



MeiraGTx Announces Positive 6-Month Data from Phase 1/2 Trial of Investigational Gene Therapy AAV-RPE65 for RPE65-Deficiency

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- AAV-RPE65 met the primary endpoint of safety and tolerability
- Statistically significant improvement demonstrated in vision-guided mobility and visual function in treated eyes compared to untreated eyes
- Dose selected for pivotal study; Company expects to meet with global regulatory authorities in the second half of 2019

LONDON and NEW YORK, May 14, 2019 (GLOBE NEWSWIRE) -- MeiraGTx Holdings plc (NASDAQ:MGTX), a vertically integrated, clinical stage gene therapy company, today announced positive data from a Phase 1/2 dose escalation trial of AAV-RPE65, the Company's investigational gene therapy for the treatment of RPE65-deficiency, a condition that causes blindness. AAV-RPE65 is a second-generation gene therapy candidate developed specifically to treat RPE65-deficiency, and optimized for transduction efficiency, potency and stability. The trial achieved the primary endpoint of safety and tolerability of AAV-RPE65. Additionally, AAV-RPE65 demonstrated statistically significant improvement across several secondary endpoints designed to assess clinical activity.

The Phase 1/2 open-label, multi-center, dose-finding trial evaluated AAV-RPE65 in patients with retinal dystrophy associated with disease-causing variants in the *RPE65* gene. The trial was conducted at two centers in the U.S. and UK, and three surgeons undertook the surgery across these sites. The trial enrolled 15 patients, including nine young adults (aged 16-24 years old) across three dose escalation cohorts, and six children (aged 5-12 years old) in a pediatric expansion cohort. Each patient was treated with subretinal delivery of AAV-RPE65 in the eye that was more affected at baseline. The patient's other eye served as an untreated control.

Significant improvement in vision was demonstrated at six months after AAV-RPE65 treatment, as measured by assessments of vision-guided mobility, retinal sensitivity, visual acuity and contrast sensitivity. Larger improvements from baseline in functional vision were observed between treated and control eyes at lower light levels. These outcomes address the core functional manifestation of RPE65-deficiency, which typically causes vision impairment beginning in early childhood that is most pronounced in low-light conditions, and is consistent with the proposed mechanism of action of AAV-RPE65.

MeiraGTx intends to meet with regulatory authorities in the second half of 2019 to define the development pathway for regulatory approval of AAV-RPE65.

"RPE65-deficiency profoundly impacts quality of life from childhood and leads to increasing disability as patients progress toward complete loss of vision," said Michel Michaelides, trial investigator, Professor of Ophthalmology, University College London, and Head of Clinical Ophthalmology, MeiraGTx. "This trial demonstrated that AAV-RPE65 has the potential to restore vision in a severely debilitating disease. These highly encouraging early data reflect the promise of gene therapy to change the lives of patients with blinding inherited retinal diseases."

Full data from the Phase 1/2 trial is expected to be presented in a scientific forum later this year.

Topline Data from Phase 1/2 Trial of AAV-RPE65

Dose escalation in adults began at a potentially therapeutically relevant dose of 1×10^{11} vg/ml in Cohort 1. Cohorts 2 and 3 were treated with increasing doses of 3×10^{11} vg/ml and 1×10^{12} vg/ml, respectively. Dose escalation was successfully completed, with three adults treated sequentially in each cohort.

In Cohorts 1, 3, and the pediatric expansion cohort, subretinal injections targeted the central retina including the fovea. In Cohort 2, subretinal injections were peripheral to the fovea.

Based on the encouraging efficacy and safety observed in adults treated in Cohort 1 (1×10^{11} vg/ml), this dose was selected for use in a pediatric expansion cohort that enrolled six children.

Patients completed assessments of functional vision and visual function at baseline, and at pre-specified follow-up periods, and are intended to be followed for a period of five years to evaluate long-term safety, efficacy and durability of response.

Safety summary:

AAV-RPE65 was demonstrated to be generally well-tolerated after six months of follow-up, with a safety profile that was consistent with other approved and investigational ocular gene therapies. Subretinal injection targeting the central retina, including the fovea, was demonstrated to be safe and well tolerated. Retinal thinning, which has been reported in other RPE65-deficiency gene therapy studies in which the fovea was detached during subretinal injection, was not observed in this study in either adults or children.

Consistent with other ocular gene therapy dose finding trials, signs of inflammation were observed in some patients in high dose cohorts, which may have been associated with decreased activity of the AAV-RPE65 treatment in these patients. Inflammation was effectively managed and resolved with a standard steroid protocol.

Efficacy summary:

Mobility testing

In the Phase 1/2 study, across all cohorts, a statistically significant improvement in functional vision at six months versus baseline was demonstrated in the treated eye compared to the untreated control eye, as measured by the change in vision-guided mobility testing across a broad range of controlled light levels (1 lux, 4 lux, 16 lux, 64 lux and 256 lux). The mobility test assessed ability to complete navigation tasks that represent real-world visually-guided activities of daily living.¹

- Across the Phase 1/2 study a statistically significant improvement in the time taken to navigate a maze was demonstrated across the full spectrum of light levels tested (n=14)² (p=0.0017).
- A statistically significant improvement in time taken to navigate a maze was also demonstrated in the subset of patients treated at 1x10¹¹ vg/ml (n=9), that included both the adults (Cohort 1) and all children treated (p=0.0039).
- Across the Phase 1/2 study a statistically significant improvement in the time taken to navigate a straight path was demonstrated across the full spectrum of light levels tested (n=14)³ (p=0.0107).
- A statistically significant improvement in time taken to navigate a straight path was also demonstrated in the subset of patients treated at 1x10¹¹ vg/ml (n=9), that included both the adults (Cohort 1) and all children treated (p=0.0078).
- Mobility testing improvement from baseline was greatest at the lower light levels.

Retinal Sensitivity

As the retina degenerates in RPE65-deficiency, patients experience progressive visual field loss. To measure visual field sensitivity, Octopus 900 full-field static perimetry was employed, and the hill of vision was calculated to determine overall change in retinal sensitivity following intervention.⁴

- Statistically significant improvement in retinal sensitivity at six months compared to baseline was demonstrated in the treated eye compared to the untreated control eye in adults and children treated at 1x10¹¹ vg/ml (n=8)⁵ (p=0.0078).
- Greater improvements in retinal sensitivity were observed in children (n=5) than adults, most likely due to the increased preservation of the retina in younger patients (p=0.00625).

Improvements in the following visual function assessments (visual acuity and contrast sensitivity) suggest that foveal cone function improved over the 6-month follow up period in children and adults treated at the 1x10¹¹ vg/ml dose.

Visual Acuity

As the retina degenerates in RPE65-deficiency, visual acuity declines, and is particularly reduced at late stages of disease as central vision is affected. Visual acuity was assessed by the Early Treatment of Diabetic Retinopathy Study (ETDRS) vision chart.

- Statistically significant improvement was demonstrated in the ETDRS letter score from baseline to six months in the treated eye compared to the untreated control eye in adults and children treated at 1x10¹¹ vg/ml (n=9). A median improvement of 4.3 letters was seen across all patients treated at this dose (p=0.0156).
- This effect was greater in the pediatric patients (n=6), who had less retinal degeneration compared to the adults. A median improvement of 5.3 letters was observed in the treated versus untreated control eyes in children (p=0.0313).

Contrast Sensitivity

RPE65-deficient patients experience poor contrast sensitivity, even at a young age. Contrast sensitivity was measured by the Pelli-Robson assessment.

- Statistically significant improvement in contrast sensitivity was demonstrated in adults and children treated at 1x10¹¹ vg/ml (n=8)⁶ (p=0.0156).

Due to the favorable safety and strong activity profile established across adults and children treated with 1x10¹¹ vg/ml in the Phase 1/2 trial, MeiraGTx has selected this dose for centrally targeted administration in a future pivotal trial.

About AAV-RPE65

AAV-RPE65 is a novel second-generation gene therapy candidate in development for the treatment of patients with RPE65-deficiency, a condition that causes severe sight impairment beginning at birth. Delivered via subretinal injection, AAV-RPE65 is designed to deliver a normal copy of the *RPE65* gene, which is essential for photoreceptor function in the eye. AAV-RPE65 has been granted orphan designation by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of Leber congenital amaurosis (LCA) caused by disease-causing variants in the *RPE65* gene. The FDA has also granted AAV-RPE65 rare pediatric disease designation for the treatment of inherited retinal dystrophy due to biallelic RPE65 disease-causing variants.

About RPE65-Deficiency

RPE65-deficiency is a rare, genetic disorder caused by disease-causing variants in the *RPE65* gene. Due to rod photoreceptor dysfunction, RPE65-deficiency causes impaired vision from birth and results in the degeneration of the entire retina over time. Most RPE65-deficient patients experience poor vision in low-light conditions from a young age and suffer from central vision loss that progresses to complete blindness by early adulthood.

RPE65-deficiency is often characterized as a specific subtype of LCA caused by disease-causing variants in the *RPE65* gene (LCA2), or a specific

subtype of Retinitis Pigmentosa (RP) caused by disease-causing variants in the *RPE65* gene (RP20).

RPE65-deficiency occurs in approximately one in 125,000 people in the U.S.⁷ There are estimated to be approximately 6,000 RPE65-deficient patients in the U.S., Japan and EU5, with almost 30% of those patients under the age of 30 years old. Approximately 50 new cases are diagnosed annually.

¹ Functional vision was assessed by the RPE65-deficiency mobility test. This assessment was developed and validated specifically to measure functional vision in RPE65-deficient patients and is accordingly responsive to changes in peripheral vision and ambient illumination. It is a standardized, reliable and valid assessment. (Rubin GS. Visually Guided Mobility in Patients Treated with Gene Therapy for Leber's Congenital Amaurosis. *Investigative Ophthalmology & Visual Science*. April 2010)

² One adult patient did not complete 24-week efficacy assessments

³ One adult patient did not complete 24-week efficacy assessments

⁴ Weleber RG. VFMA: Topographic Analysis of Sensitivity Data from Full-Field Static Perimetry. *Translational Vision Science & Technology*. April 2015

⁵ One pediatric patient was unable to complete static perimetry testing

⁶ One pediatric patient was unable to complete contrast sensitivity testing

⁷ Based on an estimated prevalence of approximately one in 500,000 people in the U.S. with LCA related to disease-causing variants in the *RPE65* gene, and approximately one in 70,000 people in the U.S. with RP due to disease-causing variants in the *RPE65* gene.

About MeiraGTx

MeiraGTx (NASDAQ:MGTX) is a vertically integrated, clinical stage gene therapy company with five programs in clinical development and a broad pipeline of preclinical and research programs. MeiraGTx has core capabilities in viral vector design and optimization and gene therapy manufacturing, as well as a potentially transformative gene regulation technology. Led by an experienced management team, MeiraGTx has taken a portfolio approach by licensing, acquiring and developing technologies that give depth across both product candidates and indications. MeiraGTx's initial focus is on three distinct areas of unmet medical need: inherited retinal diseases, neurodegenerative diseases and severe forms of xerostomia and xerophthalmia. Though initially focusing on the eye, central nervous system and salivary gland, MeiraGTx intends to expand its focus in the future to develop additional gene therapy treatments for patients suffering from a range of serious diseases.

For more information, please visit www.meiragtx.com.

Forward-Looking Statement

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding our product candidate development, our meetings with regulatory authorities regarding pathways for regulatory approval of our product candidates, timing and results of data from the Phase 1/2 trial, as well as statements that include the words "expect," "intend," "plan," "believe," "project," "forecast," "estimate," "may," "should," "anticipate" and similar statements of a future or forward-looking nature. These forward-looking statements are based on management's current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, our incurrence of significant losses; any inability to achieve or maintain profitability, acquire additional capital, identify additional and develop existing product candidates, continue operating as a going concern, successfully execute strategic priorities, bring product candidates to market, build-out the manufacturing facility and processes, successfully enroll patients in and complete clinical trials, accurately predict growth assumptions, recognize benefits of any orphan drug designations, retain key personnel or attract qualified employees, or incur expected levels of operating expenses; failure of early data to predict eventual outcomes; failure to obtain FDA or other regulatory approval for product candidates within expected time frames or at all; the novel nature and impact of negative public opinion of gene therapy; failure to comply with ongoing regulatory obligations; contamination or shortage of raw materials; changes in healthcare laws; risks associated with our international operations; significant competition in the pharmaceutical and biotechnology industries; dependence on third parties; risks related to intellectual property; litigation risks; and the other important factors discussed under the caption "Risk Factors" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, as such factors may be updated from time to time in our other filings with the SEC, which are accessible on the SEC's website at www.sec.gov. These and other important factors could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, unless required by law, we disclaim any obligation to do so, even if subsequent events cause our views to change. Thus, one should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release.

Contacts

Investors:

MeiraGTx
Elizabeth Broder
(646) 860-7983
Investors@meiragtx.com

or

Media:

W2O pure
Christiana Pascale
(212) 257-6722
cpascale@purecommunications.com



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