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PRESENTATION

Operator

Good morning, and welcome to the MeiraGTx Xerostomia Clinical Program Update. (Operator Instructions) As a reminder, today's call will be recorded.

I would now like to introduce your first speaker this morning, Alexandria Forbes, Chief Executive Officer and President. Please go ahead.

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

Thank you for joining us today as we give an update on our program to treat radiation-induced, xerostomia. I'm Zandy Forbes, the President and CEO of Meira. I'm joined by Dr. Michael Brennan, Professor and Chair of the Department of Oral Medicine and Director of the Sjögren's Syndrome and Salivary Disorders at Atrium Health Carolinas Medical Center in Charlotte, North Carolina; and by Dr. Robert Zeldin, our Chief Medical Officer.

Before we begin, please note that we will be making forward-looking statements as part of this presentation, which statements are subject to certain risks and uncertainties that may cause actual results, performance or achievements to materially differ from those forecasted. Certain of these risks are described on Slide 2 of today's presentation and in our most recent filings with the SEC.

Radiation-induced xerostomia is a serious condition resulting from the reduction in saliva production that occurs when salivary glands are damaged by ionizing radiation. Salivary glands, particularly the acinar cells are exquisitely sensitive to ionizing radiation, and almost all patients, treated with radiation head and neck cancer suffer from xerostomia during and immediately after treatment.

In the 1 to 2 years following radiation treatment, saliva production returns to an adequate level in about 60% of patients. However, in approximately 40% of patients, the salivary glands suffer permanent damage and do not recover, leaving these patients with persistent, significantly impaired salivary function and grade 2 or 3 xerostomia.

We currently plan to treat patients at least 2 years after they had undergone radiation therapy for head and neck cancer and have no evidence of recurrent disease. There are now over 170,000 of these patients in the U.S. alone. We've received orphan drug designation from the FDA for this indication in the U.S., but it is a relatively large population for a gene therapy treatment.

In addition, with around 58,000 new cases of head and neck cancer annually in the U.S., we estimate between 5,000 to 10,000 new U.S. patients eligible for treatment each year, all of whom are in the health care system with some form of health care coverage, having previously been treated for head and neck cancer. These patients are seen as follow-up by their physicians at least annually, and their #1 complaint is xerostomia.

As a result, we have a lot of interest in our potential treatment for xerostomia from those head and neck specialists whose patients have been treated for their cancer but are left with the debilitating symptoms of chronic xerostomia. This is an easily accessible population with a serious condition where the few treatments available provide limited benefit.

As Dr. Brennan will detail, Grade 2 or 3 xerostomia is an extremely debilitating condition with a number of severe sequelae. Reduced saliva production 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.

Our approach at Meira is to use AAV to deliver the nonpolarized water channel, aquaporin 1, into the salary gland. When aquaporin 1 is expressed in the duct and acinar cells of the gland, these cells become permeable to water and water flows down the concentration gradient into the duct and into the mouth.

Our gene therapy, AAV-AAV-hAQP1 is delivered directly into the salivary glands via the opening of the salivary duct into the mouth. A relatively easy noninvasive procedure delivers a small dose of the viral vector. While our current clinical program uses AAV-hAQP1 to treat radiation-induced xerostomia, we may use the same viral vector going forward to treat Sjogren's syndrome and potentially, dry eye.

We currently have 2 ongoing Phase I dose escalation studies. One is a single site study at the NIH, with whom we are partnered by [ACRADA]. The second is a multicenter Phase I study conducted by Meira, the AQUAx study. The NIH study is ongoing and has completed dosing of cohort 4 at a dose of 1 x 10 to 11 vector genomes per gland.

Treatment has been well-tolerated and appears to be safe with no dose-limiting safety events or drug-related serious adverse events reported. The 1x 10 to 11 dose, the highest reach in the NIH study at the time, was selected as the lowest dose in our AQUAx study.

The AQUAx study is an open-label, multicenter dose escalation study of a single administration of AAV-hAQP1 to one parotid gland in patients with radiation-induced parotid salivary hypofunction and xerostomia. The target enrollment is up to 30 subjects.

There are 4 dose cohorts with a minimum of 3 subjects per cohort, with the potential to treat up to nine subjects in dose expansion cohorts. The study is being conducted at five centers, four in the U.S. and one in Canada, and all subjects will be followed for one year post treatment. The study's primary endpoint is safety. Secondary endpoints include change from baseline in patient-reported measures of xerostomia symptoms and an unstimulated and stimulated salivary volume.

The AQUAx study was initiated late last year and all subjects in cohort 1 were enrolled and treated by February this year. With the COVID pandemic, no additional subjects were treated from March through November. We've now reopened 2 centers for enrollment with all 5 centers to be opened by 1Q 2021. The first patient in cohort 2 has been enrolled and sites are actively recruiting.

For the 3 subjects treated in cohort 1, follow-up visits have proceeded at site. One subject has reached the 12-month assessment and two have passed the 6-month assessment. Treatment has been well-tolerated, and no dose-limiting events or serious adverse events have been seen.

We are very pleased to report that improvements have been observed in both patient-reported assessments as well as measures of salivary volume output in the subjects treated in cohort 1, with complete resolution of symptoms in the subject who has reached the 12-month time point.

It is now my pleasure to introduce Dr. Mike Brennan, the investigator at Atrium Health's Carolinas Medical Center participating in the study. Dr. Brennan is an expert in the field of xerostomia and Sjögren's syndrome, and will give us an introduction to the clinical aspects of radiation-induced xerostomia, a feel for the patient experience and provide an overview of the 3 subjects treated in the first cohort of the AQUAx study. Dr. Brennan?

Michael T. Brennan

Good morning. My name is Mike Brennan from Atrium Health Carolinas Medical Center in Charlotte, North Carolina, and I'm one of the investigators for the MeiraGTx AQUAx trial. Today, I'm going to speak about some of the clinical perspectives in relation to xerostomia and salivary hypofunction.

First, let me talk a little bit about salivary glands and the production of saliva. As you can see in this figure, there are 3 major salivary glands: the parotids,the submandibular glands and the sublingual glands. A normal healthy adult will produce about 1.5 liters of saliva in 24-hour period with the parotids responsible for about 45% of the overall saliva produced, the submandibular glands another 45%, the sublingual glands about 5% and the approximately 600 to 700 minor salivary glands throughout the mouth producing the other 5%.

When we talk about patients with head and neck cancer who have undergone radiation therapy, xerostomia is one of the most common complications of treatment. It can be progressive, irreversible symptom and can significantly impair quality of life. Importantly, in contrast to the prototypical elderly male patient with head and neck cancer, patients with human papillomavirus-related head and neck cancer are often diagnosed in their 40s and 50s.

These patients who have been treated with radiation therapy and are potentially cured of their cancer will have the side effects of salivary hypofunction and xerostomia during the most productive years of their lives. So the public health impact is quite significant. Patients with radiation-induced xerostomia have a change in both quantity and quality of the saliva. They produce less saliva overall and often report a thicker ropier type of saliva.

These patients have dryness of the mouth that can make it difficult to eat, chew and swallow. They can also experience sore throat and changes in the quality of their voice due to decreased lubrication in the mouth. Patients may also experience burning, especially on the sides of the tongue and the insides of the lips. Because of the poor lubrication, there is mucosa friction that causes burning in areas that are in constant contact with teeth. We know that 40% of patients with dry mouth have a concurrent symptom of burning.

Because of reduced lubrication, a patient may not be able to wear or tolerate dentures, and these patients problems with speech or eating develop and are associated with decreased quality of life. Also, with less lubrication, the mouth is not cleansed as well. Plaque can build up on the teeth, and saliva as important antimicrobial and antifungal properties, so reduced salivary output can lead to dental carries, tooth loss and fungal infections in the mouth.

Saliva also has important impact on digestion as well as taste. Food may taste differently with patients often stating that everything has a metallic or salty taste.

The patient pictured on the slide returned within 1 year after radiation therapy for head and neck cancer, having experienced severe dental decay from a lack of saliva, which removes the plaque from her teeth. The long-term consequences can be debilitating for these patients and can cause significant morbidity. A key goal of therapy is to try to prevent this from happening.

Current options for the management of xerostomia are few and are of limited benefit. Patients will often try either chewing gum or sucking on lozenges to stimulate the production of saliva. Unfortunately, in this patient population, frequent gum chewing is not well-tolerated and patients experience temporomandibular joint dysfunction, which includes pain in the jaw joint, and in the muscles that control the jaw as well as headaches and clicking or locking of the jaw joint.

Also, these products only have benefit when they are actively being used, so patients will have to be using something in their mouth every hour to derive any benefit. Another option is the class of prescription medications known as parasympathomimetics. These medications stimulate the parasympathetic system, which will increase salivary flow.

Cevimeline and pilocarpine are the two medications approved for dry mouth. There are a lot of side effects with these medications, so not all patients can tolerate them. Flushing, upset stomach and sweating are examples of the more frequent side effects that limit the use of these medications.

Additionally, these medications don't work well if the patient doesn't have sufficient residual salivary function. So if the glands aren't working well enough, these types of prescription medications won't work well.

Another option is the use of saliva substitutes, but this, too, is of short-term benefit. Most patients don't like this approach and describe it as if someone else spit in their mouth. It's an uncomfortable feeling and not well-tolerated by patients, but it is an option for some to give short-term benefit.

In summary, none of these over-the-counter approaches or prescription medications really address the need of patients who lack adequate salivary function.

This is where the role of Aquaporin and AAV-hAQP1 really comes into consideration for the treatment of patients with the radiation-induced xerostomia. We, at Atrium Health, have treated the first cohort of patients in the AQUAx study, and we continue to enroll patients in the study So we've had a chance to gain some experience with administration of this therapy and its benefits.

First, the procedure of injecting the vector is very noninvasive. It includes the intraoral insertion of a very small catheter into the main duct of the parotid gland, and then injection of the vector through the catheter into the gland. Patients have tolerated the procedure very well. And thus far, there have been no serious adverse events reported.

Most importantly, the patients we have treated have responded very well to therapy. I'm really happy to say the first patient we treated had significant subjective and objective improvements. At the 12-month study, he reported he doesn't have any complaints of dry mouth and has had a significant improvement in his quality of life.

When we reviewed the questionnaires he completed, he scored 0 for xerostomia symptoms. And he had no dry mouth, no mouth pain or oral burning and improved sleep.

Another of our patients has reported that a lot of their throat symptoms have improved, but they're not quite 12 months out. So we look forward to seeing them back at 12 months to see if they have made further progress. We have also recorded improvements in salivary flow rate, which have been impressive, which is why we look forward to being able to continue to enroll in the study and provide this unique treatment to our patients.

Thank you for the opportunity to share our experience with you. I will now pass the call to MeiraGTx Chief Medical Officer, Dr. Robert Zeldin.

Robert K. Zeldin - *MeiraGTx Holdings plc - Chief Medical Officer*

Thank you, Dr. Brennan. As Dr. Brennan reported, we have encouraging results from the first treatment cohort in our Phase I study of AAV-hAQP1 in subjects with radiation-induced parotid gland hypofunction and xerostomia. The first patient treated has had an outstanding response.

He had persistent symptoms of xerostomia for 6 years after undergoing surgical resection and radiation therapy for a head and neck cancer. 12 months after treatment, he reported complete resolution of his xerostomia symptoms. Objectively, he has had a pronounced increase in salivary output.

And as Dr. Brennan has shared with us, at the 12-month visit, his tongue and oral mucosa looked normal. The other 2 subjects have completed their 6-month follow-up visits. Already, they have reported a reduction in xerostomia symptoms, and we have seen a trend in improvement in salivary output.

Combined with the favorable safety and tolerability profile, these data from subjects treated with the lowest dose to be evaluated in our Phase I study give us the confidence to initiate plans for a Phase II efficacy and safety study. We envision this as a double-blind sham-controlled study in which subjects will be randomized to receive 1 of 2 active doses of AAV-hAQP1 or will undergo administration of placebo.

The sample size and doses to be included in the Phase II study will depend on the results from subsequent cohorts in the Phase I study. Likewise, Phase II study timing will depend on Phase I study completion. We anticipate the primary efficacy endpoint will be the change from baseline to 12 months in a patient-reported measure of xerostomia symptoms. We expect change from baseline and salivary output will be a key secondary efficacy measure.

To be enrolled in the study, we expect subjects will have to be at least 18 years of age, have a history of radiation therapy for head and neck cancer, have grade 2 or grade 3 xerostomia, which is defined by symptoms as well as an objective measurement of reduced salivary output, have an accessible Stensen's duct on screening parotid gland volume assessment and have no evidence of recurrence of the primary malignancy on otolaryngology assessment.

We anticipate that subjects will be excluded from the study, if they have a history of salivary gland malignancy or they have a history of a systemic autoimmune disease affecting the salivary glands. Ultimately, the inclusion and exclusion criteria for the Phase II study will be chosen based on the totality of the results of the Phase I study.

Through our continued engagement with head and neck cancer patient advocacy groups, we'll be incorporating the patient perspective into our clinical development plan to ensure the focus is on clinically meaningful outcomes.

With such a large population of affected patients and the high unmet medical need they face, we will look to the patient voice to help guide study-related decisions. Now I'd like to hand it back to Zandy as we open up the meeting to questions.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Our first question comes from the line of Bola Amusa with Chardan.

Gbolahan Amusa - *Chardan Capital Markets, LLC, Research Division - Director of Research & Head of Healthcare Research*

It's Bola at Chardan. Congrats on complete symptom resolution at 12 months for that first patient. My first question has to do with conclusions around, let's say, dose responsiveness and efficacy, getting to the point where you want. I think in the prior Phase I with the 85 vector, there was dose responsiveness around enhanced parotid flow and improved subjective responses.

So my question is regarding the Phase II active doses you're going to choose. Can you discuss the balance of these 2 in getting the dose right? And I'm also interested in the classic therapeutic question, is there such thing as too much dose, i.e., will patients have too much saliva if you give them too much vector?

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

Thank you, Bola, for your question, and I'll actually answer the first one -- the second one first. So aquaporin 1 is a nonpolarized and polarized water channel. So it actually opens the cell for the passage of water down a concentration gradient into the salary gland.

So you can't actually overproduce saliva outside of the salts and proteins that are in the gland. So it's not really possible to have excessive saliva flow.

And with respect to dose response, theoretically, when we look in-vitro, we see quite a narrow range of dose response because there isn't such a great difference between making cells permeable with a small number of aquaporin 1 molecules compared to a larger number. This is literally making cells permeable on both sides of the membrane.

So when we're looking at dose response in these 2 initial studies, one of the things we're focusing on is safety. And so far, we haven't seen any safety issues and certainly no dose responsive safety issues. So our intention is to continue up to a dose that -- in this current study, the AQUAx study, we're doing an additional 3 cohorts.

And we will obviously continue to monitor safety, but review carefully any differences in efficacy that we're seeing in those cohorts, and the totality of that data will inform the doses that we take into the efficacy study.

Gbolahan Amusa - *Chardan Capital Markets, LLC, Research Division - Director of Research & Head of Healthcare Research*

Got it. And then just one quick one, and I'll get back in the queue. I know I think in the past, Meira discussed manufacturing capacity, either what's online or what soon will be. And I think there's been something like 10 million, 12 million or even more million doses you can produce for IRDs, and that's obviously more than needed there. Would you confirm existing or soon-to-arrive capacity can also cover risks as well?

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

Absolutely. So to note, this is another indication where it's a small local dose. So the doses that we're giving in these current ongoing studies are in the range of 1 x 10 to 11 up to 1 x 10 to 12 per gland. So that's very low. It's like an eye dose.

And we have a manufacturing process as well as capacity to supply our clinical programs but to significantly supply a very large market here. So it's the same sort of dose as eye. So when we say we can make many million eye doses, this is in the same ballpark, given we haven't fixed on an absolute dose.

Operator

Our next question comes from the line of Tyler Van Buren with Piper Sandler.

Tyler Martin Van Buren - *Piper Sandler & Co., Research Division - Principal & and Senior Biotech Analyst*

It's encouraging to see the early responses. I guess first question is on the efficacy endpoints for the Phase II study, the patient-reported measure of xerostomia symptoms and salivary output. Can you just elaborate a little bit more on precisely how those will be measured?

And I guess, did you take these measurements in the ongoing study? And is there anything you could say quantitatively about patient 1, 2 and 3 at baseline, and 6 months for patients 2 and 3 and at 12 months for patient 1?

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

Okay. Very detailed questions. So one of the things that we're hoping to learn from the dose escalation study is exactly which aspects of a wide range of PROs and a large number of questions that we're asking are the most appropriate to show the benefit that's occurring in these patients. So we haven't determined what those questions will be. That will depend on the data that we see coming out of this study.

However, patient-reported outcomes is a measure that the agency has used in the past to approve xerostomia indication -- drugs for xerostomia indications. So we feel confident that PRO-based endpoint will be one that we will use in the Phase II, and we're very pleased to see that the first in one patient, we're getting complete resolution.

So scoring zeros on the endpoints that have been assessed in this study as well as seeing particular questions across the population that may be coming up target for questions in an efficacy-based study.

I can pass you over to Robert for a bit more detail on what the PROs that have been used in this study are. Robert, do you want to go ahead and discuss the currently used PROs?

Robert K. Zeldin - *MeiraGTx Holdings plc - Chief Medical Officer*

Sure. Happy to do so. Thanks for the question, Tyler. We've incorporated a number of PROs in the ongoing study. One is a xerostomia-specific questionnaire, known as the XQ. That's an 8-item questionnaire, where each question is answered on the 0 to 10 scale.

Then we've also gone with the MD Anderson symptom inventory, the head and neck module, so the one that's specific for patients with head and neck cancer. A number of questions on that 28-item scale -- excuse me, on the 28-item questionnaire seem to be particularly relevant to our patient population. So we've included all 28 items, as Zandy has said, to explore in a Phase I, what might be the most appropriate to advance going forward.

And then finally, we've included the McMaster Global Rating Change question there, which is a 6-item questionnaire, and that one has been used the approval of one of the parasympathomimetics that was referred to by Dr. Brennan. So as Zandy said, we think that there is -- that ground has already been broken by a predecessor.

And so we have a path clearly to propose to FDA the use of such an approach also for this agent. In that case, the product was evaluated for treatment of Sjögren's syndrome. So hasn't yet been evaluated specifically for radiation-induced xerostomia, but we think could be quite applicable.

Tyler Martin Van Buren - *Piper Sandler & Co., Research Division - Principal & and Senior Biotech Analyst*

Okay. That's helpful. And then the second question is just on kinetics response. Can you just speak about the time course of response for patient 1? Did they improve over the course of that 12 months? Or did it -- were they scoring zeros early on as we try to think about how patients 2 and 3 might improve from 6 to 12 months?

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

So what I can say is that patient -- because -- patients when we start seeing effects is around the 3-month time point. I think to say that we're seeing an improvement, yes, there has been an improvement from that time point on, but we're not giving individual scores on this call. And we will be releasing that data in totality at a medical meeting. But yes, we do start seeing indications of efficacy early, and we have seen improvements over time.

Operator

Our next question comes from the line of Josh Schimmer with Evercore ISI.

Joshua Elliott Schimmer - *Evercore ISI Institutional Equities, Research Division - Senior MD & Equity Analyst*

I have think about 3 questions. First, to the last response, why would there be a delayed benefit over time given the mechanism? What might improve beyond 3 months from a physiologic basis? Two, maybe you can discuss a little bit more the natural history and maybe some of the concomitant interventions in these patients to provide a little bit more context for the patient who had a complete resolution? And how an expected that kind of an outcome would be for that type of patients?

And then Dr. Brennan, if you can provide commentary on the NIH study results? Or if you are familiar with that program or for the rest of the team. If not, when might we see some of the NIH data emerge?

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

Okay. Thanks for your question, Josh. Unfortunately, Dr. Brennan has literally just walked out to see a patient. So we -- I'll take the questions and then we can have arrange for him to potentially answer those questions afterwards. So sorry about that, Josh.

So with respect to the NIH study, Dr. Brennan is not involved in that study. And what I can say about that study that has reached this cohort and treated 2 patients in the cohort above, the NIH has said that it is safe that -- well, there's no safety issues, and they have reported that they're seeing improvements in both patient-reported outcomes as well as actual salivary volumes.

So consistent with what we've seen in this first cohort. With respect to the initial patient, that patient, as Robert mentioned, had been suffering from xerostomia for 6 years. And having heard from him and Dr. Brennan, his quality of life has completely changed.

And I think Dr. Brennan was very impressed to see the changes in mucosa, the changes in his mouth and his normalization to a person, who not only reported no symptoms on those PROs Robert went through, but also the mucosa from a physician point of view was significantly improved. So I apologize that Dr. Brennan stepped out.

Joshua Elliott Schimmer - *Evercore ISI Institutional Equities, Research Division - Senior MD & Equity Analyst*

That's helpful. And then for any biologic rationale for (inaudible)?

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

Yes. So salivary glands are interesting in that when you improve flow, you improve function, and that feeds on itself. So we've seen in animal models that if you improve Sjögren's, you can actually improve the kind of the structure and the function of glands.

So there is a reason to believe that you can see a benefit in that can improve over time. I mean we haven't said how great that line of improvement is or how big a benefit you see initially? But that doesn't mean you don't see these strong benefits very early on, but we very much want to show that you don't just have an improvement initially and then it doesn't maintain. So I think you can take away from this that benefits occur at 3 months in multiple measures, and they do improve over time in this first cohort.

Operator

Our next question comes from the line of Gena Wang with Barclays.

Huidong Wang - *Barclays Bank PLC, Research Division - Research Analyst*

I also have a few questions regarding the efficacy endpoints. Maybe first, regarding the patient reported outcome. So you mentioned that there are 3 questionnaires with 8 items, 28 and 6 items. So based on your scoring system, how much improvement did the first patient achieve? And I don't know if -- how much you can share.

And also from the clinical trial perspective, how much score improvement you think would be your goal or would be clinically meaningful? And then regarding this salivary output, can you walk us through exactly how you measure this?

And would that be certain time point? And then also, how do you measure -- is that measured by the volume of the salivary output? If you can walk through that.

And then one quick question also regarding the treatment procedure. If you can walk us the treatment procedure and then how long that procedure took?

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

Sure. So with respect to the PROs and patient 1, patients come in with a range of baselines, and this particular patient had been suffering from Grade 2, 3 xerostomia for 6 years. And what we saw was for each of those PROs, the 12-month time point, they had 0 on all of the questions.

So they went from the xerostomia score at entry Grade 2, 3 to 0 on each of the questions in the PROs. That's why we say it was complete resolution because they no longer reported any number for any of those questions.

Sorry. Gena question 2, I can't remember what question 2 was.

Huidong Wang - *Barclays Bank PLC, Research Division - Research Analyst*

The salivary output?

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

So salivary output is measured in multiple ways. And the standard salivary output measure, which is one of the ways we're measuring in this study is to do total saliva. And people spit into a little cup over a period of time, maybe 5 minutes, and you actually weigh and measure the volume of saliva that the mouth produces.

In this particular study, in addition to total saliva, we're looking at saliva from individual glands. And so a little cup, it's put over the end of the duct going into the mouth. And again, over a certain period of time, the actual volume of saliva coming out of the gland is collected, weighed and measured, and it's displayed as well as volume at a rate per minute.

Huidong Wang - *Barclays Bank PLC, Research Division - Research Analyst*

Okay. And how was the first patient -- how did the first patient do with the salivary output measurement? A little bit more quantity?

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

They had a significant improvement in the saliva production. A very clear and obvious improvement in volume that was associated with the resolution of symptoms.

Huidong Wang - *Barclays Bank PLC, Research Division - Research Analyst*

Okay. And last question regarding the treatment procedure, if you can just refresh our memory.

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

So this is fairly noninvasive, and a catheter is placed into the opening of the Stensen's duct and the viral vector, which is suspended in a buffer, which is the volume, the salivary gland can contain, that's been predetermined on a previous visit, is injected through the opening of the duct into the duct arbor -- the remaining arbor. So it's a very quick inpatient procedure, not painful and can be conducted by a dentist or an oral surgeon as it may be. But this is fairly noninvasive.

Huidong Wang - *Barclays Bank PLC, Research Division - Research Analyst*

Sorry, did you mean outpatient or inpatient procedure?

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

It's outpatient. They go into a dental -- no it's an outpatient procedure. Yes. They sit in the dental chair.

Huidong Wang - *Barclays Bank PLC, Research Division - Research Analyst*

Okay. Okay, perfect.

Robert K. Zeldin - *MeiraGTx Holdings plc - Chief Medical Officer*

Yes. This doesn't require any sort of anesthesia or anything. This is -- the duct is actually pretty easy to visualize for the health care professional. Here, he would simply insert this small catheter into the duct and then insert this very small volume of vector into the duct.

Operator

Our next question comes from the line of Luca Issi with RBC Capital.

Luca Issi - *RBC Capital Markets, Research Division - Research Analyst*

Congrats on the data. Obviously early days, but how should we think about durability beyond 12 months? What is the turnover rate of the salivary gland? And is there potential here for redosing?

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

Okay. So salivary glands actually don't turn over very rapidly at all. So both duct and the acinar cells are non-dividing. That's one of the reasons that when you destroy salivary gland cells with radiation, they don't recover. So they don't turn over, which does make them a good target for a gene therapy and for durability of that gene therapy.

We have -- a study has been done with adeno, which is obviously immunogenic viral vector, which is -- which tends to be short-lived. However, in that study that was done at the NIH, they did look 5 years post treatment, and they were able to see: a, a maintenance in response, but they also saw -- I think it was at the 1-year and out time point they did see maintenance, even with adeno of both RNA and protein in some of those patients that agreed to biopsy.

So we have no reason to believe that this wouldn't be a durable gene therapy in those nondividing cells and there's some evidence even with adeno that, that durability has foundation. Does that answer?

Luca Issi - *RBC Capital Markets, Research Division - Research Analyst*

Yes. Super helpful. Maybe just a quick follow-up here. Just trying to figure out whether you're excluding patients or neutralizing antibody in baseline? And maybe if you can give us some directional color on what percentage of the 170,000 patients in the U.S. you think are going to be eligible for this therapy?

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

Okay. Number one, on antibodies, neutralizing antibodies. This viral vector uses AAV 2 because that is one of the stickiest of the capsids and we want it only to go into the cells adjacent to the ducts and the duct itself. So one cell and doesn't tend to go into the serum.

So obviously we are looking at neutralizing antibodies in the treated patients. And we've actually -- in the NIH study, they have seen in a number of cohorts, not -- no neutralizing antibody production. And why I say that as well is the salivary gland is somewhat immune protected. And so you don't necessarily expect antibodies in the serum even if they were to be neutralizing to get into the salivary duct.

The salivary duct does not have IgG antibodies, and most neutralizing antibodies to AAV are IgG. So this isn't really an issue here in this particular treatment. So we don't screen out patients for neutralizing antibodies to AAV 2, although we are collecting samples so that we can take a look to see if there's any impact.

Luca Issi - *RBC Capital Markets, Research Division - Research Analyst*

Super helpful. And then what percentage of the 170,000 patients in the U.S. you expect to be eligible potentially for this therapy?

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

So that 170,000 patient number comes from our orphan status discussions with the regulatory agencies with the FDA, .and that 170,000 is the number of patients who are 2 or more years post-recovery from cancer and have Grade 2, 3 xerostomia.

So that is the appropriate population. And those are the patients that are within the health care system are seeing their physicians and are coming to their physicians annually. All of that was in the discussions with the agency to come to a number for orphan status, and that's what that 170,000 number is, and it's actually in the orphan document.

Operator

Our next question comes from the line of David Hoang with SMBC.

David Timothy Hoang - *SMBC Nikko Securities America, Inc., Research Division - Research Analyst*

I just had a couple. So the first one is, can you just give any color or details in how closely the symptom improvement correlates with the volume improvement in saliva and the salivary flow? Is it a case where you take a little bit of volume improvement can go a long way, in terms of alleviating symptoms?

And then in terms of my other question, if patients do have a recurrence of their cancer or do need to be treated again with radiation therapy, how do you think that might affect -- how you think that might affect their ducts if they already got the gene therapy? And then is it possible to maybe treat those patients again with the therapy?

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

Sure. So symptoms of volume and flow. So salivary flow and symptoms is quite a complicated dynamic. And just to start answering your question, xerostomia has a definition, which includes a halving of salivary volume as well as a set level. I think it's less than 200 microliters at non-stimulated level.

So there's both a volume, absolute volume component to the definition of xerostomia, but there can be as well, just a halving of the baseline level because different people have very different baseline levels. And so while there may not be a linear correlation between the absolute volume of saliva, so you double saliva or you improve saliva 10%.

So you have a 10% improvement in symptoms, there is a clear requirement for an improvement in volume to associate with a significant improvement in symptoms. That volume may vary between different subjects.

And if you look at the publication of the previous study, you can see that some patients who started with an extremely low amount of saliva, they may have doubled the 50 microliters to 100 microliters. And that doubling caused an improvement in their patient-reported outcomes.

You had another patient who started at a higher level and improved by several hundred microliters and saw a similar improvement in symptoms. So while there's no absolute linear relationship between symptoms and saliva, there is a relationship between change in volume and improvement in symptoms. Does that answer your question?

David Timothy Hoang - *SMBC Nikko Securities America, Inc., Research Division - Research Analyst*

Yes. That was great. That was really helpful.

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

With respect to recurrence of cancer. We require our patients to be free of cancer for 2 years. If someone was then treated and subsequently got a recurrence of head and neck cancer, we would -- obviously they would have to be required to be cancer-free for the next 2 years and then be eligible for treatment.

Operator

Our next question comes from the line of Alec Stranahan with Bank of America.

Alec Warren Stranahan - *BofA Merrill Lynch, Research Division - Associate*

I'd also like to offer my congrats on the early results as well. My first question was actually for Dr. Brennan, but maybe Zandy, you can speak to this as well. So just following up on the question of administration procedure.

How accessible is the injection site in most patients, given this is an inclusion criteria in the Phase II? And would you say that the procedure will be easy to implement more broadly, say, outside the setting of a clinical trial? And then I have a follow-up.

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

Sure. I think I'll pass that to Robert to answer questions about administration. Robert?

Robert K. Zeldin - *MeiraGTx Holdings plc - Chief Medical Officer*

Yes. Frankly, the duct -- I wish we had an image and in future presentations, we'll certainly plan to show it to you. It's actually readily accessible and very, very easy to administer this agent. So when Zandy speaks to the population of subjects who are experiencing these symptoms and being seen by their docs and regular follow-up, there's every reason to believe that these folks could be readily treated with this agent with minimal effort.

And the feedback regarding safety and tolerability in our experience to-date has been quite positive as we've shared no treatment-related adverse events, no dose-limiting toxicities. So pretty straightforward, easily administered and well-tolerated.

Alec Warren Stranahan - *BofA Merrill Lynch, Research Division - Associate*

Okay. Great. And then on the discrete differences between your study and the one run by the NIH. Can you give a bit more color on the that have been made in the AQUAx study in terms of choice of vector or any other lessons learned from the NIH study? And should the NIH study still be used as a point of reference moving forward once it ultimately reads out?

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

Okay. So the NIH study is a very similar study. It is the identical vector. We have an IND, which we took over from the NIH so both studies are under the same IND, using the exact same vector. The NIH study is a single site study under ACRADA agreement.

So it's only to be run at the NIH. And it has similar but not identical inclusion criteria and similar but not identical assessment. So in order to be able to more rapidly enroll patients into a multicenter study, we did open AQUAx to be able to get to additional sites. But the NIH study is the same vector in, essentially, the same population of patients that we've been discussing.

Operator

We do have a follow-up question from the line of Bola Amusa with Chardan.

Gbolahan Amusa - *Chardan Capital Markets, LLC, Research Division - Director of Research & Head of Healthcare Research*

It was actually for Dr. Brennan, but since he walks out to see a patient maybe Zandy or Robert. What I'm getting at, and I heard analysts asking questions about the model. But isn't there some read across here to Sjögren's to the extent these early data end up being let's say, robust and promising, if they evolve that way? Could you talk about the mechanistic overlap, why it may make sense to start to think about Sjögren's or not?

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

Thank you, Bola. So yes, you're absolutely right. The same viral vector, the aquaporin vector, delivered salivary gland in the same way, can be used for Sjögren's syndrome. And we -- and preclinical data indicates that the salivary cells, if you remove the salivary glands from Sjögren's and treat with this viral vector, you improve the water conductivity in those patients.

In animal models, exact same vector has shown to be effective in animal models of Sjögren's. So we can use the safety information from the 2 active at the NIH and AQUAx support the use of this exact same viral vector in additional indications (inaudible).

Gbolahan Amusa - *Chardan Capital Markets, LLC, Research Division - Director of Research & Head of Healthcare Research*

I've been on mute, but I think you've lost the audio on Meira's side. I'll go back to mute.

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

Hello. Can you hear me, Bola?

Gbolahan Amusa - *Chardan Capital Markets, LLC, Research Division - Director of Research & Head of Healthcare Research*

Yes, now I can hear you.

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

Okay. Thank you. Did you hear the answer to my question -- I mean, my answer to your question?

Gbolahan Amusa - *Chardan Capital Markets, LLC, Research Division - Director of Research & Head of Healthcare Research*

Yes. I did. It faded out at the end, but I'll leave it at that since we're coming on 9 a.m.

Operator

Thank you. We have no further questions at this time. I will now turn the call back to Dr. Forbes for closing remarks.

Alexandria Forbes - *MeiraGTx Holdings plc - CEO, President & Director*

Okay. With no further questions, thank you for joining today, and have a good day.

Operator

Ladies and gentlemen, this concludes today's conference call. Thank you for participating. You may now disconnect.