Purpose: A topically applied product, RT001 Botulinum Toxin Type A Topical Gel (RT001) is being developed for treating lateral canthal lines (LCL) also known as crow's feet. RT001, an investigational product, consists of a proprietary, purified 150 kilodalton BoNTA combined with a novel peptidyl macromolecule transport system which facilitates transcutaneous delivery. RT001 could avoid undesirable effects such as pain, erythema, swelling or the appearance of a "frozen", insincere smile associated with many available modalities for treating facial wrinkles (e.g. energy based devices or injectables).

Objective: Evaluate the safety and efficacy of RT001 for the treatment of moderate to severe LCLs associated with orbicularis occuli muscle activity.

Methods: Two randomized, controlled studies were conducted on a total of 270 subjects with moderate to severe LCLs. Two efficacy scales: the Investigator Global Assessment of Lateral Canthal Line Severity (IGA-LCL) and the Patient Severity Assessment (PSA) were utilized. One study (n=90) randomized subjects 1:1 to receive a single treatment of RT001 or placebo, while the second (n=180) randomized subjects 3:1:1:1 to receive a single treatment of RT001 or one of three controls: BoNTA alone, transport peptide alone or placebo gel. Response was defined by a stringent composite endpoint which required each subject to have a \geq 2-point improvement on both the IGA-LCL and the PSA scales. Response on the individual scales was also measured. Safety evaluations included adverse events, skin and ocular irritation, clinical laboratory tests and cranial nerves, ECG's and antibodies.

Summary: RT001 showed statistically significant improvement versus all controls. In the study comparing RT001 to placebo, 88.9% of subjects showed clinically meaningful \geq 1-point improvement versus 27.9% in control. Additionally, 44.4% of subjects treated with RT001 showed marked \geq 2-point composite improvement versus 0.0% of subjects in the control group (p<0.0001 for each). In the second study, 40.7% of subjects treated with RT001 were responders compared to 0.0%, 0.0% and 3.3% for each of the controls individually and 1.1% for the combined controls (p \leq 0.0001). Adverse events were generally mild in severity and not related to study treatment.

Conclusions: RT001 demonstrated statistically significant response and duration of effect versus controls with an acceptable safety profile, showing that BoNTA can be delivered topically to treat LCLs.