UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

Current Report Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **December 7, 2021**

MeiraGTx Holdings plc

(Exact name of registrant as specified in its charter)

Cayman Islands	**001-38520**	**98-1448305**
(State or other jurisdiction of incorporation or organization)	(Commission File Number)	(I.R.S. Employer Identification No.)

450 East 29th Street, 14th Floor
New York, NY 10016
(Address of principal executive offices) (Zip code)

(646) 860-7985
(Registrant's telephone number, including area code)

Not applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary Shares, $0.00003881 par value per share	**MGTX**	**The Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On December 7, 2021, MeiraGTx Holdings plc (the "Company") issued a press release announcing positive preliminary data from the Company's AQUAx Phase 1 clinical trial of AAV-hAQP1 for the treatment of grade 2/3 radiation-induced xerostomia. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K ("Form 8-K") and is incorporated herein by reference.

The Company hosted a live webcast on December 7, 2021 at 8:00 a.m. ET to discuss the preliminary data described above. A recording of the webcast can be accessed through the Investors & Media page of the Company's website at *https://investors.meiragtx.com*. A copy of the slide presentation used during the webcast is furnished as Exhibit 99.2 to this Form 8-K and is incorporated herein by reference.

The information in this Item 7.01 of this Current Report on Form 8-K (including Exhibits 99.1 and 99.2) shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that Section, nor shall it be deemed to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing. Additionally, information contained on or accessible through the Company's website is not incorporated into, and does not form a part of, this Form 8-K or any other report or document we file with the U.S. Securities and Exchange Commission, and any references to the Company's website is intended to be inactive textual references only.

Forward Looking Statement

This Form 8-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this Form 8-K 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 AAV-hAQP1, plans to advance AAV-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," "intend," "plan," "believe," "project," "forecast," "estimate," "may," "should," "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 September 30, 2021, 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* and the Investors & Media section of our website at *https://investors.meiragtx.com*. These and other important factors could cause actual results to differ materially from those indicated by the forward-looking statements made in this Form 8-K. Any such forward-looking statements represent management's estimates as of the date of this Form 8-K. 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 Form 8-K.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press release of MeiraGTx Holdings plc, dated December 7, 2021.
99.2	Presentation of MeiraGTx Holdings plc, dated December 7, 2021.
104	Interactive Data File (embedded within the Inline XBRL document).

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: December 7, 2021

MEIRAGTX HOLDINGS PLC

By: /s/ Richard Giroux
Name: Richard Giroux
Title: Chief Financial Officer and Chief Operating Officer

Exhibit 99.1

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

- *Clinically meaningful improvements in xerostomia symptoms and disease burden reported in two validated Patient Reported Outcome (PRO) measures*
- *6 of the 7 participants through 90-day assessments following treatment achieved clinically meaningful improvement in symptoms using both the McMaster Global Rate of Change PRO and the Xerostomia Questionnaire*
- *One participant with the maximum response evaluable at 12 months has now reached 24 months and the same level of response/xerostomia symptom improvement was maintained*
- *AAV-hAQP1 appears safe and well-tolerated at each dose tested*
- *Webcast and conference call to be held today, December 7, 2021 at 8:00 a.m. ET*

LONDON and NEW YORK, Dec. 7, 2021 (GLOBE NEWSWIRE) -- MeiraGTx Holdings plc (Nasdaq: MGTX), a vertically integrated, clinical stage gene therapy company, today announced positive preliminary data from the ongoing Phase 1 AQUAx trial of AAV-hAQP1 for the treatment of grade 2/3 radiation-induced xerostomia (RIX).

"We are very pleased to share this preliminary data from cohorts 1-3 of the AQUAx trial which provides encouraging evidence of the emerging clinical profile of AAV-hAQP1 for the treatment of radiation-induced xerostomia. While the primary endpoint of this Phase 1 trial is safety, we have seen both efficacy and durability in patients treated so far," said Alexandria Forbes, Ph.D., President and Chief Executive Officer of MeiraGTx. "The size of the effects we are seeing at these early stages in the study are clinically meaningful and appear greater than those seen to date with approved drugs for RIX and xerostomia associated with Sjögren's Syndrome. These results point to the potential for AAV-hAQP1 to be a disease-modifying one-time treatment for this large population of patients who currently have no effective treatment options for this devastating and intractable condition."

Study Design and Safety Update in the Phase 1 AQUAx Trial of AAV-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 AAV-hAQP1 to one or both parotid glands in patients with radiation-induced salivary hypofunction and xerostomia. Four unilaterally treated escalating dose cohorts with a minimum of 3 subjects per cohort have completed treatment (n=12) and four bilaterally treated escalating dose cohorts have been added to the protocol to further assess potential efficacy. One bilateral dose cohort has been treated (n=3). Six centers (5 in US, 1 in Canada) are currently open and screening patients. All subjects are to be followed for 1-year post-treatment in the present study and for an additional 4 years in the long-term follow-up study, per FDA guidelines. As of December 6, 2021, the investigational gene therapy AAV-hAQP1 has been well tolerated with no dose limiting toxicity (DLT) and no serious adverse events (SAEs) reported.

Preliminary data is presented from the 7 subjects treated in one parotid gland in cohorts 1, 2 and 3 of the unilateral dose escalation phase of the AQUAx study who have passed the Day 90 assessment.

McMaster Global Rate of Change PRO measure results:

- 6 of the 7 participants who reached the Day 90 assessment reported their symptoms of dry mouth as better following treatment
- All 6 of these participants rated changes in xerostomia scores that were important or very important to the participant (a score of 2 or more)
- 3 participants rated the change in xerostomia symptoms with the highest level of improvement (scores of 6 or 7)
- Improvement in xerostomia symptoms persisted through 1 year in two of the patients who reached Day 360
- Participant 1-1 has just reached the 24-month assessment and the highest possible score of 7 was maintained
- Participant 2-1 reported no improvement and was the only one of the 7 participants who had no saliva production at baseline
- No participant reported a worsening of xerostomia symptoms at any time point

		Dry Mouth Symptoms? Better (+), Worse (X), or Same (=)			How Much Better / Worse?		
Cohort	Participant	Day 90	Day 180	Day 360	Day 90	Day 180	Day 360
1	1-1	+	+	+	5	6	7
	1-2	+	+	+	3	3	6
	1-3	+	+	=	3	3	
2	2-1	=	=				
	2-2	+	+		2	4	
	2-3	+			6		
3	3-1	+			4		

Xerostomia Questionnaire (XQ) PRO measure results:

- 6 of 7 participants reaching the Day 90 assessment reported decreases in disease burden of 10 points or more on the XQ – indicating a clinically meaningful alleviation in disease burden; a change in disease burden score of 6 is considered clinically meaningful
- More dramatic reductions of 19, 25, 26, and 41 points were reported by 4 of 7 participants at Day 90
- In the participants who completed visits at Day 180 and 360, scores continued to improve or were stable at these later timepoints
- One participant reported complete resolution of symptoms at Day 360 following treatment with no symptoms of xerostomia (a score of 0 for all symptom scores), and has maintained the same score of 0 following the 24 month assessment

Phase 2 Study Plans:

- Based on the safety and efficacy profile of AAV2-hAQP1 in the AQUAx Phase 1 study and regulatory precedent, the Company intends to initiate a randomized, double-blind, placebo-controlled Phase 2 study evaluating two active doses of AAV2-hAQP1 in the second half of 2022
- The change from baseline to 12-months in the McMaster Global Rate of Change questionnaire is expected to be the study's primary efficacy endpoint. The change from baseline to 12-months in the Symptom-specific Xerostomia Questionnaire and in whole saliva volume are expected to be secondary and exploratory endpoints, respectively.

Grade 2/3 Radiation-Induced Xerostomia unmet medical need and market size:
There are currently 170,000 patients in the U.S. with grade 2/3 RIX two or more years out from successful radiation treatment for head and neck cancer, and an estimated 5,000 to 10,000 new patients per year in the U.S. 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.

The Company will host a conference call and webcast today at 8:00 a.m. ET.
Details of the webcast are listed below:

Title: MeiraGTx Xerostomia Clinical Program Update
Presenters:

- Alexandria Forbes, Ph.D., President and CEO of MeiraGTx
- Robert K. Zeldin, M.D., Chief Medical Officer of MeiraGTx
- Michael Brennan, DDS, MHS, FDS RCSEd, Chairman of the Department of Oral Medicine and Director of the Sjögren's Syndrome and Salivary Disorders Center, Atrium Health's Carolinas Center for Oral Health

Date: Tuesday, December 7, 2021
Time: 8:00 a.m. ET

- To register and attend the event, please click here
- For those who are unable to listen live, a replay of the call will be available by clicking here

About Grade 2/3 Radiation-Induced Xerostomia
Xerostomia is a chronic and debilitating disorder of the salivary glands in which saliva production is impaired. Xerostomia has a number of causes, including radiation therapy for head and neck cancer and certain autoimmune diseases. In the U.S., there are currently more than 170,000 patients with chronic grade 2/3 radiation-induced xerostomia, with an estimated 5,000 to 10,000 new grade 2/3 radiation-induced xerostomia patients a year in the U.S. In these patients, reduced salivary output results in a lack of lubrication and a loss of the antimicrobial and antifungal properties of saliva with consequent morbidities and significant negative impact on patient quality of life. Current options for the management of xerostomia are few and are of limited benefit so there is a high unmet medical need for a safe and effective treatment.

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 AAV-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, with efficacy endpoints including patient reported measures of xerostomia symptoms.

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[1].

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.

[1] 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

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, as well as a potentially transformative gene regulation technology. 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 diseases, neurodegenerative

diseases and severe forms of xerostomia. Though initially focusing on the eye, central nervous system and salivary gland, MeiraGTx intends to expand its focus in the future 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
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Contacts

Investors:
MeiraGTx
Investors@meiragtx.com

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

Gene Therapy for the Treatment of Radiation-Induced Xerostomia: **AAV-hAQP1 Program Update**

December 7, 2021

Forward Looking Statements

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Agenda

1. Introduction
   Zandy Forbes, PhD
   President & CEO MeiraGTx

2. Radiation-Induced Xerostomia: Disease Background and Unmet Medical Need
   Robert K. Zeldin, MD
   Chief Medical Officer MeiraGTx

3. AQUAx Phase 1 Study: Preliminary Data for AQUAx Cohorts 1 to 3
   Zandy Forbes, PhD
   President & CEO MeiraGTx

4. Treating Physician Perspective: AAV-hAQP1 Treatment and Unmet Medical Need
   Michael Brennan, DDS, MHS, FDS RCSEd
   Professor and Chair, Department of Oral Medicine
   Director of the Sjögren's Syndrome and Salivary Disorders Center
   Atrium Health's Carolinas Medical Center, Charlotte, NC

MEIRAGTx

Salivary Gland Gene Therapy Radiation-Induced Xerostomia

Robert K. Zeldin, MD

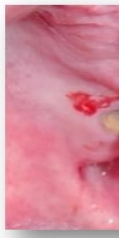
Radiation-Induced Xerostomia (RIX)
A Condition with a High Unmet Medical Need

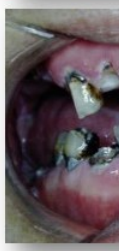
Xerostomia (Dry Mouth)

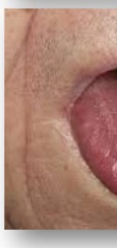
- 85% of radiation-treated patients experience reduced saliva production, 50% of whom have persistent Grade 2/3 RIX[1]
- >170,000 existing patients in the US with Grade 2/3 RIX (Orphan Status)[1,2]
- 54,000 new cases of head and neck cancer per year in the US; 650,000 worldwide[3]
- Progressive, irreversible, significantly impairs quality of life of potentially cured cancer patients

Serious, debilitating complications as a result of reduced saliva

- Difficulty eating, chewing and swallowing/taste alterations
- Severe tooth decay/periodontal disease. Increased risk of tooth loss
- Unable to wear/tolerate dentures
- Sore throat and changes in vocal quality/speech abnormalities
- Harmful changes in oral flora
- Burning mouth sensation in 40% of patients[4]







[1] 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.

[2] Cox J.D., et al. (1995). Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment for Cancer (EORTC). Int. J. Radiation Oncology Biol. Phys. 31(5):1341-1346.

[3] Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018; 68:394.

[4] Rouleau, Tanya S. et al, A retrospective, cohort study of the prevalence and risk factors of oral burning in patients with dry mouth Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:720-725

Current Treatment Options for RIX are Limited

Treatment options for management of Grade 2/3 xerostomia are limited and have no effect on gland functionality. None are disease-modifying.

- ❑ Saliva substitutes
  - Carboxymethyl cellulose and mucin
  - Short term benefit
- ❑ Mechanical and Gustatory stimulation
  - Not all patients tolerate frequent gum chewing
  - May exacerbate temporomandibular disorder symptoms
- ❑ Sialogogues: Pilocarpine (indicated for RIX) and Cevimeline (off-label)
  - Chronic, frequent dosing (x3 daily)
  - Do not improve salivary gland functionality
  - Not well tolerated
    - 20% of patients experience Grade 3 or higher side effects include flushing, upset stomach, sweating
    - Contraindicated in a variety of conditions
- ❑ Acupuncture
  - Some benefits to an extremely small subset of patients

No new treatments have been approved in 20 years – last drug approved was Cevimeline in 2000

Xerostomia Patient-Focused Drug Development Meeting (PFDD)

Xerostomia-focused meeting hosted by a consortium of advocacy and patient care groups with guidance from the US FDA on August 19th, 2021

- The goal of Patient Focused Drug Development meetings is to systematically obtain the patient perspective on specific diseases and their treatments
- The meeting provides a forum for the FDA to hear directly from patients, their families, caregivers, and patient advocates
- Attendees included 16 individuals from the FDA and over 150 patients and caregivers from both the Head & Neck Cancer and Sjogren's Disease advocacy communities
- MeiraGTx was the corporate sponsor for the event

Patient Testimonials

"Along with the fear of cancer recurrence, I fear for my dental health, my nutrition, and most importantly – my sleep. These are important factors for a healthy life."

"Aside from painful swallowing, I've had a couple of incidents of almost choking due to food getting stuck in my throat."

"If there was one symptom of xerostomia that I could eliminate, it would be the dysphagia. I never know when I would start coughing and choking."

"Sometimes the sticky saliva closes the back of my throat, and I can't speak for up to a minute. My throat is just stuck, and I'm not able to get words out."

"Sometimes I feel a sense of panic, because
blocks my airways and I struggle to clear."

"Often my mouth becomes so dry I can't enu
clearly and my lips become stiff and cracke

"Not having normal saliva production has af
in several ways, the most negative being ho
affected my sleep .... I wake up often during t
because of very uncomfortable and at times
parched mouth and throat."

"Weekly checks during my routine visits reve
serious weight loss, not surprising since extr
dryness and sensitivity."

MEIRAGTx

AAV-hAQP1
MGT016 AQUAx Phase 1 Study

MGT016 AQUAx Phase 1 Study Design

Study Design

Open label, multi-center, dose escalation study of a single administration of AAV-hAQP1 to one or both parotid glands in patients with radiation-induced parotid salivary hypofunction and xerostomia

- Four unilateral treated escalating dose cohorts with a minimum of 3 subjects per cohort
- Four bilateral treated escalating dose cohorts have been added to the protocol to further assess potential efficacy
- May treat additional subjects in dose expansion cohorts
- 6 centers (5 in US, 1 in Canada)
- All subjects to be followed for 1-year post-treatment
- Long-term follow-up study will follow patients for a total of 5 years per FDA guidelines

Cohort	Dose
1	1×10^{11} vg/gland (s
2	3×10^{11} vg/gland (s
3	1×10^{12} vg/gland (s
4	3×10^{12} vg/gland (s
1b	3×10^{10} vg/gland (b
2b	1×10^{11} vg/gland (b
3b	3×10^{11} vg/gland (b
4b	1×10^{12} vg/gland (b

Primary Endpoint

- Safety

Secondary Endpoint

- Patient reported measures of xerostomia symptoms

MGT016 AQUAx Phase 1 Study

Study Status

- All centers open for enrollment
- All four unilateral dose cohorts treated (n=12)
- One bilateral dose cohort treated (n=3)
- Completion of enrollment of bilateral cohorts in the coming months

7 participants (3 each from Cohorts 1 & 2 and 1 from Cohort 3) have data available through Day 90 following treatment:

- Treatment well tolerated
- No dose limiting toxicity
- No serious adverse events
- Improvements observed in validated patient reported assessments of xerostomia symptoms

Phase 2 Study: Design & Efficacy Endpoints

Study Design:

- Randomized, double-blind, placebo-controlled study
- Two active doses of AAV2-hAQP1

Primary Endpoint:

- McMaster Global Rate of Change at 12 months after treatment

Secondary Endpoint:

- Symptom-specific Xerostomia Questionnaire

Exploratory:

- Whole saliva volume

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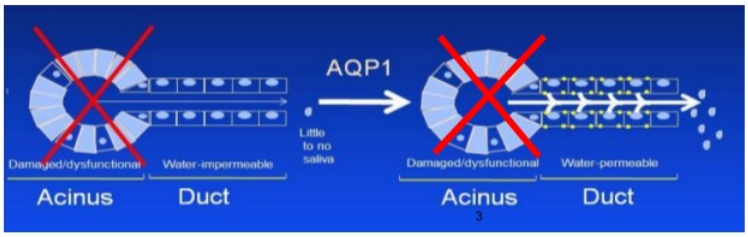
AAV-hAQP1 Clinical Development Program: Preliminary Data for AQUAx Cohorts 1 to 3

Zandy Forbes, PhD

AAV-hAQP1 - Salivary Gland Gene Therapy

Mechanism of Action:

- In normal salivary glands water flows through acinar cells into the duct. Duct cells are impermeable to water.
- Impermeable duct cells generate an osmotic gradient (lumen > interstitium)
- Acinar cells are particularly vulnerable to damage with Ionizing radiation used to treat head and neck cancer. Acinar cells are killed and disrupted following IR treatment which can result in chronic inability to produce saliva.
- Introduction of the gene encoding human aquaporin 1 (hAQP1), a water channel, into the remaining salivary gland duct via viral vector makes the duct cells and surviving acinar cells permeable to water
- Allows water to flow into the salivary duct and out into the oral cavity to moisten the mouth



Viral Vector Configuration:

Capsid - AAV2:

- AAV2 demonstrated to transduce hu salivary gland tissue more effectively known capsids
- Small volume of vector. The target c salivary gland are the single layer of remaining acinar cells around the du

Promoter – CMV promoter:

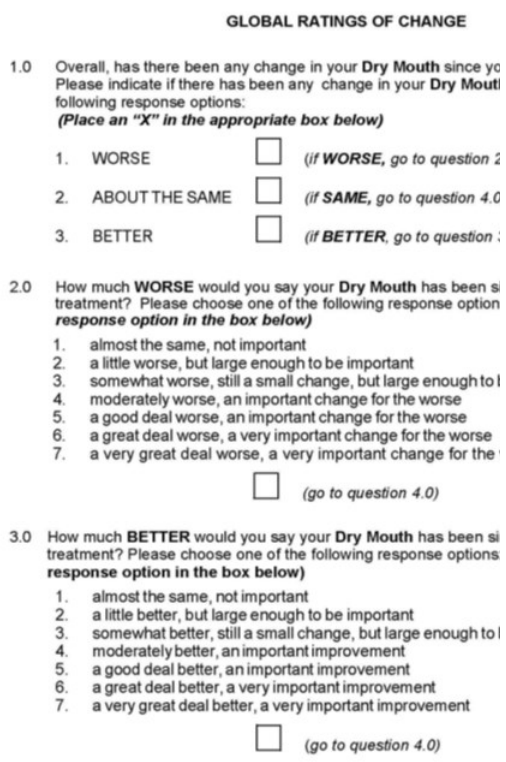
Drives strong, durable expression in sal

Gene – hAQP1:

Human water-specific channel that pr membranes with high permeability to permitting water to move in the directi osmotic gradient

McMaster Global Rate of Change PRO

- 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 patients reply "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 questionnaire is very similar to the "Global Improvement" tool accepted by the FDA to approve Cevimeline
- In the Cevimeline approval, a statistically significant difference in the "Global Improvement" tool (step 1) between the treated and the control arms was considered clinically meaningful



GLOBAL RATINGS OF CHANGE

1.0 Overall, has there been any change in your **Dry Mouth** since yo
Please indicate if there has been any change in your **Dry Mouth**
following response options:
(Place an "X" in the appropriate box below)

1. WORSE ☐ *(if **WORSE**, go to question 2*
2. ABOUT THE SAME ☐ *(if **SAME**, go to question 4.0*
3. BETTER ☐ *(if **BETTER**, go to question*

2.0 How much **WORSE** would you say your **Dry Mouth** has been si
treatment? Please choose one of the following response option
response option in the box below)

1. almost the same, not important
2. a little worse, but large enough to be important
3. somewhat worse, still a small change, but large enough to
4. moderately worse, an important change for the worse
5. a good deal worse, an important change for the worse
6. a great deal worse, a very important change for the worse
7. a very great deal worse, a very important change for the

☐ *(go to question 4.0)*

3.0 How much **BETTER** would you say your **Dry Mouth** has been si
treatment? Please choose one of the following response options
response option in the box below)

1. almost the same, not important
2. a little better, but large enough to be important
3. somewhat better, still a small change, but large enough to
4. moderately better, an important improvement
5. a good deal better, an important improvement
6. a great deal better, a very important improvement
7. a very great deal better, a very important improvement

☐ *(go to question 4.0)*

Assessment: McMaster Global Rate of Change

- 6 of the 7 participants to date reaching 90-day assessments reported their symptoms of dry mouth as better following treatment
- All 6 of these 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 level improvement scores of 6 or 7
- Improvement in xerostomia symptoms can be seen persisting through 1 year in two patients who reached Day 360
- Participant 1-1 has just reached the 24-month assessment and the score of 7 was maintained
- Only one participant, 2-1, reported no improvement and this participant had no saliva production at baseline
- No participant reported any worsening of xerostomia symptoms

		Dry Mouth Symptoms? Better (+), Worse (X), or Same (=)			How Mu
Cohort	Participant	Day 90	Day 180	Day 360	Day 90
1	1-1	+	+	+	5
	1-2	+	+	+	3
	1-3	+	+	=	3
2	2-1	=	=		
	2-2	+	+		2
	2-3	+			6
3	3-1	+			4

Xerostomia Questionnaire (XQ)

- A Patient Reported Outcome 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 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
- In the AQUAx study, 6 of 7 participants reaching the 90-day assessment reported decreases in disease burden of 10 points or more on the XQ at 90 days – indicating a clinically meaningful alleviation in disease burden
- More dramatic reductions of 19, 25, 26, and 41 points were reported by 4 of 7 participants at 90 days
- In the subjects that reached additional timepoints, scores improved or stabilized at later timepoints
- One participant reported complete resolution of symptoms at 12 months following treatment with no symptoms of xerostomia, a complete response

Summary: AQUAx Preliminary Data

Dosing in the unilateral dose escalation and first cohort of bilateral dosing phase comp

Safety

- AAV-hAQP1 treatment appears safe and well tolerated at each dose tested
- No DLT or SAEs

Efficacy

- Improvements in xerostomia symptoms and disease burden reported in two different PRO tools validated for xerostomia
  - McMaster – which has been the basis of approval of other drugs for xerostomia
  - Xerostomia questionnaire – a higher bar than the McMaster
- AAV-hAQP1 treatment response rate and effect size encouraging
- 6 of the 7 participants through 90 days following treatment achieved clinically meaningful improvement in symptoms
- One participant with the maximum response evaluable at 12 months has now reached 24 months and the same level of response/xerostomia symptom improvement is maintained

Phase 2 double-blind randomized two dose study expected to initiate 2H 2022

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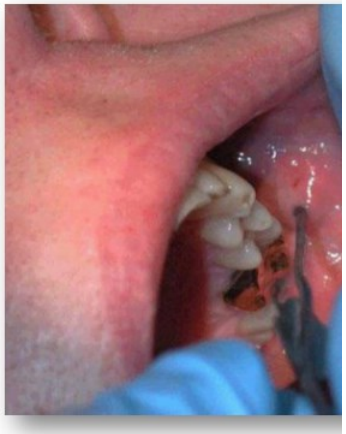
Clinical Perspective

Michael Brennan, DDS, MHS, FDS RCSEd

AAV-hAQP1 as an Office-Based Treatment

- Quick outpatient procedure
- Non-invasive: allows local administration and avoids systemic exposure
- Parotid gland is isolated and encapsulated, somewhat immune protected
- Small volume of vector required



Qualifying a patient for treatment with AAV-hAQP1 utilizes routine practices in oral medicine:

- Oral exam
- Sialometry (assessment of salivary flow rate)
- Patient-reported measures of oral dryness

Administration of AAV-hAQP1:

- Non-invasive procedure
- Easy to perform
- Well tolerated by patients

AAV-hAQP1 provides the potential for durable recovery of salivary function in patient with intractable radiation induced xerostomia in contrast to other treatments which a minimally effective

SUMMARY

- Serious debilitating condition with severe impact on health and daily living
- Intractable disease with no treatment options
- Large unmet need with >170,000 grade 2 and grade 3 xerostomia patients in the U.S. and 5,000- patients annually
- Patients are already in healthcare system under the regular care of physician
- No competitive clinical programs to our knowledge
- Small local dose, easy & non-invasive delivery
- Appears safe and well tolerated at all doses tested
- Preliminary signals of activity in two validated patient reported outcome assessments of xeros symptoms
- Endpoints that have previously supported FDA approval
- Response rate and effect size appear clinically meaningful and compare favorably with drugs the treatment of xerostomia
- Double blind, placebo-controlled multi-dose study expected to initiate 2H 2022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Audience Q&A