MeiraGTx Announces Positive Top-Line Data from the MGT009 Phase 1/2 Clinical Study Demonstrating Safety and Improvement in Multiple Domains of Vision in X-Linked Retinitis Pigmentosa Patients treated with Botaretigene Sparoparvovec (AAV-RPGR) compared to Untreated Randomized Control

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- The primary outcome of the MGT009 study is safety, and botaretigene sparoparvovec treatment was found to be generally safe and well-tolerated
- Significant improvements were demonstrated in multiple different endpoints in botaretigene sparoparvovec-treated patients across each of the three domains of vision: retinal function, visual function and functional vision
- MeiraGTx to host a conference call on Tuesday, June 28, 2022, at 8am ET

LONDON and NEW YORK, June 28, 2022 (GLOBE NEWSWIRE) -- MeiraGTx Holdings plc (Nasdaq: MGTX), a vertically integrated, clinical stage gene therapy company, today announced top-line data from the Phase 1/2 clinical study MGT009 (NCT03252847) of botaretigene sparoparvovec (formerly referred to as AAV-RPGR), an investigational gene therapy in development for the treatment of patients with X-linked retinitis pigmentosa (XLRP) with disease-causing variants in the *RPGR* gene.

Treatment with botaretigene sparoparvovec was found to be generally safe and well-tolerated, and significant improvements were demonstrated in multiple endpoints across each of the three domains of vision - retinal function, visual function, and functional vision - in participants treated with botaretigene sparoparvovec when compared to the randomized untreated control arm of the study at 6 months post-treatment.

MeiraGTx and Janssen Pharmaceuticals, Inc. (Janssen), one of the Janssen Pharmaceutical Companies of Johnson & Johnson, are jointly developing botaretigene sparoparvovec as part of a broader collaboration to develop and commercialize gene therapies for the treatment of inherited retinal diseases.

In the dose escalation and expansion phases of the MGT009 study, improvements in vision were seen in subjects treated with low and intermediate doses of botaretigene sparoparvovec compared to the randomized concurrent control arm at 6 months. Improvements were demonstrated in (i) retinal sensitivity on static perimetry, using both pointwise responder analysis as well as mean retinal sensitivity analysis; (ii) functional vision in a vision-guided mobility assessment (VMA); and (iii) other measures of visual function and functional vision, including visual acuity using ETDRS and patient-reported outcome measures.

“XLRP is characterized by early-onset visual field loss with initial difficulty in functioning in dim light conditions followed by progression to blindness and associated loss of independence by young adulthood in most patients,” said Michel Michaelides [1], BSc MB BS MD(Res) FRCOphth FACS, MGT009 trial investigator, Consultant Ophthalmologist, Moorfields Eye Hospital and Professor of Ophthalmology, at Moorfields Eye Hospital and University College London. “These data demonstrate the potential of treatment with botaretigene sparoparvovec to have a life-changing impact on vision in patients with XLRP, for which there is no currently available therapeutic option.”

“We are extremely encouraged by these data which demonstrate improvement following treatment with botaretigene sparoparvovec compared to an untreated randomized control group in a range of endpoints that are relevant to this severe disease,” said Alexandria Forbes, Ph.D., president and chief executive officer of MeiraGTx. “These data give us increased confidence in the potential for botaretigene sparoparvovec to meaningfully improve the lives of the thousands of patients with XLRP.”

Dr. Forbes continued, “As we continue to enroll the Lumeos Phase 3 study, we are leveraging our wholly-owned, end-to-end GMP manufacturing and quality infrastructure to prepare for potential commercial supply. I would like to thank the investigators, patients and families who have dedicated their time to our clinical trials and who continue to support us in our efforts to develop this important therapy aiming to make a meaningful difference in the lives of people with this serious disease.”

The Phase 3 Lumeos study (NCT04671433) of botaretigene sparoparvovec for the treatment of patients with XLRP with disease-causing variants in the *RPGR* gene is actively dosing patients.

Data Summary:

MGT009 Phase 1/2 clinical study design:

The Phase 1/2 MGT009 clinical study consists of three phases: dose-escalation, pediatric dose-confirmation, and an expansion phase. In the dose escalation phase, subjects were treated at 3 escalating doses of botaretigene sparoparvovec; a low dose of $2x10^{11}$ vg/mL, an intermediate dose of $4x10^{11}$ vg/mL, and a high dose of $8x10^{11}$ vg/mL. In the expansion phase, subjects were randomized to either immediate treatment with one of 2 doses, the low or intermediate dose, or an untreated concurrent control arm with deferred treatment. At 6 months, the untreated control subjects were randomized to receive either the low or intermediate treatment doses. Throughout the MGT009 study, a total of 42 adult male subjects were treated with botaretigene sparoparvovec at 3 doses and 3 children were treated at the intermediate dose. Each patient was treated with subretinal delivery of botaretigene sparoparvovec in only one eye.

The primary endpoint of the Phase 1/2 MGT009 clinical study is safety in all patients treated with botaretigene sparoparvovec (n=45), with exploratory efficacy endpoints measuring changes in assessments of each of the three domains of vision (retinal function, visual function and functional vision) at

pre-specified timepoints post-treatment.

Safety Findings:
Safety findings from MGT009 demonstrate that botaretigene sparoparvovec is generally safe and well-tolerated. Most adverse events (AEs) were related to the surgical delivery procedure, were transient and resolved without intervention. There were no dose-limiting events. A total of 3 serious adverse events (SAEs) were observed in the overall Phase 1/2 MGT009 clinical study. 2 SAEs were observed in the dose-escalation phase of the study (n=10; one retinal tear and one panuveitis in the low dose cohort), which have been previously reported. A single additional SAE was observed in the dose expansion phase of the study (n=32). This SAE was increased intraocular pressure and resolved on treatment. No SAEs were observed in the pediatric dose confirmation cohort.

Following the implementation of a modified prophylactic steroid regimen, a reduction in inflammation related AEs was also observed in the expansion phase of the study.

Exploratory Efficacy Findings:
MGT009 demonstrated improvements in each of the three visual domains. Based on nominal p-values ($p < 0.05$) the following endpoints were significant at 6 months compared to randomized control subjects. In the overall population of immediate treated subjects in just the randomized expansion phase of the study, using the prespecified exploratory analyses, the VMA at lux 1, patient reported outcome (PRO) extreme lighting and mean retinal sensitivity (meanRS) in the central 10 degree area of the retina, demonstrated significant improvement and BCVA approached significance ($P < 0.10$).

Further analyses reported below were conducted on the population of low and intermediate dose immediate treated subjects from both the dose escalation and the expansion phases of the study applying the Phase 3 Lumeos eligibility criteria. Based on nominal p-values ($p < 0.05$) the following endpoints were significant at 6 months compared to randomized control subjects:

Functional Vision

- Performance in the Visual Mobility Assessment (VMA) at low levels of illumination. The relative improvement in treated patients compared to untreated patients increased as illumination levels progressively got darker (nominal p-values were 0.008, 0.005 and 0.008 at lux 16, 4, and 1 respectively).
- A significant improvement was observed in the extreme lighting domain of the disease related PRO at 6 months (nominal p-value =0.020), with trends of improvements in the other patient-reported outcome domains also observed.

Visual Function

- ETDRS visual acuity (nominal p-value = 0.031).

Retinal Function using Static Perimetry

- meanRS in the central 10 degree area of the retina (nominal p-value < 0.001).

Pointwise responder Analysis of Static Perimetry Data:

Responder criteria: at least a 7dB improvement from baseline in 5 or more individual loci with the same 5 loci showing improvement at 2 timepoints following treatment**.**

- At 26 weeks 5/22 (22.7%) of the treated patients met the responder criteria compared to 0/11 (0%) in the randomized concurrent control arm. The responder rate in the treated arm further improved at 52 weeks to 10/21 (47.6%).

Based on these results, the improvements seen in each of the three visual domains is entirely in keeping with the real-life challenges patients with XLRP experience, having marked functional difficulties especially at low light levels. Additional MGT009 data will be submitted for presentation at medical meetings in the second half of this year.

Conference Call Information:
A live webcast of the call, as well as a replay, will be available on the Investors page of the Company's website https://investors.meiragtx.com/

Register for the call by clicking here

About Botaretigene Sparoparvovec
Botaretigene sparoparvovec, formerly referred to as AAV-RPGR, is an investigational gene therapy for the treatment of patients with XLRP caused by disease-causing variants in the eye-specific form of the *RPGR* gene (RPGR ORF15). Botaretigene sparoparvovec is designed to deliver functional copies of the *RPGR* gene to the subretinal space in order to help improve and/or preserve vision. Botaretigene sparoparvovec is being evaluated in the Phase 1/2 MGT009 clinical trial (NCT03252847), an open-label, multi-center dose escalation study with a randomized, multi-dose expansion cohort which included a deferred treatment control to determine the safety and efficacy of botaretigene sparoparvovec in adults and children with XLRP caused by variants in the *RPGR* gene. The Lumeos trial (NCT04671433), a Phase 3 randomized, controlled study of botaretigene sparoparvovec for the treatment of XLRP associated with variants in the *RPGR* gene, is actively dosing patients. Botaretigene sparoparvovec has been granted Fast Track and Orphan Drug designations by the FDA and PRIority MEdicines (PRIME), Advanced Therapy Medicinal Product (ATMP), and Orphan designations by the European Medicines Agency (EMA).

About X-Linked Retinitis Pigmentosa (XLRP)
XLRP is the most severe form of retinitis pigmentosa (RP), a group of inherited retinal diseases characterized by progressive retinal degeneration and vision loss. In XLRP, both rods and cones function poorly, leading to degeneration of the retina and total blindness. The most frequent cause of XLRP is disease-causing variants in the *RPGR* gene, accounting for more than 70% of cases of XLRP, and up to 20% of all cases of RP. There are currently

no approved treatments for XLRP.

About MeiraGTx
MeiraGTx (Nasdaq: MGTX) is a vertically integrated, clinical stage gene therapy company with six 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, and a transformative gene regulation platform technology which allows tight, dose responsive control of gene expression by oral small molecules with dynamic range that can exceed 5000-fold. 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: ocular, including inherited retinal diseases and large degenerative ocular diseases, neurodegenerative diseases and severe forms of xerostomia. Though initially focusing on the eye, central nervous system, and salivary gland, MeiraGTx plans to expand its focus 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 the development and efficacy of botaretigene sparoparvovec, the Phase 3 Lumeos clinical trial of botaretigene sparoparvovec and the achievement of milestones or regulatory approvals, including in light of the COVID-19 pandemic, as well as statements that include the words "expect," "will," "intend," "plan," "believe," "project," "forecast," "estimate," "may," "could," "should," "would," "continue," "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, raise additional capital, identify additional and develop existing product candidates, successfully execute strategic priorities, bring product candidates to market, expansion of our manufacturing facilities 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; the impact of the COVID-19 pandemic on the status, enrollment, timing and results of our clinical trials and on our business, results of operations and financial condition; 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 or other manufacturing issues; 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; changes in tax policy or treatment; our ability to utilize our loss and tax credit carryforwards; litigation risks; and the other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended March 31, 2022, 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.

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