MediWound Announces Positive Results from Its U.S. Phase 2 Trial of EscharEx for Debridement of Chronic Wounds

May 12, 2022

Study Met Primary and Key Secondary Endpoints with Statistically Significant Results Compared to Control Arms

Significant Improvement Across Multiple Measures Over the Current Non-Surgical Standard-of Care

No Deleterious Effect on Wound Closure and No Observed Safety Issues

End of Phase 2 Meeting with FDA Targeted for Second Half 2022

YAVNE, Israel, May 12, 2022 (GLOBE NEWSWIRE) -- MediWound Ltd. (Nasdaq: MDWD), a fully-integrated biopharmaceutical company focused on next-generation biotherapeutic solutions for tissue repair and regeneration, today announced positive results from its U.S. Phase 2 clinical study of EscharEx® for the debridement of venous leg ulcers (VLUs). The study met its primary endpoint, its key secondary endpoints with high degree of statistical significance, as well as its wound closure safety measurements. MediWound anticipates meeting with the U.S. Food and Drug Administration (the “FDA”) in the second half of 2022, for an End-of-Phase 2 meeting to discuss study results and a potential Phase 3 pivotal plan for EscharEx. U.S. key opinion leaders will join MediWound management in its coming earning call on May 17 at 8:30am EDT to discuss the data.

The study met its primary endpoint with a high degree of statistical significance, demonstrating that patients treated with EscharEx had a statistically significant higher incidence of complete debridement during the 14-day measurement period within up to 8 applications compared to gel vehicle (EscharEx: 63% (29/46) vs. gel vehicle: 30% (13/43), p-value=0.004). EscharEx efficacy superiority remained statistically significant compared to gel vehicle after adjusting for pre-specified covariates ascribed to patient baseline characteristics, wound size, wound age and regions.

The study met key secondary and exploratory endpoints. Patients treated with EscharEx had a statistically significant higher incidence of complete debridement, during the same 14-day measurement period, compared to patients treated by non-surgical standard-of-care ("NSSOC") (EscharEx: 63% (29/46) vs. NSSOC: 13% (4/30)) and the time to achieve complete debridement was significantly shorter. Estimated median time to complete debridement, was 9 days for patients treated with EscharEx and 59 days for patients treated with NSSOC (p-value=0.016). On average, complete debridement was achieved after 3.6 applications of EscharEx compared to 12.8 applications with NSSOC. Patients treated with EscharEx demonstrated significantly higher incidence of at least 75% granulation tissue at the end of the treatment period compared to gel vehicle (p-value <0.0001). Favorable trends were observed in wound area reduction and reduction of pain compared to gel vehicle.

In addition, the study showed that EscharEx was safe and well tolerated, and the overall safety was comparable between the arms as assessed by the data safety monitoring board. Importantly, there were no observed deleterious effects on wound closure and no material differences in reported adverse events. Estimated time to complete wound closure was 64 days for patients treated with EscharEx compared to 78 days for patients treated with NSSOC.

“We are thrilled to see such robust results across multiple endpoints, which demonstrate the potential significant clinical and patient beneficial impact EscharEx may have on patients' lives,” said Sharon Malka, Chief Executive Officer of MediWound. "It is gratifying to know that EscharEx, with these highly compelling results, is one step closer to potentially become a best-in-class non-surgical debridement option for the millions of patients suffering from chronic wounds. Chronic wound care is a multi-billion-dollar market opportunity, and we believe EscharEx, is well positioned to potentially be a meaningful part of that market. We believe we have a clear path forward to advance EscharEx clinical program into pivotal Phase 3 clinical trials and we look forward to meeting with the FDA and sharing these compelling clinical data.”

Dr. Robert Snyder, Chief Medical Director of the EscharEx program added, “We thank our partners, the investigative staff, and especially the patients and families for their commitment and perseverance in completing the study in the face of all the challenges posed by the COVID-19 pandemic. I continue to be impressed by the clinical data generated by the EscharEx trials. There is a great unmet need to effectively debride chronic wounds in a non-surgical and prompt manner, as debriding the wound is a critical first step for wound bed preparation towards wound healing. I believe EscharEx holds great potential to be a significant contributor in this market and welcome addition to our treatment armamentarium for chronic wounds.”

Study Design

The study was a multicenter, prospective, randomized, placebo-controlled, adaptive design study, evaluating the safety and efficacy of EscharEx in debridement of VLUs compared to gel vehicle (placebo control) and non-surgical standard-of-care of either enzymatic or autolytic debridement (NSSOC). The study enrolled 120 patients, with 119 treated, at approximately 20 clinical sites, primarily in the United States. Study participants were treated with either EscharEx (n=46), gel vehicle control (n=43), or non-surgical standard-of-care (n=30), with a three-month follow-up. The single primary endpoint was incidence of complete debridement (non-viable tissue removal), clinically assessed, within up to 8 treatment applications during the assessment period (within 14 days), compared to gel vehicle placebo control. Secondary and exploratory endpoints assessed time to achieve complete debridement, reduction of pain, reduction of wound area, granulation tissue and wound quality of life, enabling evaluation of clinical benefits compared to both gel vehicle and NSSOC. Incidence and time to achieve wound closure were assessed as safety measurements. For more information regarding this study, visit www.clinicaltrials.gov.

Summary of Study Results

Demographics and other baseline characteristics

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

Primary Endpoint
The study met its primary endpoint with high degree of statistical significance. Patients treated with EscharEx demonstrated a higher incidence of complete debridement during the 14-day measurement period within up to 8 applications compared to patients treated with gel vehicle (EscharEx: 63% (29/46) vs. gel vehicle: 30% (13/43), p-value=0.004)**.**

EscharEx efficacy superiority remained statistically significant compared to gel vehicle after adjusting for pre-specified covariates ascribed to patient baseline characteristics, wound size, wound age and regions.

Secondary and Exploratory Endpoints
The study included secondary and exploratory endpoints that provide further insight on additional efficacy parameters and can establish clinical benefits.

Patients treated with EscharEx demonstrated a significantly shorter time to achieve complete debridement compared to patients treated with NSSOC (estimated median time to complete debridement, using Kaplan Meier analysis - EscharEx: 9 days vs. NSSOC: 59 days, Log rank p=0.016), and compared to patients treated with gel vehicle (EscharEx: 9 days vs. gel vehicle: 63 days, Log rank p=0.004).

Patients treated with EscharEx demonstrated a higher incidence of complete debridement during the 14-day measurement period within up to 8 applications compared to patients treated with NSSOC (EscharEx: 63.0% (29/46) vs. NSSOC: 13.3% (4/30))**.**

Patients treated with EscharEx demonstrated a significantly lower mean number of treatment applications to complete debridement compared to patients treated with gel vehicle (EscharEx: 3.6 applications vs gel vehicle: 5.5 applications) and compared to patients treated by NSSOC (EscharEx: 3.6 applications vs gel vehicle: 12.8 applications).

The baseline pain score measure by numeric pain rating scale (NPRS) was 4, 5 and 4.7 for patients treated with EscharEx, gel vehicle and NSSOC, respectively. Patients treated with EscharEx incurred a numeric reduction in pain level from baseline to end of bi-weekly visits (raw change estimate) compared to patients treated with gel vehicle (EscharEx: 1.53 vs gel vehicle: 1.08, p=0.4). The reduction in pain was comparable to patients treated with NSSOC (EscharEx: 1.45 vs NSSOC: 1.43, p=0.9).

Patients treated with EscharEx incurred a raw change estimated reduction in wound area from baseline to end of bi-weekly visits compared to patients treated with gel vehicle (EscharEx: 3.27 cm2 vs gel vehicle: 2.31 cm2, p=0.72), and comparable wound are reduction compared to NSSOC (EscharEx: 3.49 cm2 vs. NSSOC: 4.06 cm2, p=0.79).

Patients treated with EscharEx demonstrated higher incidence of at least 75% granulation tissue by end of treatment period compared to patients treated with gel vehicle (EscharEx: 93.3% vs. gel vehicle: 55.8%, p<0.0001).

Patients treated with EscharEx demonstrated comparable raw change estimate in wound quality of life, as assessed by Wound- QoL at the end of bi-weekly visits, compared to patients treated with gel vehicle (EscharEx: 0.6 vs. gel vehicle: 0.5, p=0.78).

Safety
No deleterious effects on wound healing were observed. Patients treated with EscharEx had a non-inferior incidence rate of complete wound closure compared to patients treated with gel vehicle (EscharEx: 32.6% vs gel vehicle: 27.9%, p=0.0056) and compared to NSSOC (EscharEx: 32.6% vs NSSOC: 26.7%, p=0.0094). In addition, time to complete wound closure compared to patients treated with gel vehicle was comparable. Estimated 25^{th} percentile time to complete wound closure, using Kaplan Meier analysis, was 64 days for patients treated with EscharEx compared to 63 days for patients treated with gel vehicle (p=0.53) and 78 days for patients treated with NSSOC (p=0.47).

The Independent Data Monitoring Committee reviewed the data of all patients treated and no safety concerns were identified in the study population. EscharEx was well-tolerated and overall safety was comparable between the arms. No differences were found in reported adverse events and no serious adverse event was related to study treatment.

About EscharEx

EscharEx is a bioactive therapy for debridement of chronic and other hard-to-heal wounds in advanced stages of clinical development. Designed for the outpatient setting, EscharEx is an easy-to-use concentrate of proteolytic enzymes enriched in bromelain for topical daily applications.

EscharEx was well-tolerated and demonstrated safety and efficacy in the debridement of various chronic and other hard-to-heal wounds with only few daily applications in several Phase 2 trials. EscharEx's mechanism of action is mediated by the proteolytic enzymes that cleave and remove the necrotic tissue and prepare the wound bed for healing. EscharEx is an investigational product and currently in a U.S. Phase 2 adaptive design study.

As part of its broader EscharEx development program, MediWound is also conducting a Phase 2 open-label, single arm study being conducted at three U.S. clinical sites. The study design supports the evaluation of the clinical performance, safety, and pharmacology effect of EscharEx in the debridement of lower leg ulcers (VLUs and diabetic foot ulcers) in up to fifteen patients.

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 care, 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 topical therapeutic under development in the U.S. for debridement of chronic and hard to heal wounds. EscharEx was well-tolerated and has demonstrated safety and efficacy in the debridement of various chronic and other hard-to-heal wounds, within 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.

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, expected data timing, objectives anticipated timelines, expectations and commercial potential of our products and product candidates, including EscharEx. 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; the approval of regulatory submission by the European Medicines Agency or by any other regulatory authority, 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, 2021, filed with the Securities and Exchange Commission ("SEC") on March 17, 2022, 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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