MeiraGTx Announces Positive Clinical Data from the AQUAx Phase 1 Clinical Study of AAV2-hAQP1 for the Treatment of Grade 2/3 Radiation-Induced Xerostomia

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- *Clinically meaningful improvements in xerostomia symptoms measured by two different xerostomia PROs demonstrated across both unilaterally and bilaterally treated cohorts at 12 months*
- *Increases in whole saliva flow rates observed post-treatment, providing objective evidence of biological activity, reaching the normal range in bilaterally treated participants by 2 months and persisting through the Month 12 assessment*
- *Across assessments, greater improvements observed in bilaterally treated participants compared to those treated unilaterally*
- *Early long-term follow-up data suggest durability of improvement to at least 3 years post-treatment*
- *AAV2-hAQP1 appears safe and well tolerated at each dose tested*
- *The strong safety and encouraging, clinically meaningful activity data support further clinical development of AAV2-hAQP1*
- *Phase 2 randomized, double-blind, placebo-controlled study initiated with participants currently being dosed*
- *Webcast and conference call to be held today, June 27, 2023, at 8:00 a.m. ET*

LONDON and NEW YORK, June 27, 2023 (GLOBE NEWSWIRE) -- MeiraGTx Holdings plc (NASDAQ:MGTX), a vertically integrated, clinical stage gene therapy company, today announced positive clinical data from the completed Phase 1 AQUAx study of AAV2-hAQP1 for the treatment of grade 2/3 radiation-induced xerostomia (RIX).

“Today we are releasing data from the completed Phase 1 AQUAx study which now includes the final 12 month data from all bilaterally treated participants. The data demonstrate clinically important improvements in two different patient reported outcome questionnaires for xerostomia, as well as meaningful increases in absolute saliva production in both bilaterally and unilaterally treated cohorts at 12 months,” said Alexandria Forbes, Ph.D., president and chief executive officer of MeiraGTx. “We are also presenting additional data from our long-term follow-up study demonstrating durability of improvement in participants who have reached the 2- and 3-year post-treatment assessment, as well as supportive data showing transduction of parotid glands treated with AAV2-hAQP1 up to 24 months post-treatment and AQP1 protein expression.”

Dr. Forbes continued, “We are excited to present these data showing meaningful activity across key endpoints in participants with intractable grade 2 and 3 xerostomia which has been persistent for many years prior to treatment with AAV2-hAQP1. We have initiated a randomized, double-blind, placebo-controlled, Phase 2 study which is currently enrolling and treating participants, and we look forward to advancing the development of a potential treatment for this severely debilitating condition.”

Full data from the AQUAx Phase 1 study is expected to be reported at a scientific meeting in the second half of 2023.

Phase 1 AQUAx Trial of AAV2-hAPQ1 for the Treatment of Grade 2/3 Radiation-Induced Xerostomia

AQUAx is an open label, multi-center, dose escalation study of a single administration of AAV2-hAQP1 to one or both parotid glands in participants with radiation-induced salivary hypofunction and grade 2/3 xerostomia. There were 4 escalating dose cohorts with 3 participants per cohort for both unilaterallly and bilaterally treated participants. All participants were followed for 1-year post-treatment in the Phase 1 AQUAx study and were then enrolled in a long-term follow-up study for a total of 5 years. The primary endpoint was safety and the secondary endpoints included change from baseline to 12 months in patient-reported measures of xerostomia symptoms using the Global Rate of Change Questionnaire, or GRCQ, and the Xerostomia Questionnaire, or XQ. In addition, whole saliva flow rate was assessed. The study was conducted at 4 centers, with 3 in the US and 1 in Canada.

Treatment appears safe and well tolerated at each dose tested with no dose-limiting toxicity or treatment-related serious adverse events.

Efficacy Data presented from the 24 participants treated in the AQUAx study

- Improvements observed in both of the patient reported assessments of xerostomia symptoms, Global Rate of Change Questionnaire (GRCQ) and Xerostomia Questionnaire (XQ), in both unilateral and bilateral treated cohorts at 12 months post-treatment
- Improvements in salivary flow were seen in unilateral as well as bilateral cohorts
- Early long-term follow-up data suggest durability of improvement out to at least 3 years post-treatment

McMaster Global Rate of Change Questionnaire (GRCQ):

Bilateral Cohorts (n=12) to 12 Months

- 10/12 (83%) participants at 12 months reported symptoms of dry mouth as ”better” following treatment
- Each of these 10 participants rated changes in xerostomia scores that were “important” or “very important” with a score of 2 or more at 12 months
- 5 participants rated the change in xerostomia symptoms with the highest improvement scores of 6 or 7 denoting a “very important improvement”
- No participant reported worsening of xerostomia symptoms

Unilateral Cohorts (n=12) to 12 Months

- 8/12 participants at 12 months reported symptoms of dry mouth as “better” following treatment
- Each of these 8 participants rated changes in xerostomia scores that were “important” or “very important” with a score of 2 or more at 12 months
- 4 of these participants rated the change in xerostomia symptoms with the highest improvement scores of 6 or 7 denoting “a very important improvement”
- Improvement in xerostomia symptoms persisted through 2 years in 4 participants and 3 years in 3 participants who reached these timepoints
- No participant reported worsening of xerostomia symptoms

Combined Unilateral and Bilateral Cohorts

- Overall, the average improvement in GRCQ score was greater in bilaterally treated participants compared to those treated unilaterally
- Improvements were maintained and increased over time in both unilateral and bilateral cohorts
- A 2-point change in GRCQ is considered important by patients
- Changes of 3 points or greater are considered a substantial improvement over standard of care and “transformative” by KOLs
- Unilaterally treated cohorts achieved overall improvement of >3 points at 12 months
- Bilaterally treated cohorts achieved overall improvement of >3 points at 2 months and an overall improvement of 4 points by 6 months, with this 4-point improvement maintained at 12 months

Xerostomia Questionnaire (XQ):

Xerostomia Questionnaire (XQ) PRO measure scoring scale

- An improvement (decrease) of 8 points or more is considered clinically meaningful
- A decrease in score of 10 or greater is considered a substantial improvement over standard of care and “transformative” by KOLs

Change from Baseline Unilateral and Bilateral Cohorts

- Unilateral: 7/12 had score improvements (decrease) ≥8 at 12 months
- Bilateral: 9/12 had score improvements ≥8 at 12 months
- Overall: 16/24 (66%) had an improvement following treatment of ≥8 points
- 50% of unilaterally treated participants and 75% of bilaterally treated participants at 12 months achieved at least a 10-point improvement
- There was good concordance between the responses on the GRCQ and XQ

Average Change from Baseline Unilateral and Bilateral Cohorts

- In unilaterally treated participants, an average 13-point improvement from baseline in XQ was seen at 12 months
- In bilaterally treated participants, an average 21-point improvement from baseline in XQ was seen at 12 months
- In both groups, XQ scores improved (declined) >8 points soon after treatment, and >10 points within 2 months after treatment
- This level of benefit is considered transformative by KOLs
- The degree of improvement in scores was greater in bilaterally treated participants compared to those treated unilaterally

Whole Saliva Flow:

Bilaterally Treated Participants: Unstimulated Whole Saliva Flow

- Meaningful increase in whole saliva flow was seen in bilaterally treated participants
- The overall unstimulated whole saliva flow rate improved to an average of 0.33 mL/min which is within the normal range for unstimulated whole saliva production
- Normal unstimulated whole salivary flow rate averages 0.3-0.4 mL/min
- The average percentage change from baseline was 83% at 12 months
- Based on both absolute whole resting saliva as well as the overall percentage change from baseline – the improvement in unstimulated salivary flow in the bilaterally treated participants appears to be of a clinically meaningful size that could result in improvement in xerostomia symptoms

Unilaterally Treated Participants: Absolute Whole Saliva Measures (Stimulated)

- Increase in whole salivary flow was also observed in unilaterally treated participants despite the data being confounded by significant manipulation of the salivary glands just prior to stimulated saliva collection, and only a single treated gland contributing to the whole saliva volume
- Stimulated whole saliva in the unilaterally treated cohorts increased to greater than 0.7ml/min which is above the range of stimulated saliva flow that is considered hyposalivation
- Hyposalivation is <0.5 to 0.7ml/min for stimulated whole saliva flow

AAV2-hAQP1 Persists in Parotid Gland for at Least 24 Months After Treatment

- Biopsies were obtained in 7/15 participants enrolled in the National Institutes of Health (NIH), single site, Phase 1 study MGT001, using the same batch of drug product used in the AQUAx study
- 6/7 biopsies showed the presence of AAV2-hAQP1 genomes ≥12 months post-treatment
- There is an increase in copy number of transduced vector genomes normalized to DNA with increasing dose
- Immunohistochemistry of tissue from a core needle biopsy showed AQP1 protein expression in acinar cells transduced with AAV2-hAQP1

Initiation of Phase 2 Study:

Study Design

- Randomized, double-blind, placebo-controlled
- 120 participants: Two active doses of AAV2-hAQP1 vs Placebo. Randomization 1:1:1.
- Active Doses: 0.4E12 and 1.2E12 (n=40 per arm)

Primary Efficacy Endpoints

- Change from Baseline to 12 Months in symptom-specific XQ

Key Secondary Endpoints

- Change from Baseline to 12 Months in Whole Saliva Flow Rate
- Safety and tolerability of AAV2-hAQP1 treatment
- GRCQ is also being assessed as a secondary endpoint

Grade 2/3 Radiation-Induced Xerostomia unmet medical need and market size:

There are currently more than 170,000 patients in the U.S. with grade 2/3 RIX[1,2,3] two or more years out from successful radiation treatment for head and neck cancer. Each year in the U.S., approximately 54,000 new patients with head and neck cancer are treated with radiation[1,2], with an estimated >15,000 developing persistent grade 2/3 RIX[2,3]. Current treatment options for grade 2/3 RIX are few and are of limited benefit. The sialogogues pilocarpine (approved for RIX) and cevimeline (used off-label) are minimally effective in patients with grade 2/3 radiation induced xerostomia where the gland structure and function have been significantly impaired. No new medications for RIX have been approved in over 20 years.

MeiraGTx's xerostomia clinical program update details are as follows:

- Tuesday, June 27, 2023, at 8:00 a.m. ET.
- To register and attend the event, please click here

A live webcast of the event, as well as a replay, will be available on the Investors page of the Company's website at www.investors.meiragtx.com/.

About the Phase 1 AQUAx Clinical Trial

The Phase 1 AQUAx clinical trial is an open-label, non-randomized, dose escalation trial designed to evaluate the safety of MeiraGTx's investigational gene therapy AAV2-hAQP1 when administered via Stensen's duct to one or both parotid glands in patients who have been diagnosed with grade 2 or 3 radiation-induced xerostomia and who have remained cancer free for at least five years (or at least two years if HPV+) after receiving radiation

treatment for head and neck cancer. Primary endpoint of the trial is safety. Secondary endpoints include change from baseline in patient reported measures of xerostomia symptoms and in unstimulated and stimulated salivary flow rates.

About the Phase 1 NIH Study
The Phase 1 NIH study is an open-label, dose-escalation study evaluating the safety of a single administration of an adeno-associated virus vector encoding human aquaporin-1 to one parotid salivary gland in individuals with irradiation-induced parotid salivary hypofunction**.**

About the McMaster Global Rating of Change Questionnaire and the Xerostomia Questionnaire
The McMaster Global Rating of Change Questionnaire is a validated Patient Reported Outcome measure wherein the patient rates the severity of their dry mouth. Patients are asked, "Overall, has there been any change in your Dry Mouth since you received the study treatment?" Patients may reply, "Better", "Worse", or "About the Same". If the patient replies "Better" or "Worse", they are asked to quantify the change for better/worse on a 7-point scale, with 7 a very important change from baseline, and 1 being minimal. A two-point change is important to the patient. This PRO measure was accepted by the FDA in its review and approval of cevimeline[4].

The Xerostomia Questionnaire is a PRO measure consisting of 8 symptom-specific questions wherein the patient rates each symptom from 0 (not present) to 10 (worst possible). The responses are summed (0-80), providing an overall measure of disease burden. This PRO is refined from the Xerostomia Inventory which consists of 11 questions and for which a 6-point change in disease burden is defined as a clinically meaningful improvement. Drugs approved based on positive McMaster Global Rating of Change assessments have failed to demonstrate clinically meaningful improvement on this measure in registrational studies.

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 that allows precise, 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 diseases, including both inherited retinal diseases as well as 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**

[1] SEER, Cancer.net

[2] Marta GN et al (2014). Intensity-modulated radiation therapy for head and neck cancer: systematic review and meta-analysis. Radiother Oncol. 110(1):9-15

[3] Jensen S.B., et al. (2010). A systematic review of salivary gland hypofunction and xerostomia induced by cancer therapies: prevalence, severity and impact on quality of life. Support Care Cancer. 18(8):1039-1060

[4] Mark S. Chambers, Marshall Posner et al., Cevimeline for the Treatment of Postirradiation Xerostomia in Patients With Head and Neck Cancer, 2007. Int. J. Radiation Oncology Biol. Phys., Vol. 68, No. 4, pp. 1102–1109

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 AAV2-hAQP1, the advancement of AAV2-hAQP1 into a Phase 2 clinical trial and anticipated milestones regarding our clinical data and reporting of such data and the timing of results of data, 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 most recent quarterly report on Form 10-Q or annual report on Form 10-K or subsequent 8-K reports, as filed with the Securities and Exchange Commission. 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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