AT132 Gene Therapy for XLMTM – Commonly Asked Questions & Answers

1. What is INCEPTUS? What is ASPIRO?

Both INCEPTUS and ASPIRO are clinical studies that are being or will be conducted by Audentes Therapeutics. The Audentes gene therapy product for XLMTM is called AT132. INCEPTUS and ASPIRO form part of the clinical development program for AT132. The overall aim of the clinical development program is to evaluate if AT132 is safe and effective in XLMTM, and to get the drug approved quickly in order to benefit patients with XLMTM as rapidly as possible. Audentes will collect the necessary data in the clinical studies and then, if the outcomes from the clinical studies are positive, file an application for potential approval to sell AT132 commercially with regulatory agencies around the world (e.g. FDA in the United States, and EMA in Europe).

The INCEPTUS study is currently active, while the ASPIRO study is in final planning stages before submission to regulatory authorities (e.g. FDA in the United States, MHRA in the UK, PEI in Germany, etc) for final approval. The names INCEPTUS and ASPIRO are short 'titles' used to describe the study without using the full study name, and have meanings in Latin.

- INCEPTUS (which means "begun" or "beginning" in Latin) is a non-interventional (i.e. no gene therapy with AT132 administered) study to evaluate male XLMTM patients 3 years or younger. The goal of INCEPTUS is to determine which assessments, or tests, best identify the key characteristics of the disease. The information gathered will help Audentes determine which assessments to use in ASPIRO and other studies of AT132.
- ASPIRO (which means "to aspire" in Latin) is a study of gene therapy with AT132 for male XLMTM patients. The goal of ASPIRO is to determine if AT132 is safe to administer and has a beneficial effect on the signs and symptoms of XLMTM.

2. When will the INCEPTUS study begin to enroll patients? When will the ASPIRO study begin to enroll patients?

- The INCEPTUS study has begun enrolling patients. Information on the study centers that are open is available on the clinicaltrials.gov website.
- The ASPIRO study is expected to begin enrolling patients in 2017. The exact timing will depend on approvals of the study by various health authorities (e.g. FDA in the United States, MHRA in the UK, PEI in Germany, etc), Ethics Committees, Institutional Review Boards and other review committees (such as the U.S. Recombinant DNA Advisory Committee).

3. How many patients will be enrolled in INCEPTUS? How many patients will be enrolled in ASPIRO?

- The INCEPTUS study is currently designed to enroll up to 12–15 patients who meet the inclusion criteria.

- The ASPIRO study is not yet finalized, however, current plans are to initially enroll approximately 9–12 patients (that meet inclusion criteria), to evaluate the safety and efficacy of AT132.

4. What are the inclusion criteria for INCEPTUS?

a. Male patients
b. 3 years or younger
c. Diagnosis of XLMTM resulting from a confirmed mutation in the MTM1 gene
d. Mechanical ventilatory support required (e.g., ranging from 24 hours per day full-time mechanical ventilation, to noninvasive support such as continuous positive airway pressure [CPAP] or bi-level positive airway pressure [BiPAP] during sleeping hours)
e. Access to medical records
f. Signed informed consent by the parent(s) or legally authorized representative(s)
g. Patient and parent(s) or legally authorized representative(s) are willing and able to comply with study visits and study procedures

5. What assessments are being conducted in INCEPTUS? How many days and visits are required?

There are a series of assessments that will be conducted over 2 days every 3 months for up to 2 years. The assessments cover safety (ECG, blood draws, physical exam, height/weight, X-ray, etc), physical and movement assessments, respiratory (breathing) measurements, and questionnaires to evaluate respiratory status and quality of life.

6. What costs are covered for study visits for INCEPTUS?

Audentes will cover the costs of patient and family travel to/from the study site. These costs may include airfare, buses, trains, taxis, meals (daily stipend per person), and hotels for the patient, two parents, and a caregiver.

7. Does enrollment in INCEPTUS guarantee a patient's participation in ASPIRO?

No. There are additional inclusion criteria (such as antibody titer levels and age, among others) for ASPIRO, which must be met before a patient can be enrolled in the ASPIRO study. The intent and hope is for the majority of patients in INCEPTUS to be enrolled into ASPIRO.

8. Does a patient have to be enrolled in INCEPTUS to be enrolled in ASPIRO?

No. However, as INCEPTUS patients will already be familiar to the doctors at the study site, and data from INCEPTUS patients will have been collected for establishing a patient's baseline disease status, it is planned to give INCEPTUS patients priority for enrollment into ASPIRO.

9. If a patient is enrolled in INCEPTUS, are they obliged to enroll in ASPIRO?

No. Participation in INCEPTUS does not oblige a patient to participate in ASPIRO. Both studies are independent from each other and require separate approval from regulatory authorities in relevant countries (e.g. FDA in the United States, MHRA in the UK, PEI in Germany, etc), and then from ethics committees at specific trial sites. Each study also requires separate consent from the patients' parents (or their legally authorized representatives).

- INCEPTUS has received all of the necessary regulatory and ethical approvals, and is currently enrolling patients. ASPIRO has not yet undergone approval and, therefore, is not yet enrolling patients. Families who wish to participate in ASPIRO can only be asked to do so once the trial plans are finalized and approved, and when a detailed consent document is available.
- Participating in INCEPTUS does not obligate a patient to enroll in ASPIRO; neither does it guarantee a place in ASPIRO. However, the hope is that patients participating in INCEPTUS will agree to participate in ASPIRO (assuming that their doctors determine they meet the eligibility criteria), as this makes the data from before and after treatment easier to interpret and understand.

10. How will patients be chosen for INCEPTUS and ASPIRO?

Doctors at the study sites will evaluate patients based on protocol defined inclusion/exclusion criteria for the INCEPTUS and ASPIRO studies to determine eligibility and suitability for the studies. The choice of which patients to include in either or both studies is determined solely by the doctors at the trial sites in discussion with the patients' families. Neither Audentes nor any other members of the MTM community have any input into the choice of which patients will participate in either study.

11. If there are 12–15 patients in INCEPTUS and 9–12 in ASPIRO, how will it be decided which patients enroll in ASPIRO?

Enrollment into ASPIRO will be dependent upon when each clinical study site has the appropriate Institutional Review Board or Ethics Committee approval in place. Once a site is approved for enrolling patients into ASPIRO, the doctor at the site will work with each of their INCEPTUS patients to determine whether they meet the eligibility criteria for ASPIRO, and if so, when they might be able to enroll.

12. Will there be other clinical study opportunities for the INCEPTUS patients who don't qualify for ASPIRO or other XLMTM patients not enrolled in ASPIRO?

Although there will initially be approximately 9–12 patients enrolled in ASPIRO, if results from this initial study are positive, it may, after discussion with regulators, be possible to enroll patients into an additional study. Any plans to enroll beyond the initial patients in ASPIRO will need to be discussed with and approved by regulatory authorities in the appropriate region (e.g. FDA in the United States, MHRA in the UK, PEI in Germany, etc).

13. What happens if my child enrolls in INCEPTUS but is too old to participate in ASPIRO?

INCEPTUS enrollment is intended for those patients who will ultimately not be too old to enroll in ASPIRO. Audentes will continue to evaluate data from the clinical trials to determine if older subjects may gain benefit from gene therapy and evaluate the clinical development plan accordingly.

14. What are the challenges that have hindered earlier initiation of clinical studies?

- Audentes is working as hard and as fast as possible to initiate clinical studies of AT132.
- Gene therapy is a new and a highly innovative approach to treating disease. The manufacture of gene therapy products is very complex. There are a number of regulatory requirements which need to be met in order to confirm that product is of high enough quality, purity and safety to administer to humans, and, in particular, children. In addition, the quantities of product needed for human studies are significant, which means that the manufacturing process has to be 'scaled up' in size as we near clinical studies. This also adds complexity. Due to these challenges, Audentes has invested in a manufacturing facility for the production of AT132 for clinical studies.
- There are a number of pre-clinical studies that must be completed to assess safety of AT132. These studies must then be submitted and agreed to by health authorities prior to the conduct of studies in humans. Once this approval has been granted, the study sites must conduct their site initiation work (ethics committee approval, contract authorization, etc).
- The aim of the clinical development program (human studies) is to test the safety and efficacy of AT132 for XLMTM, and collect the data necessary to file an application for the marketing approval of AT132 in order to make it available for all patients with XLMTM as rapidly as possible.

15. What is Audentes' role as Sponsor of the INCEPTUS and ASPIRO studies?

Audentes is both the regulatory and the financial Sponsor of the INCEPTUS and ASPIRO studies. This means that Audentes is responsible for designing the clinical program, identifying trial sites, and conducting interactions with regulatory authorities (e.g. FDA and EMA). In addition, Audentes has sole financial responsibility for all aspects of the INCEPTUS and ASPIRO studies; no outside funding sources are required in order to be able to initiate, run, and complete these studies.

16. How does Audentes work with the MTM Patient Advocacy Groups?

Audentes has frequent communications with all of the MTM patient groups. This takes various forms, including emails, one-on-one phone calls, in-person meetings, and regular group discussions with the leaders of each advocacy group. The intent is to provide an open, transparent dialogue between Audentes and the patient community about the status of the clinical development program, and to help address any questions, concerns or issues that patients and their families have about the studies or gene therapy. These discussions do not include any discussion about eligibility of any

individual patients for the AT132 clinical development program (including INCEPTUS or ASPIRO) nor any other aspects of individual patients' care.