Purpose: To describe the results of a recently completed multi-center, double-masked, exploratory trial in patients with moderate to severe dry eye disease (DED) using a novel, topically applied, IL-1 receptor inhibitor.

Methods: In a double-masked, placebo-controlled trial, subjects were randomized to receive vehicle, EBI-055, 5 or 10 mg/mL. The study was powered to show a statistical trend in improvement in signs and symptoms of DED compared to baseline at week six. All other assessments included: adverse event reporting, complete blood count, urinalysis, chemistry, electrocardiogram, corneal topography, corneal thickness, visual acuity, intraocular pressure, corneal biometry, and corneal topography. Results: Topical EBI-005 was shown in an earlier study to be safe and well tolerated when administered to healthy human subjects and demonstrated a strong effect on signs and symptoms of dry eye disease. EBI-005 is a genetically engineered recombinant human IL-1 receptor antagonist (IL-1 Ra) for treatment of meibomian gland dysfunction (MGD)-associated ocular surface disease.

Results: Topical EBI-005 was safe and well tolerated. There were no patient drop-outs and no serious ocular or non-ocular adverse events. EBI-005 significantly improved signs and symptoms of DED compared to baseline at week six by up to 30% (p<0.05) and 36% (p<0.01) respectively. In addition, there was a statistical trend in improvement in signs (CFS) and symptoms (OSDI, individual patient symptom assessments, investigator global assessment) in the EBI-005 treated compared to the vehicle treated group. Safety data were equivalent at both dose levels.

Conclusions: Topical EBI-005 treatment is a promising therapy to improve signs and symptoms of moderate to severe dry eye disease. These results further validate the importance of IL-1 blockade in DED and support continued development of the drug in a planned 12-week study designed to further characterize the safety and efficacy of EBI-005 in patients with DED.

Background: DED affects 26.5 million Americans (Market Scope, 2011). Although it is more common in women and the elderly, it affects all ages and races. Signs of DED are variable and include a sensation of dryness, presence of a foreign body, irritation, burning, tearing, pain, and itching. Patients with DED are commonly stratified by clinical severity into mild, moderate, and severe groups. Therapy begins with artificial tear replacement and punctal occlusion. To date, there is no U.S. Food and Drug Administration (FDA) approved therapy for DED with proven efficacy.

Purpose: The purpose of this study is to assess the safety and efficacy of EBI-005 in moderate to severe DED.

Methods: A double-masked, placebo-controlled study. Study subjects were randomized to receive vehicle, EBI-055, 5 or 10 mg/mL and treated for 6 weeks. All other assessments included: adverse event reporting, complete blood count, urinalysis, chemistry, electrocardiogram, corneal topography, corneal thickness, visual acuity, intraocular pressure, corneal biometry, and corneal topography. Results: Topical EBI-005 was shown in an earlier study to be safe and well tolerated when administered to healthy human subjects and demonstrated a strong effect on signs and symptoms of dry eye disease. EBI-005 is a genetically engineered recombinant human IL-1 receptor antagonist (IL-1 Ra) for treatment of meibomian gland dysfunction (MGD)-associated ocular surface disease.

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Commercial Relationships: Dr. Sanjay Chowdury is a consultant to Eleven Biotherapeutics. Mr. Chowdury is a contractor to Eleven Biotherapeutics. All other consultant to Eleven Biotherapeutics. Dr. Goldstein is a consultant to Eleven Biotherapeutics. Mr. Chowdury is a contractor to Eleven Biotherapeutics. All other consultant to Eleven Biotherapeutics.

Design: Multicenter 2 centers in United States, randomized, double-masked, vehicle-controlled, environmental study.

Key inclusion criteria: Minimum age of 18 years, moderately severe dry eye (OSDI score ≥15), no serious ocular or nonocular disease (Drug Approval). Key exclusion criteria: Significant ocular or nonocular disease, contact lenses, ocular drops, topical antibiotics within 7 days of dosing. Pharmacokinetics: Plasma levels of EBI-005 were measured at each dosing interval (week 1 and 3) 0-15 minutes after dosing (p<0.05). Safety: Adverse event monitoring and general systemic safety monitoring. Ophthalmic safety assessment. Serum PK and immunogenicity. Biological assessment: Sign assessed by evaluating CFS in 5 vision sections of the cornea. Symptoms assessed using PROs. Use of rescue preservative free artificial tears monitored.

Safety and Tolerability Summary:

No treatment related serious adverse events were reported. AE’s were mostly mild, transient and self-limiting. No SAEs. Of the 25 non-safety AEs 10 were in the vehicle treated group, 6 were in the 5 mg/ml group, and 11 were in the 10 mg/ml group. Systemic plasma levels of EBI-005 remained undetectable (<2.5ng/mL) at all time points following dosing before and after administration 0 weeks of dosing. EBI-005 demonstrated a strong effect on ocular signs and symptoms in patients with moderate to severe DED. EBI-005 demonstrated a strong effect on ocular signs and symptoms in patients with moderate to severe DED. EBI-005 demonstrated a strong effect on ocular signs and symptoms in patients with moderate to severe DED. EBI-005 demonstrated a strong effect on ocular signs and symptoms in patients with moderate to severe DED. EBI-005 demonstrated a strong effect on ocular signs and symptoms in patients with moderate to severe DED. EBI-005 demonstrated a strong effect on ocular signs and symptoms in patients with moderate to severe DED. EBI-005 demonstrated a strong effect on ocular signs and symptoms in patients with moderate to severe DED.