MeiraGTx Presents Preclinical Data on its Ocular Gene Therapy Studies for the Treatment of Leber's Congenital Amaurosis, Achromatopsia and X-Linked Retinitis Pigmentosa at ESGCT 2017 Congress in Berlin

October 17, 2017

Results support MeiraGTx's clinical development strategies in all three inherited retinopathies

MeiraGTx has clinical trials in all three inherited retinopathies

New York, NY, Berlin, Oct 17, 2017 (PR NEWSWIRE) – MeiraGTx, a New York and London based gene therapy company, today announced the presentation of preclinical data from studies in animal models of Leber's congenital amaurosis (LCA2), achromatopsia, and X-linked retinitis pigmentosa (XLRP) that support the company's clinical development programs in these indications. The data will be presented at the European Society of Gene and Cell Therapy Congress in Berlin, during poster session 2 on Thursday October 19th, between 1845 and 2015 hrs (CET). Posters will be available to the public when the Congress opens today at the bcc Congress Center GmbH.

MeiraGTx has phase 1/2 clinical trials ongoing in all three inherited retinopathies at the Moorfields Eye hospital in London. All three studies are dose escalation trials, and all three clinical studies have accompanying Natural History studies.

- LCA2 (RPE65) Trial: Dosing complete in all 3 dose escalation cohorts
- Achromatopsia (CNGB3) Trial: Dosing complete of dose escalation cohorts 1 and 2
- XLRP (RPGR) Trial: Currently Dosing the 1st cohort

Tassos Georgiadis, Ph.D., from MeiraGTx, will present the LCA2 data in a poster titled "Pre-clinical toxicology of AAV2/5-OPTIRPE65, an optimized RPE65 gene therapy vector" (Poster #220). Leber's congenital amaurosis (LCA2), a childhood retinal dystrophy caused by mutations in the RPE65 gene has been the focus of various gene therapy clinical trials. Most trials showed modest improvements in (night) vision that were generally not sustained, most likely due to an insufficient level of RPE65 expression in the human RPE. To address these limitations, MeiraGTx has developed an optimized next generation vector, AAV2/5-OPTIRPE65, an AAV2/5-based vector, carrying an optimised expression cassette comprising a stronger RPE cell specific promoter, SV40 intron and codon-optimised transgene.

A head-to-head comparison between AAV2/5-OPTIRPE65 and the AAV2/2-based gene therapy vector used in MeiraGTx's first Phase I/II clinical trial measuring retinal sensitivity of Rpe65-deficient mice following subretinal delivery of either vector at increasing titres was performed. Maximum attainable scotopic responses (~90µV) were achieved with a 300-fold lower titre of AAV2/5-OPTIRPE65.

Administration of AAV2/5.OPTIRPE65 did not adversely affect retinal structure or function. Low level vector dissemination mainly to the liver was detected without pathological changes in these tissues. As expected, MeiraGTx detected some immune responses against the vector capsid, without concomitant pathology. MeiraGTx concluded that subretinal administration of AAV2/5-OPTIRPE65 is both safe and effective for use in clinical trials. The Phase I/II study is ongoing, treatment of the dose escalation cohorts has completed and dosing in pediatric patients is scheduled to start Q4 2017.

Jon Telfer, Ph.D., from MeiraGTx, will present the achromatopsia data in a poster titled, "Efficacy assessment and pre-clinical toxicology of AAV2/8-hCARp.hCNGB3, a CNGB3 gene therapy vector" during poster session 1 (Poster #218). The efficacy of AAV2/8-hCARp.hCNGB3 in Cngb3-/- mice was assessed following subretinal injection. Delivery of AAV2/8-hCARp.hCNGB3 resulted in long-term restoration of cone function, as determined by electroretinography (ERG). There was a three-fold increase in photopic b-wave amplitudes (to 85% of WT levels in animals treated at 1 month, and this was maintained for at least 9 months post-injection.

Administration of AAV2/8-hCARp.hCNGB3 resulted in a restoration of ERG at all titres planned for the clinical trial in a dose dependent manner. In toxicology studies, AAV2/8.hCARp.hCNGB3 did not adversely affect retinal structure or function. Some vector dissemination was detected as well as low level immune responses against the vector capsid, without concomitant pathology. MeiraGTx concluded that subretinal administration of AAV2/8.hCARp.hCNGB3 is safe for use in clinical trials. The Phase I/II study is ongoing and dosing of cohorts 1 and 2 has completed.

Alexander Smith, Ph.D., from MeiraGTx, will present the XLRP data in a poster titled, "Efficacy and safety of AAV2/5-hRKp.RPGR to treat X-linked retinitis pigmentosa" (Poster #226). X-linked retinitis pigmentosa due to recessive mutations in the RPGR gene is the commonest form of inherited retinal dystrophy with an incidence of ~1 in 15,000 males. Most patients present with loss of night vision before 10 years of age and progress to legal blindness by the third to fourth decade. MeiraGTx developed a proprietary RPGR gene therapy vector, AAV2/5-hRKp.RPGR, based on the AAV2/5 serotype. It carries a stable deletion mutant of the retina-specific RPGR isoform, ORF15, driven by the human rhodopsin kinase promoter.

Subretinal administration of 2 x 10^9 vg of AAV2/8-hRKp.RPGR in Rpgr-/- mice restores RPGR protein to the connecting cilia of the photoreceptor cells leading to a long-term preservation of photoreceptors and retinal function as measured by electroretinography.

On RPGR-/- human iPSC-derived retinal organoids, RPGR gene transfer led to the restoration of RPGR protein at the connecting cilia of the photoreceptors and a dose-dependent recovery of poly-glutamylated tubulin, which is absent from the RPGR-/- retinal organoids.

Subretinal administration of AAV2/5-hRKp.RPGR leads to a preservation of retinal function and structure in Rpgr-/- mice. Assessment of adverse effects suggested that subretinal administration of the vector is safe for use in the clinic. The Phase I/II study was initiated in July 2017, and treatment of cohort 1 is ongoing.

Dr. Robin Ali, Ph.D., Chief Scientific Officer of MeiraGTx Ocular Division, and President of the ESGCT, will deliver the Congress opening remarks today. In addition, Bastiaan Leewis, Manager, Industrialization for MeiraGTx, will deliver a presentation discussing considerations for building a GMP manufacturing facility.

About MeiraGTx

MeiraGTx is committed to the development of novel gene therapies to transform the lives of patients suffering from acquired and inherited disorders. The company is developing treatments for ocular diseases, including rare inherited blindness and age-related macular degeneration (AMD). MeiraGTx is also establishing treatments for xerostomia, a frequent and debilitating side effect of radiation treatment used in head and neck cancers, as well as certain neurodegenerative diseases. In addition, MeiraGTx is developing novel gene regulation platforms that promise to transform the way gene therapy can be applied and create new paradigms for biologic therapeutics.

About Moorfields Eye Hospital

Moorfields Eye Hospital NHS Foundation Trust is the leading provider of eye health services in the UK and a world-class center of excellence for ophthalmic research and education. The hospital has a reputation, developed over two centuries, for providing the highest quality of ophthalmic care and its 1,800 staff are committed to sustaining and building on our pioneering legacy and ensuring we remain at the cutting edge of developments in ophthalmology.

About UCL

The UCL Institute of Ophthalmology conducts cutting-edge science, attracting research workers of the highest international caliber. The most recent national Research Excellence Framework has once more confirmed that UCL has the strongest Clinical Medicine research of any British university. Independent auditors have shown that their partnership with Moorfield's Eye Hospital is the most productive in the world.

Forward-Looking Statements

This press release contains forward-looking statements. These forward-looking statements are based on management's expectations and are subject to certain factors, risks and uncertainties that may cause actual results, outcome of events, timing and performance to differ materially from those expressed or implied by such statements. The information contained in this press release is believed to be current as of the date of original issue. MeiraGTx expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations with regard thereto or any change in events, conditions or circumstances on which any such statements are based.

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