Purpose:

Skin scars can arise from most types of dermal injuries and represent an unmet medical need for which no approved targeted therapy exists. Associated cosmetic disfigurement and loss of function may result in a decreased quality of life.

An entirely novel approach to reduce the severity of post-surgical skin scarring has been developed that approach utilizes EXC 001, an antisense oligonucleotide drug (ASO) designed to inhibit the expression of connective tissue growth factor (CTGF). CTGF is a matricellular growth factor known to play a fundamental role in the process of tissue fibrosis and scar formation, and therefore inhibiting its expression should lead to a reduction in the severity of skin scarring. EXC 001 has been evaluated in two Phase 1 safety studies and three Phase 2 efficacy studies of skin scarring.

Materials and Methods:

One of the Phase 2 studies (study #203) was a randomized, double-blind, multicenter study conducted in the U.S. In this study, EXC 001 or placebo was administered intradermally within surgical wounds for 21 subjects who underwent elective revision of hypertrophic scars of the breast. Three separate assessments of scar severity were performed: a Physician Assessment, a Subject Assessment and an Expert Panel Visual Analog Scale (VAS), at 12 and 24 weeks post-surgery.

Results:

On all three scales, EXC 001 showed a rapid onset to scar improvement and a sustained reduction in scar severity. At 24 weeks, the EXC 001 treated scars showed highly statistically significant improvement compared to placebo on all 3 scales; the Physician Assessment ($p<0.001$), the Subject Assessment ($p=0.003$) and the Expert Panel VAS ($p<0.001$). These results clearly demonstrate the utility of EXC 001 as a novel therapeutic approach to reduce the severity of post surgical scars in patients who are known to produce hypertrophic breast scars. There were no adverse events (AE) associated with the administration of EXC 001 or changes in clinical chemistry values.

Summary and Conclusions:

When EXC 001 was administered intradermally during scar revision surgery to patients who had developed hypertrophic scars following breast surgery, a highly statistically significant improvement was noted as compared to the placebo-treated side in the clinical outcomes.