency (“EMA”) endorsed the study design as part of the agreed-upon Pediatric Investigational Plan (“PIP”) to support the indication label expansion to include pediatric patients. The primary endpoints included early eschar removal, reduction of wound area surgically excised (surgical need) and non-inferiority cosmesis and function at twelve months follow-up from wound closure. Secondary endpoints included reduction in the need for surgical excision for eschar removal (surgical need), blood loss, reduction of the need for autograft in DPT wounds and non-inferiority in cosmesis and function at twenty-four months follow-up from wound closure. Non-inferiority of the time to complete wound closure and other standard safety measurements were also compared with the SOC control arm.

The study was expanded to include burn centers in the United States following agreement with the FDA, under the same protocol with alignment to the U.S. phase 3 study (DETECT) protocol for adult population. The non-inferiority of cosmesis and function at twelve months and twenty-four months from wound closure were defined as safety measurements. In addition, reduction in surgical need was measured only by reduction in incidence of surgical excision for eschar removal.

Funding and support for this pivotal pediatric Phase 3 clinical study (CIDS) with NexoBrid is provided by the Biomedical Advanced Research and Development Authority (BARDA), under the office of the Assistant Secretary for Preparedness and Response (ASPR), within the U.S. Department of Health and Human Services (HHS), under ongoing contract number HHSO100201500035C.

Summary of Study Topline Results

Demographics and other baseline characteristics

The overall patient demographics and wound baseline characteristics were comparable across study arms.

Primary Endpoints

The study met its three primary endpoints with highly statistical significance. Patients treated with NexoBrid demonstrated a significantly shorter time to achieve complete eschar removal compared with patients treated with SOC (median time to complete eschar removal - NexoBrid: 0.99 days vs. SOC: 5.99 days, p=0.0008[1]).

Patients treated with NexoBrid demonstrated a significant reduction in surgical need for excisional eschar removal as measured by an analysis of percent wound area surgically excised for eschar removal. Patients treated with NexoBrid incurred a significantly lower percent of wound area surgically excised for eschar removal compared with patients treated with SOC (NexoBrid: 1.5% vs. SOC: 48.1%, p<0.0001).

The non-inferiority analysis of cosmesis and function of scars (quality of scars) measured by MVSS (modified Vancouver scar scale) at twelve-months from wound closure, demonstrated that NexoBrid was non-inferior to SOC (p<0.0001).

Secondary Endpoints

The study included several secondary endpoints that provided further insight on additional efficacy parameters.

Patients treated with NexoBrid demonstrated a statistically significant lower incidence of surgical excision for eschar removal compared with patients treated with SOC (NexoBrid: 8.33% (6/72) vs. SOC: 64.38% (47/73), p<0.0001).

Patients treated with NexoBrid incurred lower blood loss during the eschar removal procedure compared with patients treated with SOC, demonstrating a clear trend in favor of NexoBrid (mean volume – NexoBrid: 32.36 ml vs. SOC: 202.55 ml, p=0.134).

Patients treated with NexoBrid demonstrated significant reduction of incidence of autograft performed in DPT wounds (on a target wounds level analysis) compared with patients treated with SOC (NexoBrid: 25.93% (21/81) vs. SOC: 37.63% (26/69), p=0.05).

Patients treated with NexoBrid incurred a numerically lower percent area of DPT wound autografted compared with patients treated with SOC (NexoBrid: 15.9% vs. SOC: 22.8%, p=0.5).

Safety

No deleterious effect on wound healing was observed. Patients treated with NexoBrid had a non-inferior time to complete wound closure compared with patients treated with SOC (p=0.0149[1]). Estimated median time to complete wound closure, using Kaplan Meier analysis, was 32 days for patients treated with NexoBrid and 34 days for patients treated with SOC.

The study DSMB (Data Safety Monitoring Board) reviewed the data of all subjects and found NexoBrid to be safe and well tolerated. No safety concerns were identified in the study population.

About NexoBrid

NexoBrid (concentrate of proteolytic enzymes enriched in Bromelain) is a topically administered biological product that enzymatically removes nonviable burn tissue, or eschar, in patients with deep partial and full-thickness thermal burns within four hours of application without harming viable tissue. NexoBrid is approved in the European Union and other international markets and has been designated as an orphan biologic drug in the United States, European Union, and other international markets. Vericel holds an exclusive license for North American commercial rights to NexoBrid. In January 2019, MediWound announced positive top-line results from the acute phase of the pivotal Phase 3 U.S. clinical study (DETECT) of NexoBrid in adult patients with deep partial-and full-thickness thermal burns up to 30 percent of total body surface area. The study met its primary endpoint of complete eschar removal compared to gel vehicle as well as all secondary endpoints compared to standard of care (SOC), including shorter time to eschar removal, a lower incidence of surgical eschar removal and lower blood loss during eschar removal. Safety endpoints, including the key safety endpoint of non-inferiority in time to complete wound closure compared with patients treated with SOC, were also achieved. In addition, the twelve-month and twenty- four-month follow-up safety data of cosmesis and function were found to be comparable between the treatment and SOC arms, and no new safety signals were observed. NexoBrid is currently an investigational product in the United States.

About MediWound Ltd.

MediWound is a biopharmaceutical company that develops, manufactures, and commercializes novel, cost effective, bio-therapeutic solutions for tissue repair and regeneration. Our strategy leverages our enzymatic technology platform, focused on next-generation bioactive therapies for burn, wound care and tissue repair.

NexoBrid, our commercial orphan biological product for non-surgical eschar removal of deep, partial and full-thickness thermal burns, is a bromelain-based biological product containing a sterile mixture of proteolytic enzymes that selectively removes burn eschar within four hours without harming surrounding viable tissue. NexoBrid is currently marketed in the European Union and other international markets and is at registration-stage in the U.S. NexoBrid is supported by the U.S. Biomedical Advanced

Research and Development Authority (BARDA).

EscharEx, our next-generation bioactive therapy for debridement of chronic and hard-to-heal wounds, is a product candidate in advanced stages of development. In two Phase 2 studies, EscharEx was well-tolerated and has demonstrated safety and efficacy in the debridement of various chronic and other hard-to-heal wounds, with only a few daily applications.

MW005, our topical biological drug for the treatment of non-melanoma skin cancers, is a clinical-stage product candidate under development.

Committed to innovation, we are dedicated to improving quality of care and patient lives. For more information, please visit www.mediwound.com.

About BARDA

The Biomedical Advanced Research and Development Authority (BARDA), part of the Office of the Assistant Secretary for Preparedness and Response within the U.S. Department of Health and Human Services, provides an integrated, systematic approach to the development and purchase of the necessary vaccines, drugs, therapies, and diagnostic tools for public health medical emergencies. For more information, refer to www.phe.gov/about/BARDA. Funding and technical support for development of NexoBrid to obtain marketing approval in the U.S. including the expanded access treatment protocol (NEXT), the pivotal U.S. Phase 3 clinical study (DETECT) and the marketing approval registration process for NexoBrid in the U.S. is provided by BARDA, under the Assistant Secretary for Preparedness and Response (ASPR), within the U.S. Department of Health and Human Services (HHS), under ongoing USG Contract No. HHSO100201500035C. Additional projects for evaluation of NexoBrid funded under the BARDA contract include randomized, controlled pivotal clinical trial for use in pediatric population, establishment of a pre-emergency use data package and development of the health economic model to evaluate the cost savings impact to enable market adoption in the United States.

Cautionary Note Regarding Forward-Looking Statements

MediWound cautions you that all statements other than statements of historical fact included in this press release that address activities, events, or developments that we expect, believe, or anticipate will or may occur in the future are forward-looking statements. Although we believe that we have a reasonable basis for the forward-looking statements contained herein, they are based on current expectations about future events affecting us and are subject to risks, assumptions, uncertainties, and factors, all of which are difficult to predict and many of which are beyond our control. Actual results may differ materially from those expressed or implied by the forward-looking statements in this press release. These statements are often, but are not always, made through the use of words or phrases such as "anticipates," "intends," "estimates," "plans," "expects," "continues," "believe," "guidance," "outlook," "target," "future," "potential," "goals" and similar words or phrases, or future or conditional verbs such as "will," "would," "should," "could," "may," or similar expressions .

Specifically, this press release contains forward-looking statements concerning the anticipated progress, development, study design, objectives anticipated timelines, expectations and commercial potential of our products and product candidates, including NexoBrid. Among the factors that may cause results to be materially different from those stated herein are the inherent uncertainties associated with the uncertain, lengthy and expensive nature of the product development process; the timing and conduct of our studies of our products and product candidates, including the timing, progress and results of current and future clinical studies, and our research and development programs; our ability to obtain marketing approval of our products and product candidates in the U.S. or other markets; the clinical utility, potential advantages and timing or likelihood of regulatory filings and approvals of our products and products; our expectations regarding future growth, including our ability to develop new products; risks related to our contracts with BARDA; market acceptance of our products and product candidates; our ability to maintain adequate protection of our intellectual property; competition risks; the need for additional financing; the impact of government laws and regulations and the impact of the COVID-19 pandemic. For example, we are unable to predict how the pandemic will affect the overall healthcare infrastructure, including the ability to recruit patients, the ability to conduct the studies in medical sites and the pace with which governmental agencies, such as the FDA, will review and approve regulatory submissions. Additional government-imposed quarantines and requirements to "shelter at home" or other incremental mitigation efforts also may impact our ability to source supplies for our operations or our ability or capacity to manufacture, sell and support the use of our products and product candidates in the future.

These and other significant factors are discussed in greater detail in MediWound's Annual Report on Form 20-F for the year ended December 31, 2020, filed with the Securities and Exchange Commission ("SEC") on February 25, 2021, Quarterly Reports on Form 6-K and other filings with the SEC from time-to-time. These forward-looking statements reflect MediWound's current views as of the date hereof and MediWound undertakes, and specifically disclaims, any obligation to update any of these forward-looking statements to reflect a change in their respective views or events or circumstances that occur after the date of this release except as required by law.

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[1] Generalized Wilcoxon-Gehan test

Source: MediWound Ltd.