Gene Therapy with RGX-314 for Neovascular AMD: New Results from the Ongoing Phase I/IIa Study

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Purpose:
Neovascular age-related macular degeneration (nAMD) typically requires frequent intravitreal anti-VEGF injections to optimize outcomes. Gene therapy delivering a transgene for an anti-VEGF protein has the potential for continuous anti-VEGF therapy after a one-time administration. The ongoing, fully-enrolled RGX-314 Phase I/IIa study is evaluating the safety and efficacy signals of an AAV (adeno-associated virus) vector, AAV8, encoding a soluble anti-VEGF Fab protein in previously treated subjects with nAMD.

Methods:
Multi-center, open label, Phase I/IIa trial evaluating five doses of RGX-314 (3 x 10^9, 1 x 10^10, 6 x 10^10, 1.6 x 10^11, and 2.5 x 10^11 genome copies/eye) administered via subretinal delivery during pars plana vitrectomy. Safety and efficacy are being assessed through week 106, including at the primary endpoint at week 26; measurements include ocular and systemic adverse events, RGX-314 aqueous protein level, best corrected visual acuity (BCVA), central retinal thickness (CRT), and need for additional anti-VEGF injections post-RGX-314 delivery.

Results:
Cohorts 1 - 5 have completed enrollment (n=42). As of April 6, 2020, RGX-314 has been well-tolerated with no observed immune response or inflammation beyond what is expected immediately post-vitrectomy. Sixteen non-drug-related SAEs had been reported among ten subjects. Dose dependent protein production was observed across all five cohorts at one month and six months. Cohort 3 showed sustained RGX-314 protein production over two years with mean improvement in BCVA (+14 letters) and stable mean CRT (+2 µm). Three subjects (50%) in Cohort 3 have received no anti-VEGF injections for two years following RGX-314 administration, with one additional subject receiving no injections in year two. 73% of subjects (8/11) in Cohort 5 remained anti-VEGF injection-free at nine months. One-year data for Cohorts 4 and 5 will be presented.

Conclusions:
Among the 42 subjects with nAMD enrolled in this Phase I/IIa study, subretinal administration of RGX-314 was well-tolerated and results support the potential for a one-time administration of RGX-314 to deliver a long-term, durable anti-VEGF therapeutic effect.