Choroideremia Gene Therapy: Phase 2 Clinical Trial 48 Month Results and Overview

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Purpose:
To report the long-term 48-month follow-up of the Miami phase 2 high dose choroideremia gene therapy clinical trial (NCT02553135) and to provide an overview of the current ongoing choroideremia gene therapy clinical trials.

Methods:
The Phase 2 Miami clinical trial consists of six men (aged 32-72 years) with advanced choroideremia, who received subfoveal injection of AAV2-REP1 in the worse-sighted eye. Four of the same six patients were also treated in the better-sighted fellow eye at month 24 as part of phase 2 GEMINI trial. The primary measure was best-corrected visual acuity. Secondary endpoints included change from baseline in microperimetry, fundus autofluorescence, and OCT. Safety evaluations included adverse events, viral shedding in body fluids, and vector antibody responses.

Results:
Baseline mean ETDRS BCVA was 65.3 ± 8.8 (SD, range 56-77, 20/32-20/80) letters in the treated eyes and 77.0 ± 4.2 (69-81, 20/32-20/40) letters in the untreated eyes. At Month 36, mean BCVA in the treated eye was 69.0 ± 9.6 (55-82, 20/25-20/40) with the best outcome of +12 letters and worst outcome of -1 letter. Month 48 data completing in 3/2020 will be presented. Of the four initially untreated eyes that received treatment at Month 24; best outcome at Month 36 was +3 letters and worst outcome was -2 letters. No serious adverse event occurred. The phase 2 GEMINI and phase 3 STAR study designs and outcome measures are discussed.

Conclusions:
Sustained improvement or maintenance of BCVA is achievable in advanced choroideremia with high-dose AAV2-REP1. Bilateral sequential high-dose AAV2-REP1 treatment delivered with intraoperative OCT has a good safety profile. The multicenter bilateral sequential phase 2 and the randomized phase 3 clinical trials are ongoing.