OVERVIEW

The ***Sofusa® Lymphatic Delivery System (SLDS)*** is a new method of treatment designed to deliver injectable medicines directly into lymphatic and systemic capillaries just beneath the epidermis via a proprietary microneedle and microfluidics system. In 2015, the Sofusa team partnered with a design firm to translate insights gained from real patients into an elegant and functional wearable armband design for the delivery system. This breakthrough design has now been realized by combining micro-fabrication techniques (associated with silicon chip manufacturing) with precision molding and traditional drug delivery manufacturing capabilities.

How is the SLDS different from other microneedle systems? Nanostructured polymer patterns layered on top of our microneedles have been shown to activate cellular pathways (Kam et al., 2013) and dramatically enhance absorption of large molecules up to 150kDa (10-fold, Walsh et al., 2015) through the epidermis. This results in Sofusa's unique biodistribution profile - higher lymphatic concentrations and lower systemic concentrations - relative to intravenous (IV) infusions, subcutaneous (SC) injections, and intradermal (ID) injections. In addition, our proprietary microfluidics system enables precise and customizable flow profiles to optimize and tune drug levels over time.

What is the problem with current treatment methods? Many therapeutic targets are located peripherally or in systemic organs, and drug delivery via the systemic (blood) circulation provides adequate exposure in these targets. However, it is more difficult to achieve adequate drug exposure to targets that reside primarily in the immune system (lymph nodes or lymphatic capillaries), or in a micro-tumor environment. Many formulation approaches (e.g. lipid conjugates, nanoparticles, intradermal injections) have been attempted to improve the relative lymphatic/systemic biodistribution ratio, but with limited success. Historically, the primary option to improve target exposure was to deliver higher systemic doses and/or prolonged the half-life. This often results in trade-offs between maximum efficacy/response and toxicity or tolerability. In addition, traditional injections or infusions deliver a bolus of drug, which results can result in a high C_{max} or "burst" that can result in adverse events.

How do we solve these problems? The Sofusa ("soft transdermal infusion") system enables maximal drug exposure to immune system targets by delivering higher concentrations of directly via lymphatic capillaries to lymph nodes. The significance of intra-lymphatic targeting has now been validated in pre-clinical studies with an improved clinical response in both RA and oncology models. We have also demonstrated in solid tumor models that access to lymphatic capillaries resulted in increased tumor penetration and an improved response with a significantly lower dose vs intravenous infusion. By accessing lymphatic capillaries and increasing the exposure of immune targets to the drug, Sofusa has potential to improve clinical response, to lower AE's/dosing, or both. In addition, with precise and tunable flow profiles, we may reduce burst-associated adverse events AND improve the overall patient experience by avoiding the pain and anxiety associated with traditional injections.

The Sofusa Lymphatic Delivery System is a strategic asset for Sorrento with broad potential application, and we are open to partnering opportunities to accelerate development and use of this exciting platform technology.