# ADULT (PARENTS OR LEGAL GUARDIANS) CONSENT TO PARTICIPATE IN A NON-INTERVENTIONAL RESEARCH STUDY

**STUDY TITLE:** A Multicentre, Longitudinal, Observational Natural History Study to Evaluate Disease Progression in Subjects with Usher Syndrome type 1B (USH1B)

**PROTOCOL NUMBER:** TIGEM3-UshTher-NHS

**STUDY DRUG:** Not Applicable

**SPONSOR:** Fondazione Telethon

**CENTER NAME:** ***Insert Center name**
**INVESTIGATOR (STUDY DOCTOR):** ***Insert Investigator name, address, phone #**
**PHONE NUMBER:**

*As an adult patient or as the parents or guardian of a child under 18 years old (in your capacity as legal representative), you will be asked to read and sign this form to give permission for your child to participate in this study. Your child will also be asked to sign an assent form. The word "you" and "my" throughout this document refers to you or your child.*

**This information sheet and informed consent form must be read together with the Annex 1, regarding personal data processing (that is an integral part of it).**

## 1. INTRODUCTION

You are being asked to take part in a research study. This study is a "non-interventional" study, which means the study only involves doing tests, answering questions; there is no drug, therapy, or treatment being tested. You will continue to see your regular doctor for your routine visits and care as you are already doing. You should inform your regular doctor of your participation in this study.

This form explains the purpose of the study so that you can make an informed decision as to whether you would like to take part. If you decide to take part, your data will be collected and analyzed for the purposes described below.

Please read this form carefully and make sure that you take your time to consider this information and have all your questions answered before you make your decision to participate.

## 2. PURPOSE

You have been asked to take part in this study because you have been diagnosed with Usher Syndrome type 1B.

The purpose of this study is to gain data to support a new way to follow the progression of the disease, and to understand the way the disease progresses over time using a variety of assessments and technologies.

## 3. NUMBER OF PATIENTS / LENGTH OF TIME IN STUDY

About 50 patients, from 3 centres in Europe are expected to take part in this study. You will be in the study for about 2 years.

## 4. VOLUNTARY PARTICIPATION

Taking part in the study is entirely voluntary. It is up to you whether or not you want to take part.

If you decide to take part, you must sign the consent at the end of this form. Even after signing the consent, you are free to leave the study at any time without giving a reason.

If you decide not to take part or if you withdraw from the study at a later time, there will be no penalty or loss of benefits to which you are otherwise entitled. Your decision would not change the routine medical care you would otherwise receive.

## 5. STUDY PROCEDURES

You will be asked to sign this informed consent form before any tests or procedures are performed.

You will be asked to notify the investigator in case you take any of the following not recommended mediciation throughout the study:

- Plaquenil
- Thioridazine
- Clofazimine
- Deferoxamine
- Phenothiazine
- Chlorpromazine
- Cisplatin
- Valproic acid
- Any other drugs with known visual side effects

Please, talk with your study doctor about this.

During the study, you will visit your study doctor approximately every twelve months. At each study visit, study staff will record assessments of your disease and general health noted in your medical notes and data from the study tests will be collected.

A typical study visit may take up to 2 days to complete all required procedures. Your study staff will inform you of the time requirement during scheduling. You will be asked to stop wearing your contact lenses for a period of time before you attend each study visit (4-5 days).

The tests and procedures that will be performed in this study are part of the routine care for your disease, meaning they may be performed by your regular doctor during your routine visits. However, these tests and procedures may occur more frequently for the purposes of this study. Other, like the questionnaires, are administered specifically for the purposes of this research study. The study visits are described below.

**Baseline Visit**

Informed Consent

It is very important for you to review this document closely and fully understand what will be required of you to participate during the study period. If you have any questions about any of the study procedures or study requirements, please ask the study doctor or study staff. If after you read the consent and have all of your questions answered; you wish to participate in the study; you will be required to give your written consent by signing and dating this form in front of the study staff and or the study doctor to participate in the study.

Eligibility
The study doctor will review the entrance criteria of the study to determine if you are eligible to participate.

Demographics
Questions about your background including your gender, age and ethnic origin will be collected for the purpose of this study.

Medical History
Questions about your medical history will be collected including any illnesses or diseases you have or have had in the past, any surgeries, procedures, or treatments you have had, and any medication, nutritional supplements, or other substances used, such as alcohol, tobacco, and other substance use that you have taken or are currently taking. Moreover, any previous ocular test and investigation will be collected and recorded. This information will be used only for the purposes of this research study.

Family History and Vision-related Family History
Information about your family members' general health, and vision related conditions your family members may have will be collected. This will include questions about retinitis pigmentosa and any other eye or vision problems that your first degree relatives such as your parents, siblings and children; and second degree relatives such as grandparents, uncles, aunts, nephews, nieces, half siblings and grandchildren may have, or may have had.

Pregnancy Assessment
For females, who are capable of becoming pregnant, you will be asked if you are pregnant.

Clinical Outcome Assessments (NEI-VFQ25 Questionnaire)
Study staff will ask you a number of questions related to your loss of vision, ability to perform certain activities, physical and emotional well-being, quality of life. These questionnaires will take approximately 20-30 min to complete.

Vision Test (Refraction and Best Corrected Visual Acuity)
If you wear contact lenses, you will be asked not to wear them the day of your study visits. Your study doctor will have you look through a series of lenses to help you see as clearly as possible. The lenses will be placed in a pair of trial glasses. You will be asked to read letters of different sizes from an eye chart using the trial glasses. You will sit or stand at a defined distance away from the screen or chart, and read each letter that appears. You will be given as much time as you needed.

Visual Field Assessments
These assessments will test how sensitive your vision is to light at specific locations on your eye. During the test you will be asked to look straight ahead at a spot in the middle of a screen. You will be asked to push a button each time you see a spot of light appear elsewhere in your vision. Each eye will be tested separately for each assessment. The total time for each eye that these tests will take is approximately 30 minutes

Ophthalmic examination

Your study doctor will examine your eyes with different instruments that use light and magnification to examine the health of your eyes in general. Your pupils will be enlarged with eye drops for these procedures. You will be given eye drops to numb your eyes. Your study doctor will use a pen shaped handheld electronic device to test your eye pressure by gently touching the surface of your eyes with the sterile cover tip.

Microperimetry
You will be asked to look into a screen and press a button whenever you see a light everywhere. Some of the lights may be easy to see and others will not. The test takes approximately 10-15 minutes.

Retinal Images
Three types of pictures will be taken of your retina during the study. Your pupils will be dilated with drops for these procedures.

- Spectral-domain optical coherence tomography (sd-OCT)
  This machine uses an invisible light to show the thickness of the retina. You will sit in front of the machine and look at a spot on a screen. The equipment will scan your eyes without touching you. This test will take about 10 minutes.

- Fundus Autofluorescence and Fundus Photograph
  The fundus camera is a specialized low power microscope with a camera attached, designed to take pictures of your eye. You will sit in front of this specialized camera and it will take photographs of the back of your eyes without touching you. This test will take about 10 minutes.

Images of your retina are information that can identify you like your fingerprint, since they reproduce your retina, which is a physical feature different in each individual. These medical images collected during the study will be processed and results will be reported as necessary for the purpose of the study. Medical images will be analyzed also at the Coordinating Centre:

Eye Clinic
Multidisciplinary Department of Medical, Surgical and Dental Sciences
University of Campania Luigi Vanvitelli
Via S. Pansini, 5
Naples, Italy

, and retained for at least 15 years after analysis. The images will be identified by a code; the coded images will be sent to this central reading center; only authorized staff will have access to your images and results.

Multifocal Electroretinography (mfERG)

Before this test, you will receive eye drops that will dilate (enlarge) your pupils as described above. For the test, a special contact lens, designed to pick up the electrical signal from the eye (like an antenna), will be placed on the front of your eye(s). A drop of anesthetic will be given before applying the contact lens, which will numb your eye so you do not feel the contact lens. Your eyes will be kept open during the procedure by the contact lens but they will not feel dry. White and black hexagons will be displayed in front of you. The test will take approximately ten minutes.

Electroretinography (ERG)
This test is performed to determine how well your retina responds to light. You will receive drops in your eyes for this test to enlarge your pupils and to make your eyes numb. You will be asked to sit in a completely dark room and/or have your eyes covered for about 40 minutes to allow your eyes to completely adjust to the dark. Your study doctor will gently place an electrode on the surface of each eye. Readings will be taken after flashes of light are directed towards your eyes. This test will be done in a dark room and then in a lit room for different measurements. The test will take approximately one hour to complete.

If no signal has been detected during previous examination, you will not undergo this procedure.

After the above-mentioned tests, the study doctor will determine if you are still eligible to participate in the study. If you are eligible you will be asked to return to the study clinic for a visit every twelve months starting from the baseline visit. These visits will include some or all the tests performed at the baseline visit.

During the study you must tell your study doctor right away if you:

- Have any accident or injury
- Have any medical treatment including surgeries, hospitalizations, or emergency hospital visits
- Become pregnant
- Notice any symptoms or illnesses that are new or different
- Add or change any medicines you are taking, including vitamins, herbal treatments, or over-the-counter medicines (such as, cough or cold medicines)

After you enroll in the study, if you decide not to continue your participation, your study doctor will ask you to return to the study site for some end of study procedures.

## 6. PREGNANCY & NURSING

For females who become pregnant your study doctor will collect information about your pregnancy. While you are pregnant or are nursing during the study, certain changes will be made to the assessments mentioned in section 5 to ensure there is no risk to you and your baby from being in the study

The safety of the eye drops that are administered to dilate your pupils and to numb your eyes during the assessments has not been studied in pregnant women. The effects of most of them have not been studied in pregnant animals. Due to the small amount of drug administered to the eye, and the small amount that is absorbed into the system, these drugs are frequently used in eye exams during pregnancy when the potential benefits are felt to outweigh the risks. In this study if you become pregnant, no eye drops will be used for the period that you are pregnant.

It is not known whether many of the drops used to numb and dilate eyes pass into the breast milk of nursing mothers. Thus, in this study if you are nursing, no eye drops will be used for the period that you are nursing.

The assessments that do not require eye drops present no potential threat or harm to a developing fetus or a nursing infant. Some of the assessments that are usually performed with eye drops may still be performed without the use of eye drops. In this case there would be no potential risk to the fetus or the nursing infant. Any tests that require eye drops will be eliminated while you are pregnant or nursing.

If you have any questions at any time, please discuss them with your study doctor.

.

You will not be given any eye drops while you are pregnant or nursing. You will undergo the following procedures without any eye drops while you are pregnant or nursing.

Vision Test
There are no eye drops used for this test, thus there will be no change to the way this test is performed.

Intraocular Pressure Assessment
The eye pressure test is usually performed after a drop of numbing medicine is put in the eyes, but this test can also be done without this eye drops with only minimal discomfort. However if you prefer to decline undergoing this assessment during your pregnancy you may do so by letting your study doctor know.

Visual Field Assessments
There are no eye drops used for this test, thus there will be no change to the way this test is performed.

Spectral-domain optical coherence tomography (sd-OCT)
This test is usually performed after the pupils are enlarged with eye drops. However the test can be done without using drops, thus no drops will be used while you are pregnant or nursing.

Ophthalmic examination This is usually performed after the pupils are enlarged with eye drops. The study doctor will examine the general health of your eyes without enlarging your pupils.

There are some assessments in this study that cannot be done without the use of eye drops, thus these assessments will not be performed during the time that you are pregnant or nursing.

Assessments not performed while you are pregnant or nursing are:

- Microperimetry (MP1)
- Multifocal electroretinography (mfERG)
- Electroretinography (ERG)
- Dilated ophthalmic exam (you will still have an eye exam un-dilated)
- Dilated fundus photography

## 7. RISKS AND DISCOMFORTS

There are some known discomforts and risks associated with the procedures being performed in this research study. Your study doctor will explain them to you, and you are encouraged to ask questions at any time. You will be monitored carefully for any side effects from the study procedures. If you experience any side effects from any procedures during the study, it is important that you let your study doctor or study staff knows immediately.

Eye drops
The eye drops used to numb and enlarge your pupils may cause your eyes to sting or burn. The dilating drops may make you particularly sensitive to bright lights and have blurry vision. It may take a few hours for the drops to wear off. In very rare cases people may experience allergic reactions to the drops, which may include swelling and red eyes. Some of the dilating drops may cause temporary high blood pressure, and/or a temporary fast heartbeat.

mfERG / ERG
You may feel a slight discomfort during the ERG test, like the feeling of having a hair in your eye. You may still feel like there is something in your eyes for a little while after the test is completed. There is a

very small chance that the electrode your study doctor uses during the ERG procedure can cause a small scratch on the surface of your eye. Excessively rubbing your eyes after the test while your eyes are still numb can also scratch your eye. If you do experience this type of scratch, it will usually heal within 24 hours. You should inform your study doctor if your eye hurts after testing, especially when you blink.

Study Visit
You may feel tired after you take part in some or all of the study procedures mentioned above. Please let the study doctor or study staff knows if you need a break to rest between these study procedures.

## 8. BENEFITS

You will not receive any direct benefit from taking part in this study. However, the collection of the information from this study may help develop future treatments for patients with Usher Syndrome type 1.

## 9. COSTS

There are no additional costs for you to be in this study.

## 10. COMPENSATION FOR PARTICIPATION

You will not be compensated for being in this study nor will you be required to pay any money for participating in this study.

Discuss with the Study Doctor if you can be considered in order to receive reimbursement for reasonable travel and food costs incurred due to your participation in the study.

## 11. WITHDRAWAL FROM STUDY / END OF STUDY

The study doctor or the Sponsor may remove you from the study at any time for certain reasons, such as in the interest of your safety. The Sponsor may also end the study at any time.

If you stop taking part in the study or are withdrawn from the study, any data about you (including your personal health information) that has already been collected will remain part of the study database and may not be removed. This is in order to maintain the reliability of the study's results and to satisfy legal and regulatory requirements.

## 12. CONFIDENTIALITY AND PRIVACY

All of your personal data collected during the study will be processed in a confidential way, in accordance with the Code for the Protection of Personal Data (Legislative decree no.196/03). For further details, please refer to Annex 1 that is an integral part of this document.

We will take all reasonable steps to make sure that the personal information in your medical record is kept confidential. Your personal information may be shared with others if required by applicable law or regulation. In addition, study information collected about you and your medical record (which may include your name) may be directly accessed and copied by the following people:

- The Sponsor and its authorized representatives:
  - the study monitor and auditors who ensure that the study is being performed correctly and the information collected about you is accurate
- Government health and regulatory agencies involved in keeping research safe for participants and reviewing the Sponsor's submission package

- Independent ethics committees, who are responsible for approving this study and ensuring that your rights and well-being are safeguarded.

By signing this consent form you are giving your permission for these people to access your study information.

To the extent permitted by law and regulation, all information that is collected about you and leaves the study site will have your name, address, contact details, and any other information that could identify you removed so that you cannot be recognized by it. However, your record that is identified by a study number may be linked to any participating family members' medical records that are also identified by study numbers. Your age may also be recorded to help identify your study record.

The Sponsor and those working for the Sponsor will use the results of this study and your coded information collected during this study. Some information will also be recorded on data forms that will be entered into a database. This information will be used for activities related to the study, for example to evaluate the progression of the disease over time as measured by a number of vision related assessments. The associations between the different measurements will also be studied. The Sponsor / UshTher Consortium may publish or present the study results at scientific or medical meetings, and submit this information to regulatory or health authorities. The Sponsor / UshTher Consortium may also use the information about the results of this study for other research purposes which may include:

- Developing a better understanding of the disease
- Improving the design and efficiency of future clinical trials

These uses of information will not reveal your identity.

If information from this study is published or presented at scientific or medical meetings, your name and other personal information will not be used.

Your personal data, including any sensitive personal data, will be retained for as long as is required to:
- Complete the study,
- Publish data related to the study,
- Support any regulatory applications.

Fondazione Telethon and your study doctor will control health data collected for the purposes of this study and will be jointly responsible as 'data controllers'. The study information collected will be recorded in your medical notes. Personal data, including sensitive data, such as your race and your health information, will be collected and processed, but only for research purposes in connection with this study. Some information will also be recorded on data forms that will be sent to a data processing office and entered onto a computer.

## 13. SOURCE OF FUNDING

The study is being conducted by the Sponsor, Fondazione Telethon and UshTher Consortium within the Project "Clinical trial of gene therapy with dual AAV vectors for Retinitis Pigmentosa in patients with Usher syndrome type IB" funded by European Commission .

## 14. REVIEW OF STUDY

The design of this study has been reviewed and been given favorable opinion by an independent ethics committee.

Name of ethics committee:

## 15. CONTACTS FOR QUESTIONS

If you have questions about the research study, you may use the contact reported in the first page of this document.

If you have any questions relating to privacy, ethical issues, potential conflicts of interest of the study doctor, or your rights as a research subject, you should contact the **Independent Ethics Committee, reported in the paragraph "REVIEW OF STUDY"** through the Investigator.

**CONSENT STATEMENT**

A. I understand that responsible individuals from the Sponsor, those working for the Sponsor, study staff, ethics committees, and health and regulatory authorities, may review sections of any of my medical notes and data collected during the study where it is relevant to my taking part in this research. I permit these individuals to have access to my records.

B. I understand that my taking part in this study is voluntary. I am free to withdraw at any time, without giving a reason. This will not affect my medical care or legal rights.

C. I have read and understand the above study document and have had time to consider the information. I have had the chance to ask questions and have had these questions answered to my satisfaction. I understand that I will receive a copy of this signed and dated consent form.

D. I agree to the transfer of my personal data, including sensitive data, to the Sponsor, companies working for the Sponsor, and to regulatory authorities both within and outside Europe. I understand that this data may be sent to countries that do not have the same level of data protection as the **EU**.

E. I agree that study data, including my coded medical information, may be used and shared for legitimate study and scientific purposes, including, if I do not object, for future use in medical or pharmaceutical research.

I agree to take part in the above study. By signing this form, I agree that:

| | |
|---|---|
| The study has been explained to me. | Yes☐ No☐ |
| All of my questions were answered. | Yes☐ No☐ |
| Possible harm and discomforts and possible benefits (if any) of this study have been explained to me. | Yes☐ No☐ |
| I understand my genetic data may be accessed and used. | Yes☐ No☐ |
| I understand that I have the right not to participate and the right to stop at any time. | Yes☐ No☐ |
| I understand that I may refuse to participate without consequence. | Yes☐ No☐ |
| I understand that I have a choice to not answer any specific questions. | Yes☐ No☐ |
| I am free now, and in the future, to ask any questions about the study. | Yes☐ No☐ |
| I understand that there may be risks in having study procedures performed. These risks have been explained to me. | Yes☐ No☐ |
| I understand that if I become pregnant or begin nursing I can continue in the study. I will not be given eye drops during the time I am pregnant or nursing, and I will not undergo the study assessments which require the use of eye drops. | Yes☐ No☐ |
| I have been told that my personal information will be kept confidential. | Yes☐ No☐ |
| I understand that information in my medical records and coded study data may be transferred and processed to third parties who may be in non-EU countries that do not ensure an adequate data protection level. | Yes☐ No☐ |
| I understand that no information that would identify me will be released or printed without asking me first. | Yes☐ No☐ |
| I understand that I will receive a copy of this signed and dated consent form. | Yes☐ No☐ |

**All signatories must sign and date the form personally.**

Printed Name of Patient

Signature of Patient | Date

I hereby consent to participate in this study:

Printed Name of Patient

Signature of Patient | Date

For Assent Subject (if applicable):

Printed Name of Mother/Guardian/Legally Authorized Representative | Relationship to Patient

Signature of Mother/Guardian/Legally Authorized Representative | Date

Printed Name of Father

Signature of Father | Date

Printed Name of Witness*(if applicable)

Signature of Witness*(if applicable) | Date

*In compliance with Ministerial Decree 15 July 1997 "Acknowledgment of EU guidelines on Good Clinical Practice for the conduction of investigational clinical trials.
A witness must be present during the entire process of obtaining informed consent if the subject has consented but is unable to read or write..

**PHYSICIAN STATEMENT:**

I acknowledge that I have discussed the above study with this participant and answered all of his/her questions. They have voluntarily agreed to participate. I have documented this action in the patient's medical record. A copy of this signed document will be placed in the patient's medical record. A copy of this signed document will be given to the patient or the patient's legally authorized representative.

Printed Name of study doctor Conducted Consent Discussion

Signature of Study Doctor Conducted Consent Discussion Date

**ANNEX 1 TO ADULT (PARENTS OR LEGAL GUARDIANS) CONSENT TO PARTICIPATE IN A NON-INTERVENTIONAL RESEARCH STUDY**

**NOTICE AND INFORMED CONSENT AUTHORIZING THE USE OF PERSONAL DATA**

Data Controllers of personal data and purposes of processing

The study site (Insert the name of the site without name of division) and the Fondazione Telethon which has sponsored the study described to you, each of them for their own competence area and in accordance with the responsibilities set forth in the Good Clinical Practices rules (GCP Guidelines and Legislative Decree n. 211/2003) will process your personal data as Data Controllers, in particular those regarding your health and, only if essential in relation to the objective of the study, other data regarding your origin, gender, weight and height exclusively for the study carrying out and for purposes of pharmacovigilance. The Principal Investigator will be qualified as Data Processor for the part of the processing for which the Institution is the data controller.

For the purposes mentioned above, your data will be collected by the study site and forwarded to the Sponsor and such involved third-parties (individuals or companies) acting on behalf of Sponsor. Some of the above recipients may also be established in non-EU countries that do not ensure an adequate data protection level. An updated list of companies to whom your personal data will be transferred is available at the Sponsor and can be accessed upon request through the Investigator.

The processing of personal data relevant to your health, gender, origin and lifestyle is essential for carrying out the trial: any refusal to give information will not permit your participation in it.

Nature of the data

The Investigator who will look after you during the study will identify you by the assignment of a code: your data that will be collected during the study, with exception of your name, will be transferred to the Sponsor, recorded, processed and kept together with this code, your birth date, your gender. Only the Investigator and authorized subjects will have the permission to connect this code to your name, by a list that will be kept by the Hospital/Institution for at least 15 years, according to the applicable laws.

Methods employed in processing

The data processed also through electronic tools, will be disclosed only and exclusively in anonymous form, for example through scientific and statistics publications and scientific conventions. Your participation in the study involves that, in compliance with the provisions about clinical trials on drugs, Sponsor's personnel or personnel working for companies that perform monitoring and audit activities during the study on behalf of the Sponsor, as well as the Ethics Committee and the national and foreign Health Authorities will have the permission to access your data including in your original clinical documentation, in ways such as to guarantee the privacy of your identity.

Exercise of the rights

You will be able to exercise the rights pursuant to Art. 7 of the "Code for the Protection of Personal Data" (i.e. to have access to your personal data, to complete, update, and correct these, or to refuse their treatment for legitimate reasons, etc.) by contacting directly the study site (insert PI name or a responsible office and phone number) or, through it, the Sponsor. You have the right to stop your participation in the study at any time without giving explanation: in this case, biological samples linked to you will be destroyed. No further data regarding you will be collected, but the data already collected will still be used as they are necessary to determine, without modifying them, the results of the research.

CONSENT

By signing off this form, I authorize that my personal and confidential data can be made available (direct access) for the purpose of quality checks by the Sponsor's personnel and people delegated by the Sponsor itself, or local and international Regulatory Authorities for inspective purposes. In addition, I give my consent to the transfer of my personal data within and outside the European Union for the purposes of the study in the limits and in the ways described in the information sheet that I received together with this document.

I hereby consent to participate in this study:

**All signatories must sign and date the form personally.**

| | |
|---|---|
| Printed Name of Patient | |
| Signature of Patient | Date |
| For Assent Subject (if applicable): | |
| Printed Name of Mother/Guardian/Legally Authorized Representative | Relationship to Patient |
| Signature of Mother/Guardian/Legally Authorized Representative | Date |
| Printed Name of Father | |
| Signature of Father | Date |
| Printed Name of Witness* (if applicable) | |
| Signature of Witness*(if applicable) | Date |

*In compliance with Ministerial Decree 15 July 1997 "Acknowledgment of EU guidelines on Good Clinical Practice for the conduction of investigational clinical trials.

A witness must be present during the entire process of obtaining informed consent if the subject has consented but is unable to read or write.