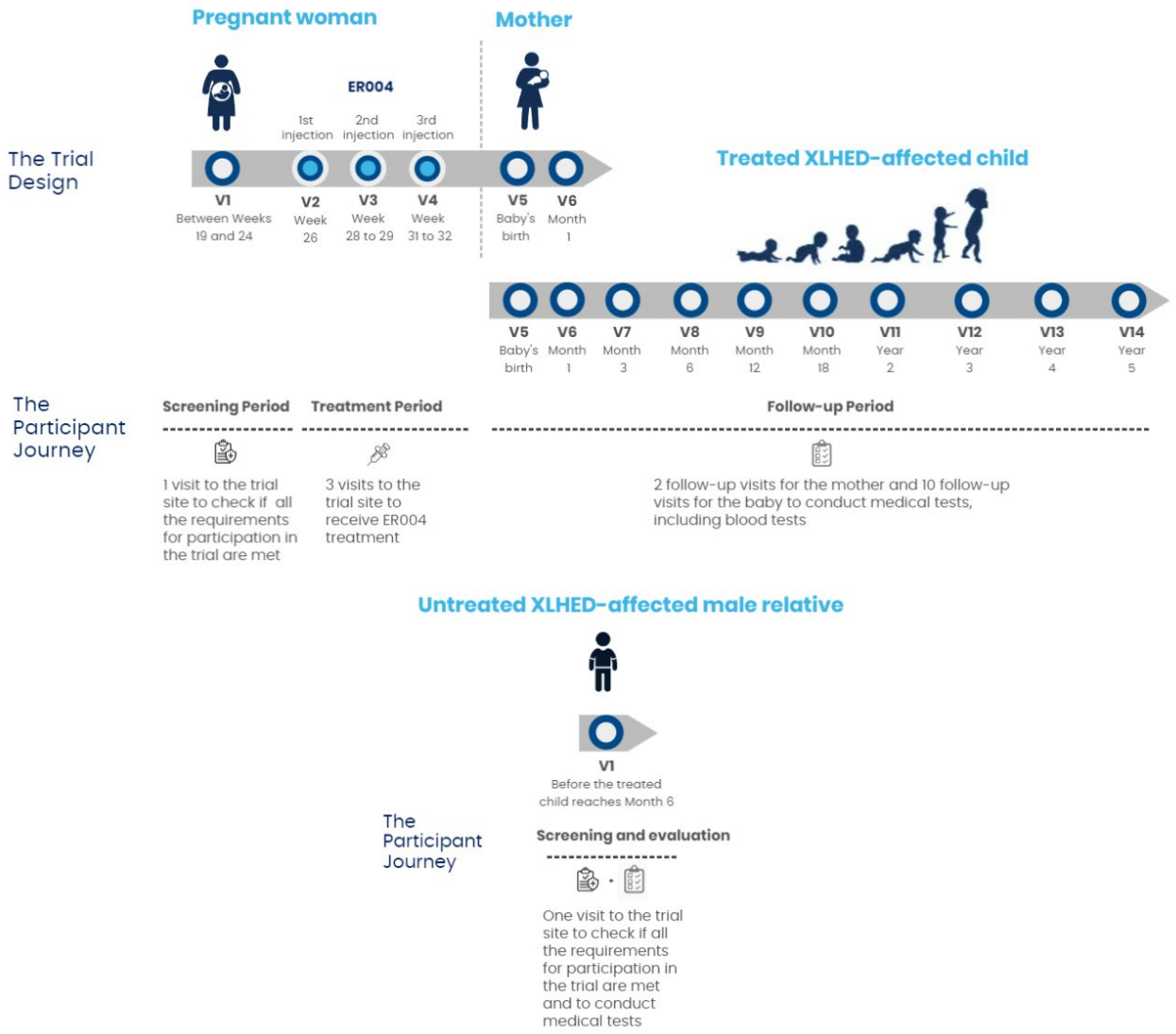
Trial title	A prenatal trial for XLHED affected boys.
Disease	X-linked Hypohidrotic Ectodermal Dysplasia (XLHED),
Treatments	Three rounds of ER004 injections into the amniotic fluid at pregnancy weeks 26, 29 and 32.
Participants	Treated group: • Pregnant woman (aged 18 years or over) with a confirmed genetic diagnosis of XLHED AND expecting a baby boy with XLHED. Comparator group • XLHED-affected male blood relative of the pregnant woman (aged between 6 months and 75 years),
Trial dates	From 26 April 2022 (first participant first visit) to January 2029.
Trial Locations	France, Germany, Italy, Spain, United Kingdom, United States.
We do research to improve patient care. This trial will help us to answer important questions about treatment of XLHED.	

This document is a brief summary of a clinical trial protocol. It is written in plain language for the general public, providing answers to the following questions:

- What is the purpose of the trial?
- What are the objectives of the trial and how are they evaluated?
- How is the trial conducted?
- Who can take part in the trial?
- What is the trial treatment and how it is administered?
- What are the possible benefits and risks in taking part in the trial?

What is the purpose of the trial?	This is a prenatal trial for X-linked Hypohidrotic Ectodermal Dysplasia (XLHED) affected boys. The purpose of the trial is to evaluate how prenatal treatment of male fetuses with ER004 works and how it is tolerated. ER004 is an experimental medicine for XLHED not yet approved for use in humans, except in clinical studies. ER004 is made in a laboratory to replace an important protein called EDA1 (Ectodysplasin-A1), missing in people affected by XLHED. Absence of this protein during the baby's development in the womb leads to some important structures not forming properly (sweat glands, hair, teeth etc).
What are the objectives of the trial and how are they evaluated?	The main objective of the trial is: • To evaluate the effect of prenatal treatment with ER004 on the sweating ability of treated boys. This is assessed by measuring the amount of sweat produced by XLHED affected treated boys at given times during the trial and up to 5 years of age. In addition, the trial will allow: • To evaluate if treatment with ER004 is tolerated by both the mother and her son. This is assessed by evaluating the number, frequency and type of side effects experienced by

	both the mother, up to 1 month after delivery, and by her son, until he is 5 years of age. • To evaluate the effect of ER004 on teeth development of XLHED-affected treated boys up to 5 years of age. • To evaluate the potential effects of prenatal treatment with ER004 on other symptoms of XLHED.
How is the trial conducted?	This is an open-label Phase II trial. Approximately 20 pregnant women expecting a baby boy with XLHED will participate in the trial. The trial for the pregnant woman and her XLHED-affected son consists of 3 different periods: • A screening period during which the pregnant woman comes for a single visit to the trial site to check that both her and her unborn son are eligible for participation in the trial. During this visit, she will get a chance to discuss in person with the trial doctor prior to giving her consent or deciding not to participate. • A treatment period during which the pregnant woman visits the trial site 3 times to receive a total of 3 injections of ER004 into the amniotic fluid, approximately 3-week apart. • A follow-up period which starts when the treated boy is born and lasts until he is 5 years old. Regular visits at the trial site will take place during which trial doctors will conduct various tests and measurements to evaluate the effects of the treatment and its tolerability. The "comparator group" consists of XLHED-affected male blood relatives who will not receive ER004. The XLHED-affected male blood relative is asked to come to the clinical site for one visit only, to allow doctors to conduct non-invasive medical tests. The picture below summarizes the information presented above:



Who can take part in the trial?	To take part in the trial, participants must fulfill several conditions including the following: Treated group • Pregnant woman (aged 18 years or over) with a confirmed genetic diagnosis of XLHED AND expecting a baby boy with XLHED. Comparator group • XLHED-affected male blood relative of the pregnant woman (aged between 6 months and 75 years), who has not previously received the ER004 treatment.

What is the trial treatments and how it is administered ?	ER004 treatment is given before birth, in a procedure that closely resembles an amniocentesis. Three rounds of injections into the amniotic fluid take place over 3 visits, approximately 3 weeks apart, at pregnancy weeks 26, 28-29 and 31-32. No more ER004 administration will take place after the baby is born.
What are the possible benefits and risks in taking part in the trial?	ER004 is an experimental medicine, not yet approved. Previously, 6 XLHED-affected boys received prenatal treatment with ER004. Some preliminary results have been reported in scientific journals (Schneider 2018 and Schneider 2022). They suggest that ER004 has the potential to prevent or reduce the severity of some XLHED symptoms. So far, ER004 has not been found to have any major side effects, but it is a product in development and may therefore have unknown side effects. Side effects can come from the ER004 treatment and from the injection procedure itself. The trial doctor closely monitors the pregnant woman and her unborn son throughout the trial to check they are safe.

Cinical Trial identification	
Protocol number	ER004-CLIN01/F60082AI201 (EDELIFE)
Protocol version	5.0 dated 23 September 2022
Full trial title	A prospective, open-label, genotype-match controlled, multicenter clinical trial to investigate the efficacy and safety of intra-amniotic ER004 as a prenatal treatment for male subjects with X-linked hypohidrotic ectodermal dysplasia (XLHED).
Registry ID	ClinicalTrials.gov: NCT04980638 EDELIFE Trial - ClinicalTrials.gov EudraCT Number: 2021-002532-23 EDELIFE Trial - Clinicaltrialsregister.eu
Who sponsors this trial?	
Name and contact details of the sponsor	**EspeRare Foundation** Campus Biotech, Avenue Secheron 15, CH-1202 Geneva, Switzerland. **Pierre Fabre Médicament** Les Cauquillous, 81500 Lavaur, France.
Additional Information	• *Research articles from Prof Schneider and colleagues: Schneider 2018; Schneider 2022* • *Link to EDELIFE Trial Website: edelifeclinicaltrial.com*

Glossary	
Amniocentesis	A procedure used during pregnancy to take out a small sample of the amniotic fluid for testing.
Amniotic fluid	Liquid that surrounds the baby during pregnancy.
Comparator group	Trial participants who have not received the treatment and will serve as a reference.
Genetic diagnosis of XLHED	DNA testing to identify the changes (mutations) on the *EDA* gene.
Open-label trial	A type of trial in which both the doctors and the participants are aware of the treatment being given.
Phase II trial	Trial designed to assess whether an experimental treatment is safe and whether it works.
Prenatal trial	A clinical trial to test a treatment given to unborn babies while they are in their mother's womb.
Side effects	Glossary: Side effects are unwanted medical events (such as headache) that happen during the trial and that are related or possibly related to trial treatment.
X-linked Hypohidrotic Ectodermal Dysplasia (XLHED)	Rare genetic disease characterized by a reduced ability to sweat, missing teeth, and fine sparse hair. The disease is caused by specific changes (mutations) in a gene called *EDA* which makes a protein called EDA1 (Ectodysplasin-A1). If EDA1 protein is absent or not working correctly during the baby's development, important structures like sweat glands, hair, teeth do not form properly.