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

December 13, 2022

- *Clinically meaningful improvements in xerostomia symptoms and disease burden reported in patient reported outcome (PRO) measures in both unilateral and bilateral cohorts*
- *Increases in whole saliva flow rates were seen in both unilateral and bilateral cohorts*
- *Overall degree of improvement was greater in bilateral compared to unilateral cohorts*
- *AAV2-hAQP1 appears safe and well tolerated at each dose tested*
- *Webcast and conference call to be held today, December 13, 2022, at 8:00 a.m. ET*

LONDON and NEW YORK, Dec. 13, 2022 (GLOBE NEWSWIRE) -- MeiraGTx Holdings plc (NASDAQ:MGTX), a vertically integrated, clinical stage gene therapy company, today announced positive clinical data from the ongoing Phase 1 AQUAx study of AAV2-hAQP1 for the treatment of grade 2/3 radiation-induced xerostomia (RIX).

“We are very encouraged by the clinical data in both unilateral and bilateral cohorts demonstrating the safety, efficacy and durability of AAV2-hAQP1 in grade 2/3 radiation-induced xerostomia,” said Alexandria Forbes, Ph.D., president and chief executive officer of MeiraGTx. “Not only does this therapy continue to be safe and well tolerated, but we are seeing durability of effect at 2 and even 3 years for patients who have reached those timepoints.”

Dr. Forbes continued, “These updated data from all 24 patients treated in our AQUAx Phase 1 study suggest that our novel gene therapy, AAV2-hAQP1, could have a disease modifying effect in this large and underserved patient population. We look forward to further advancing this wholly-owned program into a Phase 2 study in the first half of 2023.”

Study Design and Safety Update in 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 patients with radiation-induced salivary hypofunction and grade 2/3 xerostomia. Enrollment of the AQUAx study was completed in the first quarter of 2022 and consisted of four unilaterally treated dose escalating cohorts with 3 subjects per cohort and four bilaterally treated dose escalating cohorts with 3 subjects per cohort. As of the cutoff date of November 30, 2022, all 12 unilaterally treated participants have undergone their 12-month assessment, with 3 having completed their 24-month assessment and one having completed their 36-month assessment in the long-term follow-up study. All 12 bilaterally treated participants have undergone their 6-month assessment. To date, treatment has been well tolerated with no dose limiting toxicity (DLT) or treatment-related serious adverse events (SAEs), and improvements have been seen in validated patient reported assessments of xerostomia symptoms and in whole salivary flow rate.

The study is being conducted at 4 centers, 3 in the US and 1 in Canada. All participants are to be followed for 1-year post-treatment and will then enter a long-term follow-up study for an additional 4 years. The study’s primary endpoint is safety. Secondary endpoints include change from baseline in patient reported measures of xerostomia symptoms as well as whole salivary flow rates.

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

- Clinically meaningful improvements in xerostomia symptoms reported consistently across two validated PROs assessing xerostomia symptom severity
- Meaningful increases in whole saliva flow rates observed post-treatment, providing objective evidence of biological activity of AAV2-hAQP1 treatment
- Early long-term follow-up data suggest durability of improvement 2+ years post-treatment

Global Rate of Change (GRCQ):

Bilateral Cohorts (n=12) to 6 Months

- 10/12 participants reported symptoms of dry mouth as “better” at the 6 month timepoint
- Each of these 10 participants rated changes in xerostomia scores that were “important” or “very important” (a score of 2 or

more)
- 3 participants rated the change in xerostomia symptoms with the highest improvement scores of 6 or 7 denoting a “very important improvement”
- No participant reported any worsening of xerostomia symptoms

Unilateral Cohorts (n=12) to 12 Months

- 8/12 participants who reached the 12-month assessment 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” (a score of 2 or more)
- 4 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 can be seen persisting through 2 years in all 3 patients who have reached that timepoint
- Participant 1-1 reached the 3-year assessment and the maximum score of 7 was maintained
- No participant reported any worsening of xerostomia symptoms

Combined Unilateral and Bilateral Cohorts

- 18/24, or 75%, of all unilateral and bilateral treated participants reported symptoms of dry mouth as “better” following treatment
- Each of these 18 participants rated changes in xerostomia scores that were “important” or “very important” (a score of 2 or more)
- In the overall cohorts the average improvement in scores was greater in bilateral participants compared to unilateral participants
- Unilateral cohort achieved overall improvement of >3 points at 12 months
- Bilateral cohort achieved overall improvement of >3 points at 2 months and an overall improvement of 4 points by 6 months
- A 2 point improvement in the GRCQ is considered clinically meaningful and an improvement of 3 or more is considered a substantial improvement over standard of care and “transformative” by KOLs
- Overall improvement in scores was maintained and increased over time in both unilateral and bilateral cohorts

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

- 7/12 unilateral participants had improvements in XQ severity score of >8 at 12 months
- 10/12 bilateral participants had improvements in XQ severity score of >8 at 6 months
- Overall, 17/24 participants showed an improvement following treatment of >8 points in the XQ score
- 6/12, or 50%, of unilateral participants at 12 months and 10/12, or 83%, of bilateral participants at 6 months achieved 10 point or greater decline

Average Change from Baseline Unilateral and Bilateral Cohorts

- In unilateral participants an average 13-point improvement from baseline in XQ was seen at 12 months
- In bilateral participants an average 22-point improvement from baseline in XQ was seen at 6 months
- Improvement in XQ severity score was observed rapidly post-treatment
- The degree of improvement in scores was greater in bilateral participants compared to unilateral participants

Whole Saliva Flow:

Bilateral Treated Subjects

- Meaningful increase in whole saliva flow was seen in bilateral treated patients at 6 months
- The average percentage change from baseline was 100% in bilateral patients at 6 months

- The overall flow rate improved to an average of 0.4mL/min which is in the normal range for unstimulated whole saliva production
- Based on both absolute and percent change from baseline in whole resting saliva, the improvement in unstimulated salivary flow in the bilateral treated patients are of clinically meaningful size

Unilateral Treated Subjects

- Whole saliva was collected using gum stimulation, however this was directly following extensive manipulation and citric acid stimulation and collection from individual glands which confounded the stimulated whole saliva data
- Despite this, an increase in the absolute and percentage change from baseline in whole saliva flow was seen in unilateral treated patients following treatment of only one parotid gland

Phase 2 Study Plans:

- Based on the favorable safety and efficacy profile of AAV2-hAQP1 in the AQUAx Phase 1 study, the Company intends to initiate a randomized, double-blind, placebo-controlled, Phase 2 study evaluating the bilateral administration of two active doses of AAV2-hAQP1 in the first half of 2023
- Based upon regulatory interactions, we anticipate the Phase 2 study's primary efficacy endpoints will be the change from baseline to 12 months in salivary flow rate and key secondary endpoints will be the change from baseline to 12 months in the XQ and GRCQ PROs at 12 months

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 50,000 new head and neck cancer patients are treated with radiation[1,2], with an estimated >14,000 developing persistent grade 2/3 RIX[2,3]. Current treatment options for 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, December 13, 2022, 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 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, plans to advance AAV2-hAQP1 into Phase 2 clinical trial and anticipated milestones regarding our clinical data and reporting of such data and the timing of results of data, 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 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. Unless otherwise stated or the context otherwise requires, the information herein is as of December 13, 2022.

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