ELU42: THE FIRST SMALL MOLECULE TO PROMOTE REGENERATIVE TISSUE REPAIR VIA STEM CELL RECRUITMENT AND DYNAMIC WNT PATHWAY MODULATION

ELUCIDERM INC.
CHANGING THE WORLD OF WOUND HEALING

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ABSTRACT

BACKGROUND: ELU42 is currently being evaluated for the treatment of diabetic foot ulcers in a Phase I/IIA clinical trial (ELU42-01-01). ELU42 (XAV939 + DHA77) is a first-in-class small molecule designed to accelerate regenerative healing by targeting PARP-1, -2, and -5 enzymes. Its active component, XAV939, has been shown to significantly limit fibrosis (scarring), promote stem cell activation, and enhance keratinocyte migration—key processes in wound repair. In preclinical porcine models, topical application of ELU42 has demonstrated exceptional regenerative effects in healing acute wounds (including full-thickness excisions), chronic wounds, and burn injuries, and also in the repair of rabbit ear elastic cartilage. These studies establish ELU42 as the first small molecule Wnt modulator that promotes the regeneration of healthy tissue with little to no scarring—an ultimate goal in wound healing.

METHOD: To elucidate the mechanism of action of ELU42 on cutaneous wound healing, we performed excisional wound surgery on C57BL6 mice and treated them with ELU42 or saline every other day. Mice were sacrificed at Day 2, Day 5, and Day 7 following injury. Tissues were processed for RNA isolation and immunostaining from each time point. To assess gene expression changes, RNA sequencing followed by WNT signaling and wound healing RT PCR arrays were performed. Immunostaining was performed on paraffin-embedded tissues for β-catenin and SOX9 protein expression during the wound healing process.

RESULTS: Our preclinical data revealed that the topical application of ELU42 to acute open wounds resulted in an early suppression of fibrosis with a simultaneous angiogenic surge, followed by a timed rebound of collagen and Wnt-driven polarity. This "one-two punch" transforms wound healing from scar-prone repair into true architectural regeneration. On Day 2, pro-fibrotic genes, including COL1α1 and COL3, were suppressed in the wound healing process, and by Days 5 and 7 a balancing of Wnt signaling occurred. Activation of CXCL3 and CXCL5 cytokines in the early phase following injury resulted in the recruitment of SOX9-positive stem cells at a later stage of wound healing. It is our hypothesis that the pleotropic Wnt-driven properties of ELU42 drive a unique, complex mechanism of action that activates multiple signaling pathways that promote more complete regenerative tissue repair.

CONCLUSION: This mechanism of action study revealed a unique multi-faceted regulation of regenerative wound healing, which includes a dynamic modulation of the fibrotic response, activation of angiogenesis, and activation of stem cell recruitment into the wound bed to facilitate regeneration of tissue. These findings position ELU42 as a breakthrough treatment for both acute and chronic open wounds, as well as third-degree burns and blast injuries, the latter of which offers the potential to redefine point-of-care intervention for military and emergency settings.

WNT SIGNALING PATHWAY: AN ATTRACTIVE TARGET FOR CHRONIC WOUNDS

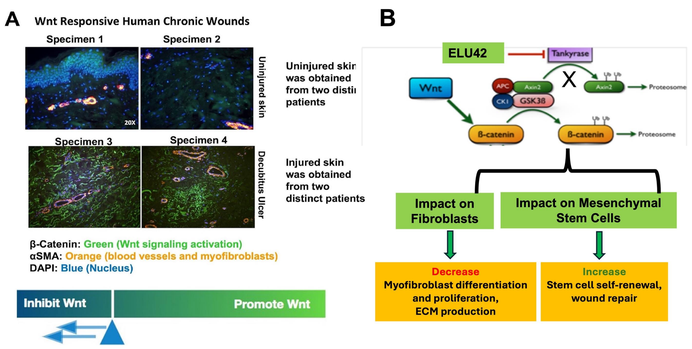

Figure 1. Wnt signaling pathway activation in non-healing wounds makes it an essential target for wound healing. A. Constitutive activation of Wnt signaling pathway in human chronic wounds. A representative image of uninjured skin (specimens 1 and 2) and decubitus ulcer (specimens 3 and 4) stained with β-catenin (green), α-SMA (orange), and DAPI (blue). Strong expression of β-catenin was identified in the chronic wounds represented by decubitus ulcer whereas no β-catenin expression was identified in uninjured human tissue. α-SMA stained the blood vessels and DAPI was used for nuclear staining. **B.** ELU42 is a Wnt signaling inhibitor that targets Tankyrase 1 and 2. Wnt signaling inhibition promotes repair by increasing stem cell renewal and suppressing myofibroblast activation.

ELU42: FIRST IN A GENERATION OF NOVEL, POTENT, AQUEOUSLY SOLUBLE, TOPICAL "SPRAY-ON" SMALL MOLECULE WNT SIGNALING MODULATOR

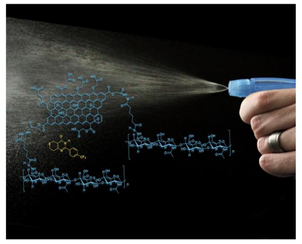

Figure 2. ELU42: Eluciderm Inc. has developed a **patented, portable, safe, bacteriostatic, and topical** Wnt signaling modulator for acute and chronic open wounds, as well as third degree burns.

ELU42 SPRAY-ON WNT MODULATOR APPLIED TO WAGNER 1-2 DFU PHASE I/IIA CLINICAL TRIAL (NCT07396376)

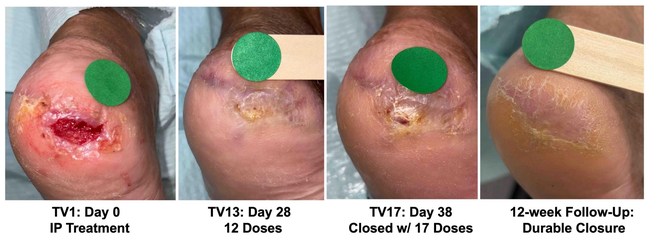

Figure 6: ELU42 demonstrated breakthrough status in Phase I/IIA DFU Clinical Trial. A. ELU42 spray-on was applied to Wagner 1-2 DFU following a two-week screening period applying standard of care with offloading and applying the IP-ELU42. **The first subject reached complete healing with 17 doses of ELU42 and has remained healed 12 weeks post-IP dosing, without recurrence, demonstrating durable DFU closure.** Visit poster (Dr. Delgado *et al.*) for full progress on clinical trial.

ELU42 ACTIVATES SOX9 AXIS RESTORING TISSUE ARCHITECTURE BY ORCHESTRATING INFLAMMATION AND REGENERATION

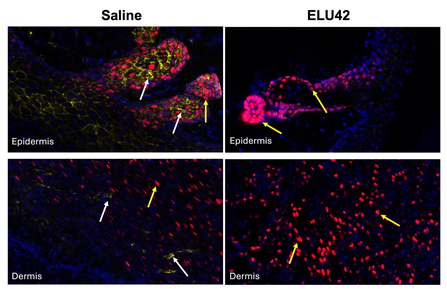

Figure 5. ELU42 recruits SOX9 positive progenitor/stem cells in the wound bed. Immunostaining of mouse tissue **7 days** following injury and ELU42 application identified recruitment of SOX9-positive stem cells (yellow arrow) while inhibiting β-catenin (white arrows) in the late (remodeling) phase of wound healing, suggesting a role of stem cells in promoting regenerative repair with ELU42 application.

ELU42 ACTS AS A MASTER REGULATOR THAT MODULATES THE GENE SPECTRUM DURING THE WOUND HEALING PROCESS

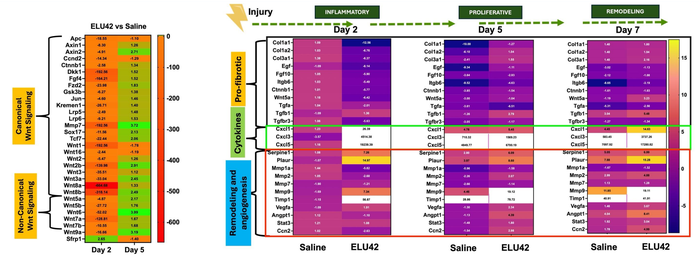

Figure 3. ELU42 dynamically modulates a distinct gene expression profile during the wound healing process. A. Both canonical and non-canonical Wnt signaling pathways were inhibited with ELU42 treatment and reset to basal level expression by Day 5 of wound healing, as demonstrated by **Wnt signaling RTPCR array**. **B. Wound healing RTPCR array** demonstrated that ELU42 promotes regenerative repair by **inhibiting** pro-fibrotic genes, activating **pro-angiogenic genes** (*Angpt1* and *Vegf*), and modulating **tissue remodeling genes** (*Mmps* and *Timps*) in the wound healing process, observed at Days 2, 5, and 7 following injury. **A significant surge of** ~20,000 fold for *Cxcl5* chemokine was identified at Day 2 following injury with ELU42 treatment. *Cxcl5* levels increased with saline treatment by Day 5 (~5000 fold) and Day 7 (~7000 fold) but not as much as with ELU42 treatment (~7000 fold and ~17,000 fold at Day 5 and Day 7, respectively).

ELU42 ACTIVATES CXCL5 AXIS RESTORING TISSUE ARCHITECTURE BY ORCHESTRATING INFLAMMATION, POLARITY, AND REGENERATION

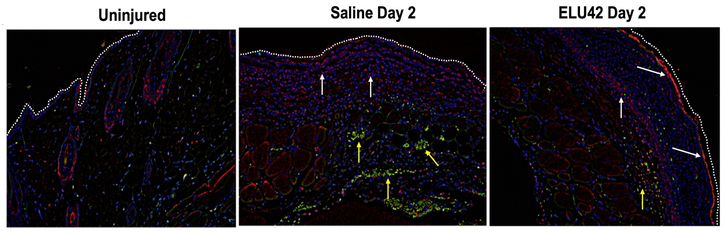

Figure 4. ELU42 upregulates CXCL5 in the murine epidermis following injury. Immunostaining of mouse tissue **2 days** following injury and ELU42 application identified recruitment of CXCL5-positive cells (white arrow) in the early phase of wound healing, suggesting a role of chemokine CXCL5 in promoting epidermal cells (keratinocytes) recruitment and organization promoting regenerative repair. Myofibroblast activation (yellow arrow) was suppressed following ELU42 application indicating downregulation of fibrotic response.

CONCLUSIONS

ELU42 achieves a Restorative Reset by targeted Tankyrase (PARP5) inhibition that decouples the early fibrotic β-catenin response and awakens non-canonical regenerative programs (Wnt5a, Sox9, CXCL5). These Preclinical models and early DFU SuperHealer™ Clinical Trial (NCT07396376) data show accelerated closure, neo-vascularization, adnexal regeneration, and restoration of native collagen architecture— evidence that transient, local Wnt modulation followed by appropriately timed pro-regenerative cues (FGF-2, IL-4, CSF-1) can produce functional healing with reduced scar formation and enhanced dermal integrity.

REFERENCES

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