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**Abstract Title:** Oral Synthetic *cis*-Retinoid Therapy in Subjects with Leber Congenital Amaurosis (LCA) due to Lecithin: Retinol Acyltransferase (*LRAT*) or Retinal Pigment Epithelial 65 Protein (*RPE65*) mutations: Preliminary Results of a Phase Ib Open Label Trial

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Date trial started: November 2009

Human subjects: compliance with Declaration of Helsinki

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**Purpose:** To assess safety and efficacy of an oral synthetic *cis*-retinoid prodrug (QLT091001) in subjects with LCA due to mutations in the Lecithin:Retinol Acyltransferase (*LRAT*) or Retinal Pigment Epithelial 65 Protein (*RPE65*) genes. There are no proven therapies for this progressive retinal degeneration. QLT091001 has been shown to restore vision in mouse and dog models with LCA.

**Methods:** In this ongoing, IRB approved, proof-of-concept clinical trial, subjects with LCA are treated daily for 7 days with oral QLT091001 at the Montreal Children's Hospital. Visual function testing, ophthalmic and physical examinations, electrocardiograms and laboratory tests are completed before and after treatment at predetermined time points.

**Results:** Nine of 12 planned subjects with LCA due to *LRAT* or *RPE65* mutations have been enrolled. Preliminary results show improvements in Early Treatment of Diabetic Retinopathy Study (ETDRS) best-corrected visual acuity (BCVA) and Goldmann visual fields (GVF). In some cases, BCVA and GVF improvements have persisted for up to 11 months beyond the end of treatment. Many subjects reported meaningful improvements in their activities of daily living (ADLs). There were no serious adverse events. Transient headache and photophobia were reported and reversible elevations in triglyceride levels and reduction in HDL were recorded.

**Conclusion:** In this study, seven days of oral QLT091001 was generally well-tolerated and led to rapid and sustained vision improvements, as well as subjective improvements in ADLs.

Adverse events were transient and/or reversible. We have identified a population of dormant photoreceptors that rapidly respond to external manipulation. We are currently enrolling the remainder of the LCA subjects and expect to report on the full study results upon study completion.

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