- EspeRare Foundation
- History of XLHED treatment
- Upcoming clinical trial
ER004

EspeRare Foundation
EspeRare Foundation – who we are

Who?
• Founded by 3 experienced pharma executives
• Team of 12 employees & expert consultants

Where?
• Geneva, Switzerland, 2013

How?
• Not-for-profit
• Financed through both private & public funds

Why?
✓ To fast-forward drug development
✓ To leverage equitable not-for-profit business model
✓ To deliver accessible treatments with fair pricing for children with rare diseases

“A world in which patient engagement, great science, big data, pharmaceutical excellence and health authorities come together to address the medical needs of children affected by rare diseases, ultimately alleviating the healthcare burden of their conditions“
ER004

History of XLHED treatment
Ectodysplasin (EDA) in normal development (non-XLHED)

A protein called "ectodysplasin" is needed for glands, hair, teeth, & skin to develop properly. This is happening very early in life.

Ectodysplasin (EDA) is missing in XLHED

In XLHED, ectodysplasin is missing. Because of this glands, hair, teeth, and skin do not develop properly.

EDI200/ER004 as a replacement for Ectodysplasin (EDA)

In animal studies EDI200 replaced ectodysplasin and helped glands, hair, teeth, and skin to develop. This is now being testing in human clinical trials.
EspeRare makes plans to relaunch development of treatment

- EDI200 developed by Edimer Pharma
- Validated *efficacy* in animal models
- **First clinical study:** Well tolerated in XLHED adults (Ph I, 2012)
- **Second clinical study:** Treating new-born XLHED babies does not work (Ph II, 2013-16)
- Edimer closes down 2009 to 2016
- 3 babies treated *in utero* by Prof. H Schneider 2016
- Promising results 2016
- EspeRare makes plans to relaunch development of treatment 2018
History of the treatment – first antenatal interventions

Mother 1
- pregnant with twins
- 1 intra-amniotic injection, at week 26
- 1 intra-amniotic injection, at week 31

Mother 2
- 1 intra-amniotic injection only, at week 26

- ✓ sweat function
- ✓ dentition
- ✓ eye health
- ✓ respiratory function
- ✓ salivation
- ✗ hair

History of the treatment – first antenatal interventions

Wet baby sleeping bag from one of the treated twins, showing sweat production

Maarten and Linus, the treated twins, with their older brother Joshua (April 2018)

One of the treated twins, being examined by Prof Holm Schneider during a check-up (May 2019)
ER004
Upcoming clinical study
Purpose of the pivotal antenatal clinical trial
- Generate safety and efficacy data
- Aim is to submit dossier for marketing authorisation
  o Data generated in the upcoming trial
    + all data generated so far
- Health Authorities support (FDA, EMA)
  o faster approval process

Who’s eligible?
Pregnant women expecting a baby boy affected by XLHED

How many patients will take part in the study?
15 to 20 in total

How long will the study last?
- Subject monitoring:
  o close follow-up during the first 6 months
  o yearly visits for 5 years
When is the treatment given?

- ER004 does not work in newborn babies
- ER004 seems to be working in fetuses
- Antenatal treatment

How is the treatment given?

- Intra-amniotic injection
  - Procedure similar to amniocentesis
- 3 injections during pregnancy: **weeks 25, 28 and 31**
- No post-birth treatment planned

How is the diagnosis made?

- **Mother**: to be **genetically confirmed** as XLHED carrier
- **Baby**: amniocentesis and/or ultrasound diagnosis (count of tooth buds)
Where will the study take place?
1. Germany first
2. Rest of the world (e.g. UK, FR, USA)

What are the potential challenges?
- To date, no approved treatment given as an intra-amniotic injection
  - Unchartered territory, program is opening a new regulatory pathway
- Small window of opportunity to receive treatment
- Short time between screening and enrolment into the study
- Travel: challenging, but there will be a support program available to families
What are the potential benefits and how will we assess them?

- Sweat ability is the main anticipated benefit
  - non-invasive sweat volume test
  - non-invasive sweat pore density test
  - from 6-months of age

- Other potential benefits that will be probed
  - Teeth
  - Eye health
  - Skin health
  - Salivation
  - Respiratory function
  - Growth and development
  - Quality of life
What do we monitor potential side effects?
- Safety is paramount (mother and baby)
  - blood tests
  - frequent vital signs and clinical monitoring
- Independent Data Monitoring Committee to independently assess subjects’ safety

When will you know if the study is successful?
Anticipated study duration: 4 years from start
<table>
<thead>
<tr>
<th>Study number</th>
<th>Title and clinical trial number</th>
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<tbody>
<tr>
<td>ECP-001</td>
<td>Evaluation of Phenotypic and Genetic Properties in Male Subjects Affected by Hypohidrotic Ectodermal Dysplasia (NCT01108770, NA)</td>
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<tr>
<td>ECP-003</td>
<td>Evaluation of Phenotypic and Genetic Properties in Male Subjects Affected by Hypohidrotic Ectodermal Dysplasia (NCT01293565, 2013) (Jones 2013)</td>
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<td>ECP-005</td>
<td>Evaluation of Phenotypic and Genetic Properties in Male Subjects Affected by Hypohidrotic Ectodermal Dysplasia: Intrafamilial Variation (NCT01386775, 2011)</td>
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<td>ECP-007</td>
<td>Natural History and Outcomes in X-Linked Hypohidrotic Ectodermal Dysplasia (NCT02099552, 2013)</td>
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<td>ECP-015</td>
<td>Sweating ability and genotype in individuals with X-linked hypohidrotic ectodermal dysplasia (NCT01109290, 2011) (Schneider et al. 2011)</td>
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<td>ED10</td>
<td>Early respiratory and ocular involvement in X-linked hypohidrotic ectodermal dysplasia (NCT01308333, 2013) (Dietz et al. 2013)</td>
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<td>ED12</td>
<td>Genotype-Phenotype Correlation in Boys With X-Linked Hypohidrotic Ectodermal Dysplasia (Burger et al., 2014)</td>
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<tr>
<td>ECP-012</td>
<td>Evaluation of Phenotypic and Genetic Properties in Male Subjects Affected By Hypohidrotic Ectodermal Dysplasia (NCT01629927, 2012) (Burger et al. 2014)</td>
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<tr>
<td>ECP-014</td>
<td>Phenotypic Properties in Individuals affected with X-linked Hypohidrotic Ectodermal Dysplasia: Symptoms and Facial Recognition</td>
</tr>
<tr>
<td>ECP-002</td>
<td>A Phase 2 open-label, dose-escalation study to evaluate the safety, pharmacokinetics, immunogenicity and pharmacodynamics/efficacy of EDI200, an EDA-A1 replacement protein, administered to male infants with X-Linked Hypohidrotic Ectodermal Dysplasia (XLHED)</td>
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<tr>
<td>ECP-004</td>
<td>A Phase 1 open-label safety and pharmacokinetic study of EDI200, an ectodysplasin-A1 replacement molecule, in X-Linked Hypohidrotic Ectodermal Dysplasia (XLHED) adults</td>
</tr>
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**Upcoming Clinical Study**

**Your contribution is priceless!**

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Thank you!

Questions?

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