Signs of functional vision recovery in an advanced stage RP patient after optogenetic therapy

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Purpose:
Retinitis pigmentosa (RP) involves progressive degeneration of rod and cone photoreceptors. Over 100 different genes have been associated with RP, and there are currently no approved therapies for halting the disease progression. GS030 is an investigational treatment combining a gene therapy and a medical device currently in clinical development to treat RP.

Methods:
The drug product GS030-DP is an optogenetic gene therapy targeting retinal ganglion cells (RGCs) and encoding an optimized form of channelrhodopsin Chrimson R (ChR-tdT). GS030-DP is administered via intravitreal injection (IVT) to allow the expression of optogenetic protein ChR-tdT in the preserved RGCs. Visual interface stimulating glasses GS030-MD encode images of the visual scene and modulate an amplified light source to stimulate the genetically engineered retina in real-time.

PIONEER is a Phase 1/2a, open-label, non-randomized, dose-escalation study to evaluate the safety and tolerability of GS030 combined therapy in subjects with end-stage non-syndromic RP, and vision of light perception or no light perception. Subjects are treated only in their worse-seeing eye. Three dose-escalation cohorts (5E10, 1.5E11, 5E11 vg/eye) include 3 subjects each, and an extension cohort will include up to 9 subjects at the highest tolerated dose. The therapeutic use of the stimulating goggles starts 8 weeks after injection.

Results:
As of February 2020, optogenetic vector administration was completed in the six subjects of the first two cohorts. Up to 1 year after treatment administration, there were no serious adverse events or study discontinuations. The most common adverse events were mild anterior chamber inflammation responsive to corticosteroid treatment. The use of GS030-MD to stimulate ChR-tdT showed no safety concerns. A subject was able to perceive, locate, count, and touch different objects using the vector-treated eye alone whilst wearing the light-stimulating goggles. The subject could not detect visually any objects before the treatment or after treatment in the absence of goggles.

Conclusions:
This is the first reported case of functional recovery in a neurodegenerative disease after optogenetic therapy.