

Dear XLMTM Community,

Last year, the ASPIRO clinical trial began, and dosed boys affected by X-Linked Myotubular Myopathy (XLMTM) with an investigational gene therapy product. Today, interim data from this clinical trial was shared with healthcare providers at a major medical and scientific conference, ASGCT (American Society of Gene and Cell Therapy).

We are sharing this letter as part of our commitment to open communication. Because of the considerable interest in these early findings within the XLMTM community, we recognize the need for clarity regarding information as it becomes publicly available. Therefore, we wanted to answer some questions you may have and provide context to the press release issued this morning (also found at www.audentestx.com under investors/press releases).

What are the goals of the ASPIRO investigational gene therapy clinical trial?

- To learn about the safety of the investigational gene therapy product
- To learn whether gene therapy is effective for the long-term production of myotubularin, the missing or defective protein in XLMTM
- To determine the appropriate amount, or dose, of the investigational gene therapy product

How many participants have been dosed in the clinical trial to date?

- Six (6) participants have been dosed with the investigational gene therapy product, at the first dose level
- One (1) participant has been randomized to the delayed control arm of the clinical trial, meaning that they will receive a dose yet to be determined later in the clinical trial
- All dosed participants have been given the first dosage level being assessed in the clinical trial
- All participants were previously enrolled in INCEPTUS, a non-interventional assessment clinical trial

What are the early, interim findings in the clinical trial?

It is Important to Note:

- We cannot make any conclusions on the interim findings of the clinical trial until after all enrolled subjects are dosed and evaluated for the duration of the study, and the full scope of data is collected and analyzed
- Making conclusions about interim data may not accurately predict the full risk/benefit profile of an investigational product
- After all enrolled subjects are dosed and evaluated for the duration of the study, and the full scope of data is collected and analyzed, more complete information about the safety and efficacy of this investigational gene therapy product will become available to the community

Safety Findings to Date:

Ongoing safety assessments are critical to proper determination of potential safety issues and adverse events.

- There have been a total of 24 adverse events (AEs) reported in ASPIRO, which have been manageable with medical treatment.
 - Six (6) of these adverse events were classified as serious adverse events (SAEs) of which five (5) occurred in one participant and the remaining one occurred in the the delayed treatment control participant who has not been dosed
 - Seven (7) adverse events (not serious adverse events) that were possibly or probably related to the investigational product occurred in a total of two participants.

- Eleven (11) additional adverse events (not serious adverse events) occurred which were not related to the investigational product

Specific details of the adverse events are included in the Press Release

Preliminary Efficacy Findings to Date:

Of the participants dosed:

- Two (2) participants continue to show improvement at 24 weeks, as measured by:
 - Increase in CHOP-INTEND neuromuscular function scores
 - Decrease in ventilation requirements
 - Increase in respiratory pressure measures
 - Some developmental milestones reached (head control, sitting unassisted, rolling over)
- One (1) participant shows improvements at 12 weeks, as measured by:
 - Increase in CHOP-INTEND neuromuscular function scores
 - Decrease in ventilation requirements
 - Increase in respiratory pressure measures
 - No age appropriate developmental milestones reached by week 12
- Preliminary data including baseline assessments were provided for the three (3) additional participants who had 4 weeks or fewer of assessments

*It is important to understand that regulatory agencies have not approved the Audentes investigational gene therapy product as safe or effective, as it is still undergoing formal assessment in clinical trials.
The investigational gene therapy product is not approved for commercial sale and is only being used in clinical trial settings.*

Why was the interim data released at a medical conference, and not at a forum where patients could attend?

- It is customary and appropriate to have clinical trial data first released at a peer reviewed medical or scientific conference, and then it is distributed a wider public audience shortly afterwards
- Every major medical conference has similar “rules” as far as how this type of data is shared; this process also may impact future publications of data
- Physicians are medically trained to understand data coming out of clinical trials, and the data shared is written for a physician and healthcare provider audience

When will the next release of findings from the ASPIRO clinical trial take place?

- The next planned release of additional safety and efficacy assessments will take place later in 2018, and the intent is to include muscle biopsy data from first 3 participants dosed

Where can general information about the clinical trial design be found?

- USA: Visit ClinicalTrials.gov and enter the term “ASPIRO”
 - <https://clinicaltrials.gov/ct2/show/NCT03199469?term=aspiro&rank=1>
- Europe: Visit EU Clinical Trials Register at www.clinicaltrialsregister.eu
 - Please note we anticipate the clinical trial will be listed shortly

We would like to ask for your continued partnership in helping the XLMTM community understand the need to refrain from any discussions (including social media, and other online or offline communications) about how the children in ASPIRO may be doing while the clinical trial is in progress. This includes a sincere request to the XLMTM patient community to please refrain from proactively asking parents of children enrolled in ASPIRO for information regarding their child's medical status during the conduct of the study. This is critical in helping to maintain the integrity of the data coming out of the trial. Our hope is to demonstrate the safety and efficacy of this gene therapy product such that it will benefit children and families affected by XLMTM in the shortest time possible. We do this best by running a robustly controlled and scientifically disciplined clinical trial and we need your help in making sure this occurs.

We hope this information is helpful in answering some of the questions you may have.

- If parents of children in the clinical trial have questions, we suggest they directly contact their clinical trial doctor and staff with questions
- For general inquiries, Patient Advocacy at Audentes Therapeutics can be contacted at: patientadvocacy@audentestx.com

Again, this investigational gene therapy product is not approved by regulatory agencies as safe or effective and it will continue to undergo formal assessment in the clinical trial. We look forward to sharing further information at a suitable time point.

Sincerely,

Suyash Prasad MD, Pediatrician, Senior Vice President and Chief Medical Officer

Glossary of terms

Adverse Event (AE):

Any undesirable experience/medical occurrence associated with use of an investigational product. Participants in clinical trials report these to the clinical trial physician. The physician and staff will determine if it is related to the use of the investigational product.

Serious Adverse Event (SAE):

Any type of an adverse event which: results in death, is life threatening/poses the risk of death, requires hospitalization, causes persistent or significant disability/incapacity, results in birth defects, or another condition which clinical trial physicians determine represents significant hazards.

- More information may be found at: <http://www.hhs.gov/ohrp/policy/advevntguid.html>.

Interim:

Early, incomplete, short-term.

Cohort:

A group of participants in a clinical trial, who are similar and observed over the same period of time. They may be similar in terms of age, dose given, clinical symptoms, or other defined characteristics. In ASPIRO, cohorts are similar in terms of the dose received.

CHOP-INTEND:

An assessment tool used to measure neuromuscular function, including motor skills. CHOP-INTEND stands for, "Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders."

MIP:

Maximal inspiratory pressure, or the greatest amount of pressure one can create while inhaling a breath.

MEP:

Maximal expiratory pressure, or the greatest amount of pressure one can create while exhaling a breath.

Non-interventional Assessment Clinical Trial:

A type of clinical trial which does not administer investigational products.