Late-Breaking Phase 1/2 Data Demonstrates Safety Profile of Investigational Gene Therapy Botaretigene Sparoparvovec (AAV-RPGR) and Sustained Vision Improvement in Patients with X-Linked Retinitis Pigmentosa (XLRP)

October 01, 2022

Results from the Phase 1/2 MGT009 study presented at the American Academy of Ophthalmology (AAO) 2022 Annual Meeting set the stage for Phase 3 LUMEOS trial of botaretigene sparoparvovec in XLRP, which is actively dosing patients

LONDON and NEW YORK, Oct. 01, 2022 (GLOBE NEWSWIRE) -- MeiraGTx Holdings plc (Nasdaq:MGTX), a vertically integrated, clinical-stage gene therapy company, announced today the primary results from the Phase 1/2 study evaluating the investigational gene therapy botaretigene sparoparvovec (formerly AAV-RPGR) in patients with the inherited retinal disease X-linked retinitis pigmentosa (XLRP) associated with the retinitis pigmentosa GTPase regulator (RPGR) gene.

Treatment with botaretigene sparoparvovec was found to have an acceptable safety profile and efficacy assessments in this proof-of-concept study demonstrated improvements in retinal sensitivity, visual function and functional vision.[1] These findings were presented in a late-breaking oral presentation today at the Retina Subspecialty Day program of the American Academy of Ophthalmology (AAO) 2022 Annual Meeting (Abstract #30071754) by Professor Michel Michaelides.

“We are excited to present these promising Phase 1/2 data from our investigational gene therapy, botaretigene sparoparvovec in the late breaking session at this year’s AAO meeting,” said Alexandria Forbes, Ph.D., president, and chief executive officer of MeiraGTx. “The treatment appears to be safe and well-tolerated, and the improvements observed in each visual domain at six months post-treatment underscores the potential of botaretigene sparoparvovec to address a significant unmet need for those living with XLRP. We look forward to advancing this program which is currently dosing patients in Phase 3 LUMEOS trial.”

“Botaretigene sparoparvovec therapy is intended to deliver a healthy copy of the *RPGR* gene to replace a disease causing one, and potentially restore vision for patients living with XLRP,” said Michel Michaelides, B.Sc., M.B., B.S., M.D. (Res), FRCOphth, FACS, Consultant Ophthalmologist, Moorfields Eye Hospital, Professor of Ophthalmology, University College London and MGT009 study investigator‡. “The results presented so far show a positive effect of the therapy compared to the randomized untreated control arm, providing us with increased confidence in its potential to treat the underlying cause of XLRP.”

MeiraGTx and Janssen Pharmaceuticals, Inc., part 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.

The primary endpoint of the MGT009 study (NCT03252847) was safety, with secondary endpoints measuring changes in assessments of three domains of vision—retinal sensitivity, visual function and functional vision—at specified time points post-treatment.[1] In the study’s dose escalation and expansion phases, sustained or increased functional improvement in each visual domain was observed in participants treated with botaretigene sparoparvovec compared to the randomized untreated control arm of the study at six months post-treatment.[1]

Analyses of the pooled low and intermediate dose cohorts demonstrated improvement in retinal sensitivity in the treated eyes compared to untreated eyes in the randomized concurrent control arm as measured by both full-field static perimetry and microperimetry.[1] An improvement in mean retinal sensitivity as measured by static perimetry in the central 10-degree area of the retina was observed at six months in the treated eye compared to untreated eyes in the randomized concurrent control arm [in the full analysis of pooled low and intermediate doses across adults: 1.96 decibel (dB); (±95% CI: 0.59, 3.34); and in the sensitivity analysis when applying the Phase 3 criteria: 2.42 (0.91, 3.93)].[1]

As part of the study, patients performed a functional vision assessment using a visual mobility maze to assess their ability to navigate through simulated real-life obstacles across a broad range of controlled light. At week 26, improvement in walk time was observed between the treated eyes in the low and intermediate dose cohorts and the untreated eyes in the randomized concurrent control arm at low illumination levels (full analysis nominal p-value < 0.05 at lux 1 and lux 16; in the sensitivity analysis when applying the Phase 3 criteria nominal p-value < 0.01 at lux1, lux 4 and lux 16).[1]

The safety profile of botaretigene sparoparvovec observed in MGT009 was consistent with previous reports.[1] Botaretigene sparoparvovec demonstrated an adverse event (AE) profile that was anticipated and manageable.[1] Most AEs were related to the surgical delivery procedure, were transient and resolved without intervention.[1] There were no dose-limiting events.[1] A total of three serious adverse events (SAEs) were observed in the overall Phase 1/2 MGT009 clinical study; two SAEs, which were previously reported, were observed in the dose-escalation phase of the study (n=10; one retinal detachment and one panuveitis in the low dose cohort), and a single additional SAE of increased intraocular pressure was observed in the dose escalation phase and resolved with treatment.[1]

Further sensitivity analysis was conducted on study participants by applying the Phase 3 LUMEOS (NCT04671433) study eligibility criteria that corroborated the endpoints selected for the Phase 3 study.[1] Currently, the LUMEOS study of botaretigene sparoparvovec for the treatment of patients with XLRP with disease-causing variants in the RPGR gene is actively dosing patients.

Session Details:
Saturday, 8:55AM - 9:30AM CT

Section X: Late Breaking Developments, Part II

Presentation details:
Abstract Title: Ph1/2 AAV5-RPGR (Botaretigene Sparoparvovec) Gene Therapy Trial in RPGR-associated X-linked Retinitis Pigmentosa (XLRP)
Presenter: Michel Michaelides, Professor of Ophthalmology, UCL Institute of Ophthalmology in Dept. of Genetics
Date and Time: Saturday, October 1, 2022, at 9:00 a.m. CT (10:00 a.m. ET)

About the Phase 1/2 MGT009 Clinical Trial and Botaretigene Sparoparvovec
The Phase 1/2 MGT009 clinical trial (NCT03252847) study was an open-label, multicenter dose escalation study that enrolled patients aged five years and older with XLRP caused by disease causing variants in the retinitis pigmentosa GTPase regulator (RPGR) gene at multiple sites in the United States and the United Kingdom. The primary endpoint was safety and tolerability; secondary endpoints assessed retinal function, visual function, functional vision and quality of life measurements.

The clinical study was composed of three parts: dose-escalation, pediatric dose-confirmation and an expansion phase. In the dose escalation phase, subjects were treated at three escalating doses of botaretigene sparoparvovec; a low ($2x10^{11}$ vg/mL), an intermediate ($4x10^{11}$ vg/mL), and a high ($8x10^{11}$ vg/mL) dose. In the expansion phase, 42 adult male patients were randomized to either immediate treatment with one of two low or intermediate doses or an untreated concurrent control arm with deferred treatment. At six months, the untreated control arm was randomized to receive either the low or intermediate treatment doses. Botaretigene sparoparvovec was administered through subretinal delivery in only one eye. The adult patients received treatment at three doses, and the pediatric cohort (n=3) was treated with an intermediate dose of botaretigene sparoparvovec.

Botaretigene sparoparvovec has been granted Fast Track and Orphan Drug designations by the U.S. Food and Drug Administration (FDA) and PRIority MEdicines (PRIME), Advanced Therapy Medicinal Product (ATMP) and Orphan designations by the European Medicines Agency (EMA).

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.

‡*Dr. Michaelides is a scientific founder of, and consultant to, and has a financial relationship with MeiraGTx.*

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, repay our debt obligations, 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 June 30, 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.

[1] Michaelides, M et al. Ph1/2 AAV5-RPGR (Botaretigene Sparoparvovec) Gene Therapy Trial in RPGR-associated X-linked Retinitis Pigmentosa (XLRP). Abstract #30071754. Presented at the 2022 American Academy of Ophthalmology Annual Meeting.

Contacts

Investors:
MeiraGTx
Investors@meiragtx.com

Media:
Jason Braco, Ph.D.
LifeSci Communications
jbraco@lifescicomms.com