espeRare

ANNUAL REPORT 2024

The EspeRare Foundation exists to tackle the critical gaps in rare disease treatment. As a non-profit biotech, we use a patient-centered, partnership-driven approach to uncover the potential of existing technologies and healthcare products. Our focus spans both pre-natal and pediatric applications, with the overarching aim of ensuring all patients – no matter how rare their condition – can access the treatments they deserve.

Daring to Care for the most vulnerable

EspeRare is driven by a singular purpose: to transform the outlook for children diagnosed with rare and life-threatening diseases, starting as early as pre-natal treatment.

Each minute, a child is born into a world without a cure for their condition. A quarter of them will not reach the age of five. With effective therapies available for only a fraction of rare diseases, and even fewer designed with children in mind, the need for action is critical.

This is why we are focused on bringing to life and accelerating the development of innovative and accessible treatments to children affected by these underserved diseases. We put the patients and their families at the center of everything we do. The patient community guides how we tackle diseases from product selection to supporting clinical testing and helping develop new strategies for distribution.

EspeRare

For further information on EspeRare, please visit www.esperare.org

> Never remain on the sidelines of this march of living hope."
>
> **- Pope Francis**

Word of the Executive Committee

In a world increasingly shaped by uncertainty, where pediatric and women's health are facing deprioritization and deepening disregard, EspeRare remains resolute in its mission: to transform how science serves those too often overlooked. We believe that therapeutic innovation must not only be cutting-edge but also equitable, reaching under-resourced and underserved populations that traditional drug-development pathways routinely overlook.

This year, EspeRare has doubled down on its pioneering approach, advancing ER004 (p.17-22) in the prenatal field and initiating ER008 (p.23), a new program targeting preeclampsia and fetal growth restriction– just as the World Health Organization adopted its first-ever resolution on rare diseases, a milestone that underscores the urgency and relevance of our mission. Our contributions to the Lancet Commission on Rare Diseases have helped elevate rare and fetal conditions from the periphery of global-health discussions to their rightful place on the international agenda.

Once considered niche, our work in rare and prenatal diseases is now increasingly acknowledged as a bellwether for the future of personalized and equitable healthcare. By demonstrating a sustainable model for innovation in underserved patient populations, we are redefining the boundaries of what is possible in medicine and therapeutic innovation.

Yet pioneering is not without its challenges and responsibilities. Trailblazing means taking on scientific, regulatory, and ethical complexities that others often avoid. In 2024, we initiated foundational work on the ethical and regulatory framework for prenatal therapy development (p.16), a necessary step to ensure that innovation in this space is responsible, patient-centered, and sustainable.

At the heart of our model lies a collaborative spirit and we extend our deepest gratitude to our partners and supporters and funders, whose engagement and generosity make these joint achievements possible.

These efforts reflect EspeRare's values-driven model, daring, compassionate, and impact-focused. The pages that follow showcase the concrete achievements of this past year that embody our mission to make hope a reality for those who need it most.

Thank you for trusting us, as we will continue to push the boundaries of innovation, guided by our unwavering dedication to humanity. Our heartfelt gratitude extends to our strong network of invaluable donors, funders, partners, and passionate team whose support has been instrumental in our achievements and has given us the courage to strive for enhancing our impact even further.

Sincerely,

Beatrice Greco
Founder and Board Member

Caroline Kant
Founder and Executive Director

Sharon Terry
President of the Board

Addressing rare diseases

A MAJOR GAP IN THE MEDICAL LANDSCAPE

In Europe, up to 30 million people are impacted by a rare disease, which is defined as one that impacts **1 in 2,000 individuals,** or in the US, less than 200,000 people.*

Rare diseases are **chronic, progressive, degenerative,** and **often life-threatening.** Due to their low prevalence and high complexity, their management requires special combined efforts.

* Source: Orphanet and the US Orphan Drug Act

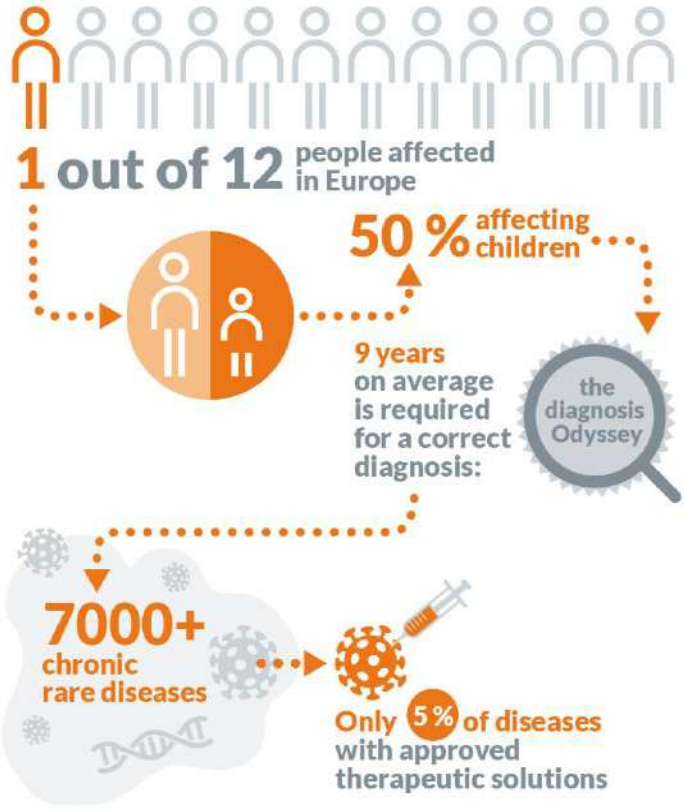
DRUG DEVELOPMENT: A LONG, COMPLEX AND COSTLY PROCESS

Developing new treatments is expensive and lengthy. It requires tight coordination across a wide selection of research and development (R&D) activities and expertise. Recent reports estimated an average expenditure of **$2.6 billion** and a time frame of **10 to 15 years** to bring a new drug to the market.*

* Source: PhRMA

INSUFFICIENT EFFORTS IN DRUG DEVELOPMENT FOR RARE DISEASES

While significant progress has been made, drug development efforts **remain insufficient to address medical needs in rare diseases.** Therapeutic development suffers from the heterogeneity and complexity of these diseases, the limited number of patients, the fragmentation of medical expertise and the lack of pathophysiological understanding.



Creating a rapid response for children with life-threatening rare diseases

A FOCUS ON UNMET NEEDS

EspeRare is driven by the urge to improve the lives and healthy development of children suffering with rare genetic diseases.
By building off an extensive drug development infrastructure – made up of in-depth scientific knowledge, patient registries, diagnostic tests, and more – we can develop significant, novel approaches to therapeutic development. This model creates rapid results with immediate impact on patients with rare diseases.

> “As a not-for-profit organisation, our priorities are not determined by the size of the market. They are solely defined by high unmet medical needs and great science. Above all, we strive to apply our patient-centric model and pharma know-how to advance and accelerate new treatments for underserved patients” –
>
> **Caroline Kant**
> Founder and Executive Director

RESCUING EXISTING DRUGS TO ACCELERATE NEW TREATMENT R&D

EspeRare brings life to discontinued, pre-existing treatments, developing them into effective treatments for rare diseases. The drugs we select have been discontinued due to changes in therapeutic focus, lack of efficacy in the original indication or unwillingness to invest the necessary funds to pursue their development, and may be at any stage of development themselves.

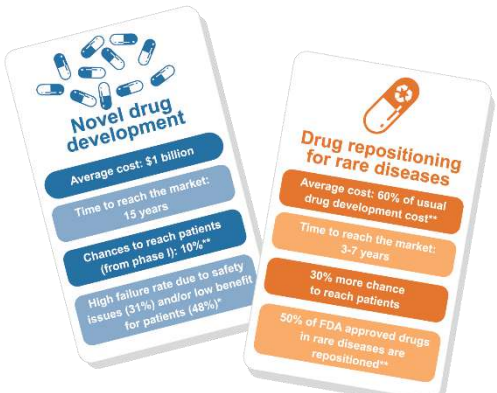
Our goal is to develop treatment opportunities that remain both economically attractive for commercial partners, as well as beneficial and accessible for patients and the healthcare system at large. These combined goals guarantee the greatest patient coverage.

Rationale for drug repositioning:

- The biological response from existing drugs is already known and recorded. The data on this response can help match drugs to other health conditions.
- Many steps in the drug development process – eg: drug activity, safety profile in humans – are already demonstrated during the initial development of the drug, saving time and cost during new treatment development.

Outcomes from repositioning drugs:

- Faster and lower risk approach
- Less costly and more accessible treatments
- Accelerated development of new therapies for rare diseases.



** Ref: M. Hay et al., Nature Biotechnology 32, 40–51 (2014)*
*** Ref: Anne Pariser, Director at CDER*

Our patient-centred approach

KEEPING PATIENTS AT THE CORE OF WHAT WE DO

EspeRare stands out in our ability to **collaborate closely with patient organisations** throughout every stage of the development journey. This is largely due to the Foundation's not-for-profit model and our strategic partnership with Genetic Alliance, a vast network comprising over 1,200 disease advocacy organisations.

By working in collaboration with these organisations, we can keep patients at the centre of our approach, ensuring that their **lived experiences are acknowledged** and **integrated** as an invaluable part of our continued progress.

Our approach prioritizes interests of patients by securing their safety, maximising medical benefits, facilitating access to treatment, and enhancing overall care.

A COLLABORATIVE AND ACCELERATED PATHWAY

For each of our drug development programmes, we develop Product Development Partnerships with the equivalent patients' community, medical experts and commercial partners.

Through these relationships, we can:

- mobilise research, clinical experts and biomedical centres of excellence to conduct pre-clinical and clinical development activities
- integrate the "patient voice" through collaborative work with patient advocacy groups
- ethically engage industry partners to manage transition into late clinical development and commercialisation
- interact directly with regulatory agencies and health authorities to best pave the way to drug/therapy approval and patient access to treatment

In every programme, our aim is to forge reliable partnerships with patient organisations, fostering drug development centred around the needs of patients.

EMPOWERING PATIENT ADVOCACY IN RARE DISEASES

Particularly in rare conditions, patient advocacy contributions are key at each stage of drug development:

Given the scarcity and fragmentation of medical expertise, patients are highly knowledgeable and can have a strong influence on drug development. Advocacy organisations collect and share the natural history data, and can provide feedback on characterisation of the disease and unmet medical needs.

Through their support and research efforts, fundraising and advocacy activities actively develop expert networks, manage disease related knowledge, engage in and support biomedical research. They also support the market launch of new treatments and equitable access to healthcare.

PATIENT ADVISORY COUNCIL (PAC)

For each of our programmes, we put in place a Patient Advisory Council (PAC). The PAC serves as a patient advisory board to EspeRare team members, senior management, and partners. Within the PAC's shared governance, patient representatives take an active part in the development of a drug or treatment.

The framework enables patient representatives to:

- ✓ Share views with the patient community concerning the therapeutic programme
- ✓ Receive regular programme updates and information to foster patients' and families' access to key programme insights
- ✓ Provide input into development activities with co-development partners
- ✓ Make recommendations to help plan, implement and refine efforts towards meaningful patient involvement.

A SNAPSHOT OF OUR PARTNER NETWORK

Pharma and Biotech Partners

Pierre Fabre · edimer · NIH National Institutes of Health · Boehringer Ingelheim · MERCK · MMV Medicines for Malaria Venture

Biomedical and R&D Partners

IQVIA · Universitätsklinikum Erlangen · Necker · PRECISION for medicine · LEON BERARD · UNIVERSITÉ DE GENÈVE · CHUV · Unil UNIL | Université de Lausanne · HE VD IG · ALMA MATER STUDIORUM UNIVERSITÀ DI BOLOGNA · GIG CYMRU NHS WALES · Washington University in St.Louis · INSTITUT DE MYOLOGIE · Great Ormond Street Hospital Charity · Cedars Sinai

Patient Organisations

Genetic Alliance · EURORDIS RARE DISEASES EUROPE · EDIN Ectodermal Dysplasias International Network · nfed NATIONAL FOUNDATION FOR ECTODERMAL DYSPLASIAS · AFMTELETHON · ed · Duchenne Parent Project · IRDiRC · Duchenne UK · aade · ACTION DUCHENNE · ed · Associazione Nazionale Displasia Ectodermica

Funders and Sponsors

LOTERIE ROMANDE · Fondation Prim'Enfance · alps group · McKinsey&Company · ASHOKA · Schweizerische Eidgenossenschaft Confédération suisse Confederazione Svizzera Confederaziun svizra Swiss Confederation Innosuisse – Swiss Innovation Agency · KIWANIS CLUB MONTHEY · 2&D CREATIVE · Same but Different · the ella fund · WATCHESTV VIVA WATCHMAKING

Thank You

Amerah

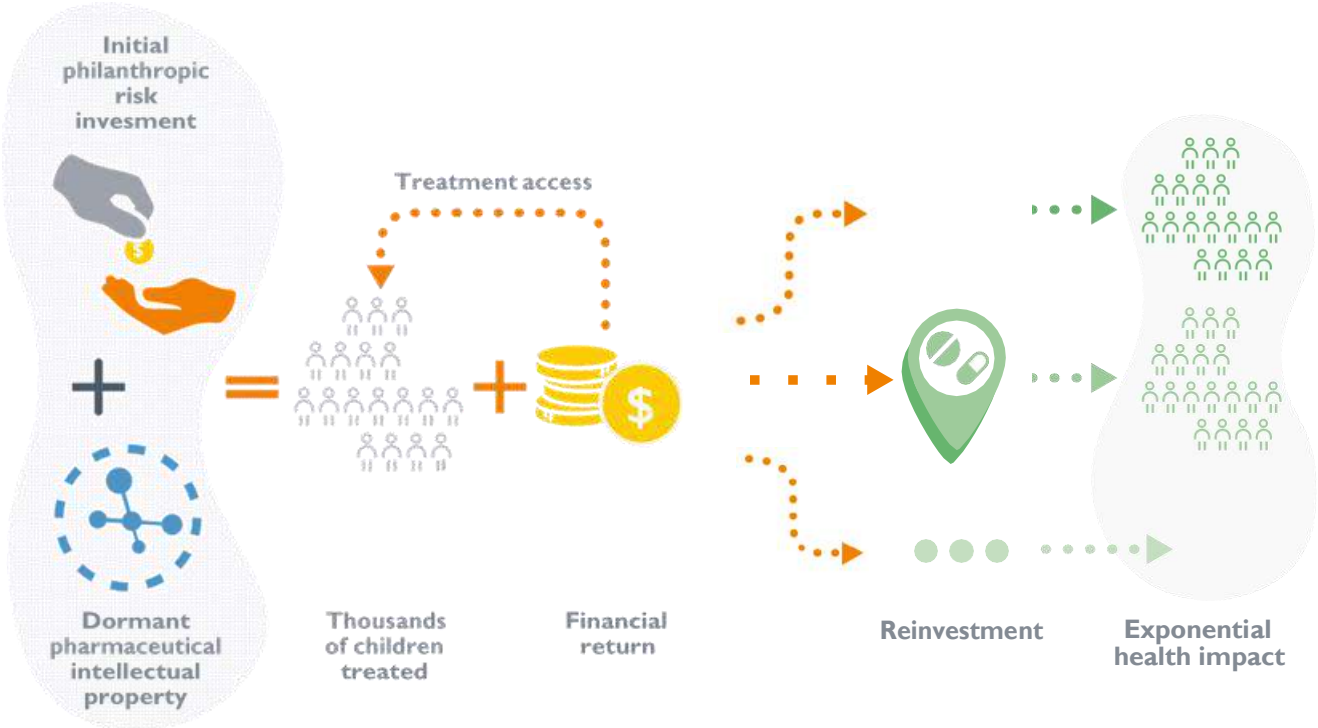
Our alternative, sustainable business model

IMPACT OF OUR NOT-FOR-PROFIT BUSINESS MODEL

As an organisation of public interest, we are committed to using our funding resources in a socially responsible and not-for-profit manner. Our venture philanthropy model multiplies the impact of philanthropic investments and pharmaceutical know-how to address the unmet needs of millions of children with rare diseases and their families

We reinvest all of our profits to further achieve our mission of developing treatments for underserved rare disease patients, improving their quality of life and driving access to medicines it develops. All financial returns that EspeRare generate are being used to strengthen the organization and its portfolio of therapeutic programs and collaborative partnerships.

These financial returns enable us to establish ourselves as a major drug development player within the paediatric rare disease space, to confirm the viability of our novel not-for-profit model, and to underpin our ability to accelerate accessible treatments for these vulnerable patients.



Innovative approach to advance treatments and care for patients

ESPERARE'S DIGITAL PLATFORM FOR THE IDENTIFICATION AND DEVELOPMENT OF RARE DISEASE TREATMENTS

Our "in silico" approach enables us to identify novel therapeutic opportunities for already existing drugs. To this end, we have supported the development of a collaborative digital platform, which systematises discovery and creates a more efficient drug development structure:

- generating essential data
- formulating new medical application hypotheses for existing drugs
- facilitating the speed at which we can make innovative discoveries

This digital platform consists of a combination of the following:

Discontinued treatments database

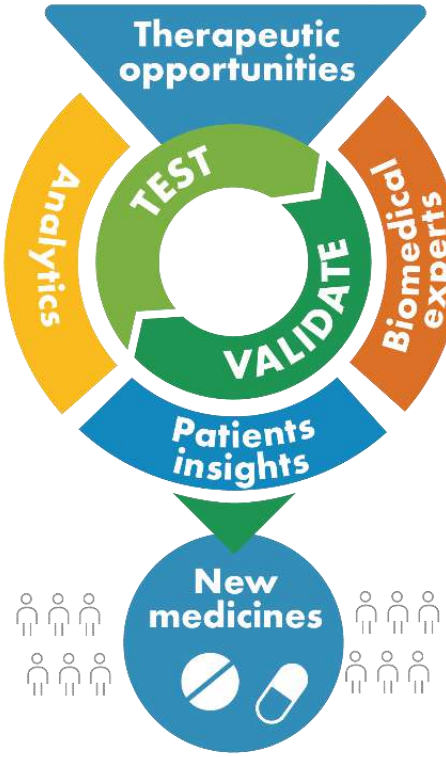
This database compiles data on 2'000 existing drugs that have the potential to be "redeveloped" to treat rare diseases. It then combines existing data about these drugs, for example: their initial disease(s) of development; safety and toxicity profiles; their biological mechanism of action. A collaboration with the National Institute of Health (US) has enabled us to access data on all drugs developed worldwide.

Rare disease analytics system

This system integrates biomedical data on the molecular pathophysiology of targeted rare diseases. The information is extracted from scientific literature and specialised databases. This technical understanding cascade is then validated and enhanced by integrating data and insights from EspeRare network of biomedical experts.

Patients' Vault

This platform integrates patients' insights, supporting our patient-centric goals. By working hand-in-hand with the patients' community, new therapeutic approaches and their development can benefit from the unique insight offered by lived-experience.



Project made possible thanks to the generous support of :

Genetic Alliance

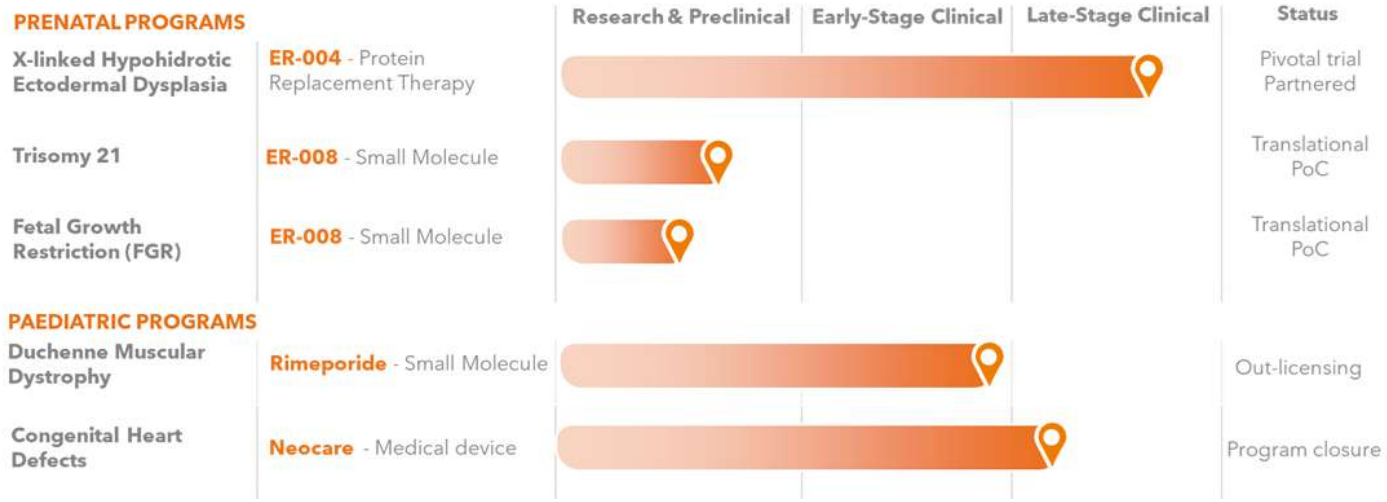
NATIONAL INSTITUTES OF HEALTH

LOTERIE ROMANDE

We are currently seeking like-minded partners and funders to further develop the digital platform.

Our portfolio of treatments

PROGRAMME PORTFOLIO STATUS TIMELINE



Since our establishment in 2013, we have been on a mission to discover and develop new medicines for rare diseases by rescuing dormant therapeutic opportunities. Supported by public and philanthropic funding, and through collaboration across the rare disease ecosystem, the Foundation advances a dynamic and patient-centric portfolio of therapeutic programmes.

The groundbreaking protein replacement therapy, ER-004, EspeRare has rescued is poised to become **the first effective prenatal treatment for patients with X-linked hypohidrotic ectodermal dysplasia (XLHED) (p.17-22).** The EDELIFE clinical trial is actively recruiting patients across six designated countries and is progressing toward therapeutic registration (p. 21).

Rimeporide, a candidate showing promising therapeutic potential in children with Duchenne muscular dystrophy, is currently in Phase II planning. EspeRare is **actively seeking a commercial partner for Rimeporide to advance the programme into Phase II/III (p. 26-29).**

Following a comprehensive internal and external review, **EspeRare has discontinued development of NeoCare (p.31)**. This strategic decision reflects the evolution of clinical standards and enables the reallocation of resources to higher-impact rare and prenatal medicine projects.

Building on the innovative pathway established by ER-004, EspeRare is **reinforcing its maternal-fetal health strategy with ER-008, a novel programme addressing Fetal Growth Restriction (FGR) and Pre-eclampsia p. 23)** two leading causes of prenatal complications. To support responsible and sustainable innovation in the prenatal space, the Foundation has also launched a dedicated **Prenatal Ethics and Regulatory Platform (p. 16).**

EspeRare continues to grow our rare disease portfolio by:

- Collaborating with pharmaceutical companies, academic institutions, and patient organizations to evaluate and co-develop opportunities aligned with our mission;
- Advancing our Digital Platform, a biomedical informatics engine that systematically identifies and assesses drug rescue and repositioning opportunities

Prenatal Therapy

ESPERARE IS UNIQUELY POSITIONED TO ADVANCE PRENATAL THERAPIES

Over the past decade, EspeRare has been dedicated to improving the lives of children living with rare diseases, driven by a deep commitment to their well-being. Since 2018, it has embarked on a remarkable journey into the realm of prenatal medicine with its ER-004 programme (p. 16-21). This initiative marks a significant milestone in **EspeRare's journey: a pioneering therapy that addresses a disease before birth.**

ER-004 programme is currently in its final stage of clinical development aiming to address symptoms associated with X-linked ectodermal dysplasia – a condition that poses life-threatening challenges such as the inability to sweat, amongst others. Through this ground-breaking development, EspeRare is advancing the development of ER-004, a novel protein replacement therapy administered into the amniotic fluid surrounding the fetus.

Should the outcome of the ongoing EDELIFE clinical study be favorable, ER-004 will become the first-ever therapy capable of addressing the symptoms of a genetic disease before birth.

Currently, regulatory approval for prenatal therapies is yet to be achieved, leaving a gap in accessible prenatal treatment options. Through the ER-004 programme, EspeRare and its partner Pierre Fabre are set to transform the current landscape. By 2027, they aim to bring this innovative treatment to the market in Europe and the United States, setting a precedent and a way forward for other prenatal therapies.

> "Through our ER-004 programme, EspeRare opens a new frontier in medical innovation, introducing a pioneering approach to treating diseases in utero and paving the way for therapeutic breakthroughs before birth. With this programme, we are not just developing a treatment; we're nurturing hope for a healthier future where every life has a chance to thrive from the very beginning.
>
> **Caroline Kant**
> Founder and Executive Director

THE PRENATAL PERIOD – A WINDOW OF OPPORTUNITY TO ENHANCE THERAPEUTIC EFFECTS

The prenatal period, occurring before a baby's birth, presents a crucial therapeutic window for addressing severe medical conditions at the fetal stage. This unique timeframe is characterized by distinct properties of both the growing fetus and the maternal environment within the womb.

Treating certain genetic diseases before birth targets their earliest manifestation, thereby potentially preventing the onset of irreversible pathology. This innovative approach holds promise for conditions that begin prenatally, like specific fetal development disorders, which can only be effectively treated during this stage.

Furthermore, intervening before birth not only addresses previously untreatable conditions but also holds the promise of improving the effectiveness of treatments currently administrated postnatally. By doing so, it can lead to long-term enhancements in quality of life and result in better outcomes, including significant cost-savings for patients, their families, and healthcare systems.

ESPERARE'S PRENATAL THERAPY INITIATIVE: PIONEERING A NEW PATH IN HEALTHCARE

The development of ER-004 marks a pivotal moment in modern medicine, where therapeutic development and medical breakthroughs converge to offer hope to those living with rare diseases present at birth. EspeRare stands at the forefront of this advancement, pioneering prenatal therapy with a blend of cutting-edge genetic diagnosis, targeted treatments, and patient-centred care. The ambition is clear: to enhance the quality of life for paediatric patients right from birth, guided by a framework of ethics and responsible therapeutic development tailored to this emerging field of medicine.

Nested in the vibrant innovation Campus Biotech hub of Geneva, EspeRare finds itself at the nexus of global health and scientific diplomacy – a position that fuels its mission to drive progress in prenatal therapy beyond its initial pioneering efforts.

With a focus on international collaboration and collective expertise, the Prenatal Therapy Initiative aims to break new ground in the development and accessibility of treatments for rare diseases and other neglected conditions amenable to prenatal therapy, focusing on three key components:

- **Prenatal Biotech portfolio**
  The Initiative aims at repurposing postnatal therapies for prenatal use in severe conditions, swiftly translating scientific breakthroughs into tangible solutions for patients with high unmet needs.

- **Research and Technology Innovation**
  Through partnerships with scientists and researchers worldwide, the Initiative aims to further the development of innovative solutions in the nascent prenatal biomedical field, positioning itself as a beacon of progress in global prenatal therapy development.

- **Ethics and Oversight Observatory**
  Guided by EspeRare's ethos, the Initiative seeks to uphold the highest standards of patient care and safety. By collaborating with global health experts and regulatory bodies, EspeRare is currently formalize and champion responsible practices in prenatal therapy development worldwide.

EspeRare's Prenatal Therapy Initiative aims to impact healthcare on a global scale. The goal is not just to offer hope and healing but to ensure that unborn children affected by severe conditions can enter the world in good health, promoting equity and inclusion from the very beginning.

campus biotech

Ethics and Regulatory Observatory

SHAPING RESPONSIBLE INNOVATION IN PRENATAL MEDICINE

Prenatal therapies are rapidly transitioning from theoretical possibilities to clinical reality, offering transformative potential for conditions that are currently untreatable after birth. Yet as these interventions emerge, ranging from gene and enzyme therapies to cell-based approaches, they also raise complex ethical and regulatory questions that are not yet fully addressed by existing frameworks.

The maternal-fetus dual-patient nature of prenatal medicine, the time-critical window for intervention, and the long-term implications for both the child and the pregnant woman make this an especially delicate and high-stakes domain. While important ethical discussions have emerged around specific technologies or clinical steps, current efforts remain fragmented and reactive, lacking the cohesive, anticipatory framework needed to guide the field of prenatal therapy as a whole.

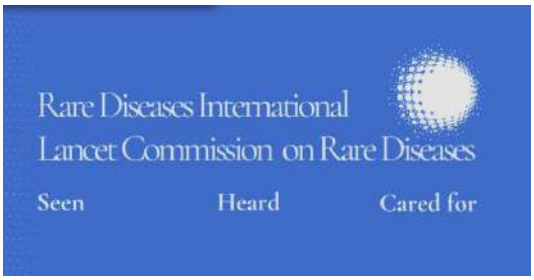
To address this gap, EspeRare established the foundation of a dedicated Ethics and Regulatory Observatory in 2024. This initiative brings together leading international experts in bioethics, human rights, and regulatory science to anticipate challenges and support the emergence of sound, inclusive governance. A cornerstone of this work is the development of a Points to Consider (P2C) framework: a practical, cross-disciplinary reference designed to guide ethical reflection and decision-making across the full research-to-care continuum.

Built around nine core principles, the P2C addresses key issues such as risk–benefit evaluation in dual-patient contexts, informed proxy consent, long-term follow-up, the role of human rights in prenatal policy, and the need for a lifecycle approach to governance. The P2C is not technology-specific but modality-agnostic and intended to support ethical innovation across a wide range of prenatal therapies, from early-stage research to real-world clinical use.

This foundational work lays the groundwork for broader stakeholder consultation in 2025, including academic symposia, professional society engagement, and dialogue with patient organisations and regulators. EspeRare is also advancing academic partnerships to support new research capacity in Switzerland, ensuring that rigorous ethical analysis continues to inform scientific progress in this emerging field.

The Observatory's relevance is further underscored by the launch of the Rare Diseases International–Lancet Commission on Rare Diseases, which brings global attention to the healthcare disparities and policy gaps faced by millions living with rare conditions. As prenatal therapies gain traction within the rare disease space, EspeRare's proactive contribution to international efforts supports the development of therapies that are not only scientifically sound, but ethically robust and societally trusted.

> "As prenatal therapies move closer to mainstream clinical practice, we urgently need governance frameworks that are as innovative as the science itself anticipatory, inclusive, and grounded in human rights. EspeRare's Points to Consider offers a vital starting point for navigating this complex and fast-evolving landscape."
>
> **Prof. Bartha Maria Knoppers, OC, OQ, PhD, FRSC, FCAHS**
> Director, Centre of Genomics and Policy, McGill University



X-Linked Hypohidrotic Ectodermal Dysplasia (XLHED)

A LIFE-THREATENING DISEASE WITH A WIDE RANGE OF DEBILITATING SYMPTOMS THAT PERSIST THROUGHOUT LIFE

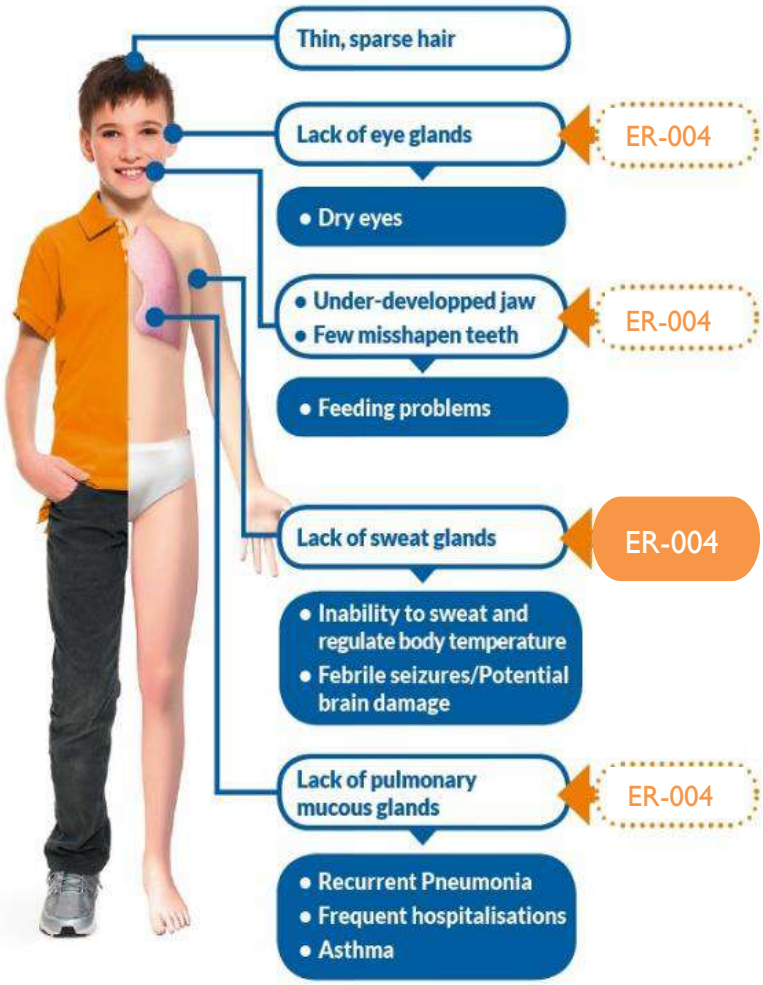
XLHED is a rare genetic disorder caused by a defect in the EDA gene inherited on the X-chromosome. Individuals with XLHED lack a functional EDA-A1 (EDA protein, essential to the normal development of a dermal layer during fetal development). Consequently, the development of ectodermal structures such as skin, teeth, glands and hair are impaired. As boys have one single copy of this gene on their X-chromosome, they usually display the full spectrum of the syndrome as opposed to girls that are in general less affected.

XLHED is a life-threatening disease, particularly in the first years of life when infants are at risk of sudden death due to hyperthermia and/or pneumonia. Disease morbidity, including psychosocial challenges, persists into adulthood.

XLHED represents also an important medical and healthcare burden. Recurrent infections, hyperthermic episodes and other health issues cause frequent hospitalizations, especially in the first part of childhood. It is estimated that, in the United States, direct hospital costs amount to over $ 50'000 in the first 3 years of life alone and dental costs amounting to up to $150'000 throughout an affected individual's lifespan can be expected.

Consequences of organ damage, treatments related to hair, dentition issues as well as psychosocial challenges require important and costly medical care throughout the life of individuals affected by XLHED.

The incidence of XLHED is estimated to be ~4/100,000 male births.



ER-004 PROGRAMME IN X-LINKED HYPOHIDROTIC ECTODERMAL DYSPLASIA

The development of ER-004 (previously named EDI200) was stopped by Edimer Pharmaceuticals, due to the treatment's lack of efficacy when treating newborns with XLHED.

EspeRare has revived ER-004 using a novel intra-amniotic administration route. It has also entered into a partnership with Pierre Fabre and launched a clinical study with the aim of bringing this protein replacement therapy to the mark

DEVELOPMENT TIMELINE

2017

Edimer Pharmaceuticals closed its operations due to minimal results in applying ER-004 to neonates. EspeRare was then approached by Edimer Pharmaceuticals to revive ER-004's clinical development of this programme in XLHED, then stalled.

The development of ER-004 in XLHED using an intra-amniotic administration approach before birth was accepted in the European Medicines Agency's PRIority Medicines scheme. Furthermore, ER-004 also benefits from Orphan Drug Designation in the EU and the US and Fast Track Designation by the FDA in the US.

2018

EspeRare sought advice from the EMA to present all data collected and to understand whether this pioneering intra-amniotic administration route can be developed. The EMA agreed with EspeRare's proposal that prenatal treatment of XLHED through intra-amniotic drug administration was the way forward to develop ER-004 into a treatment for XLHED.

2019

A similar meeting was conducted with the FDA, who were supportive of ER-004 as a prenatal treatment for XLHED. This gave EspeRare the green light to actively start seeking a co-development partner and finalise a robust clinical development plan.

2020

EspeRare and the Pierre Fabre Group signed a co-development agreement. As partners, we committed to an Ethical Charter that governs our relationship and placed the XLHED patient community at the heart of the development. Together, we established a clinical trial to bring ER-004 to the market in the EU and the US.

Pierre Fabre

2021

EspeRare and the Pierre Fabre Group successfully launched the EDELIFE pivotal clinical trial to probe the safety and efficacy of ER-004 as a prenatal treatment for XLHED, with a first center opening for enrolment in Erlangen, Germany, in November 2021. Research activities were conducted in collaboration with Dr. Pascal Schneider at the University of Lausanne to address gaps in the understanding of the ER-004 therapeutic approach. EspeRare and the laboratory of Dr. Schneider were awarded an Innosuisse grant for this research from the Swiss Confederation in June 2021.

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra
Swiss Confederation
Innosuisse – Swiss Innovation Agency

2022

In 2022, pivotal trial investigator sites opened in the rest of the world (France, Italy, Spain, the UK, and the USA) and the first patients were treated. The edelifeclinicaltrial.com website was launched, serving as a source of information on study description, design, eligibility criteria and contact details of investigators and patient website was launched, serving as a source of information on study description, design, eligibility criteria, and contact details of investigators and patient representatives. EspeRare's focus turned to boosting recruitment and completing all development activities in time to take ER-004 to market.

2023

In 2023, the study recruited another two patients. The patient-focused Edelife website underwent updates, accompanied by the launch of a global digital campaign aimed at further increasing awareness of the Edelife study. Market access activities were initiated: a Natural History study was launched, and a mock Health technology authority meeting was conducted, both to gain a better understanding of the natural course of the disease and to collect feedback and plan for reimbursement. On the regulatory front, a first discussion took place with the FDA, leveraging the Breakthrough Therapy Designation, to engage the Authority in helping EspeRare streamline this challenging and unique development.

2024

Edelife recruited another 7 subjects, bringing the total of subjects recruited in the study to 10. We conducted what should be our last consultations with the FDA and the EMA to refine our development plan, both with clinical and drug product-related queries. Both Agencies were supportive of our tailored development plan, and we now have a global development plan that aims to satisfy both Agencies' requirements.

2025 & beyond

In 2025, we will obtain results from the Edelife study, on which the filing for both the FDA and the EMA will be based. While Edelife will carry on recruiting subjects, our focus will shift to submission-readiness activities, which will also include manufacturing of our first ER004 commercial batch. Submission of our Marketing Application dossier to both the FDA and the EMA is planned for late 2026, and approval for the second part of 2027-early 2028.

> "I sincerely wish that efforts of all partners involved in the development of a treatment for XLHED will be rewarded when ER-004 can be made available to XLHED families as the first successful treatment to prevent or reduce symptoms of the disease"
>
> **Pascal Schneider**
> PhD-PD, UNIL

ER-004 - A "SINGLE COURSE" THERAPY TO INDUCE NORMAL ECTODERMAL DEVELOPMENT IN BABY BOYS WITH XLHED

ER-004 – AN INNOVATIVE PROTEIN REPLACEMENT THERAPY (PRT)

Ectodysplasin-A1 (EDA-A1) is an essential protein for the normal development of ectodermal structures in the foetus and is missing in patients with XLHED. Without this protein, XLHED-affected individuals have many serious, life-long health challenges, with the inability to sweat being the biggest of these challenges, potentially threatening the lives of small children.

ER-004 is a novel in-utero therapy to replace EDA1. ER004 is a man made synthetic form of the EDA-A1 protein, administered by intra-amniotic injections during the late stage of foetal development. The protein is given through the mother's abdomen into the amniotic sac where it is swallowed by the baby.

R-004 has already demonstrated a significant improvement in the normal development of key ectodermal structures such as glands, teeth and hair. Six patients treated with ER-004 before birth by Prof Holm Schneider at the University Hospital Erlangen in Germany were born with normalized sweat gland function and the initial results obtained in the first three patients were published in New England Journal of Medicine, as well as the International Journal of Molecular Sciences.

This breakthrough in medicine opens the door to a brighter future for couples who are carriers of the XLHED gene variant, as is the case of Laura and Milo Reiser, an American couple from Oregon.

THE REISER FAMILY STORY – HOW ER-004 CHANGED MY SON'S LIFE

After having their first baby girl, Evie, who was unaffected by XLHED, the couple decided to have another child. The genetic test done at 8 weeks in the pregnancy confirmed they were expecting a boy. When the Reisers reached out to Prof. Holm Schneider, they received the news that their unborn baby boy was affected by XLHED.

The couple was ready to face the difficulties this medical condition meant for their son, until Prof Schneider asked if they were willing to consider treating their son with an experimental medicine named ER-004, to which Laura answered:

> "I was like 'yes, I've been wanting to be part of this for 15 years!' We knew that it would work and that it would change his life. Otherwise, we would not have done it".

Despite the pandemic and a storm of mixed emotions from happiness to fear, Laura was determined to fly across the Atlantic Ocean to Germany so that their unborn son could receive the ER-004 treatment during the last couple of weeks of his fetal development.

Her motivation grew the moment she was put in contact with Emily, another mother whose son Finley had been treated pre-birth by Prof Schneider a few months earlier and who had been born healthy.

> "I don't think I would've committed to doing it if I didn't have the opportunity to talk with Emily beforehand. She was able to answer so many questions".

Laura received three injections of ER-004 during her stay in Germany, along with other usual tests such as blood drawings, ultrasounds and COVID tests. She felt really welcomed and supported by the whole team of Prof Schneider.

She tested positive for COVID on the day she welcomed her son Bennett:

"Bennett was so cute and so very tiny. He didn't have any effects from COVID and tested negative for it."

To the delight of the Reiser family, it did not take long to confirm that Bennett could sweat:

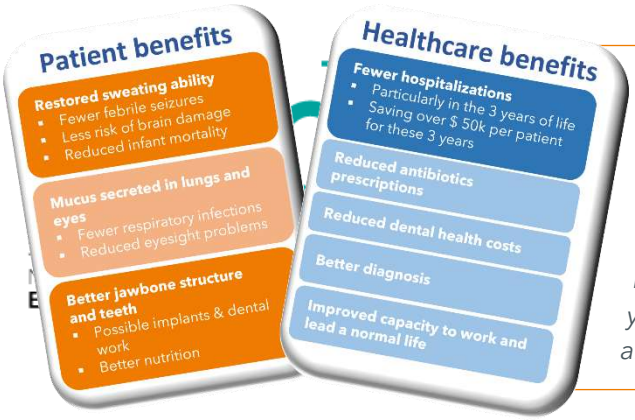
"At two months, we went on a little trip, and we slept on one of those egg crate mattresses. Bennett was sleeping next to me and he was drenched in sweat. So we knew that he could sweat from that moment.

"I knew that it would work. I had no doubt, because I knew Emily's son, Finley, and the other twin boys who were treated could sweat. Also, I had built a really good relationship with Dr. Schneider, and I totally trusted what he was doing," Laura reported.

Moreover, so far, Bennett has not had any respiratory problems, shows an increased number of meibomian glands in his eyes and has tooth buds. All are encouraging signs that the treatment has not only restored Bennett's ability to sweat but might also have improved the functionality of other ectodermal structures that are affected in XLHED patients.

Laura, who went through this journey with Prof. Holm Schneider, has expressed her willingness to help other pregnant women who are considering taking part in the trial and support them in building a new future for their children, saying that the ability to sweat and regulate body temperature is the most wonderful gift we can offer to those children.

> "Bennett's the sixth baby in the world, I believe, to have something like this done, not just for ectodermal dysplasia, but any sort of prenatal therapy. It's just amazing. It's going to take enough people willing to do it, to get to where it is available for other purposes as well. So, to me to be the sixth is pretty incredible. I hope he understands one day what it took" -
>
> **Laura Reiser**
> Bennett's mother

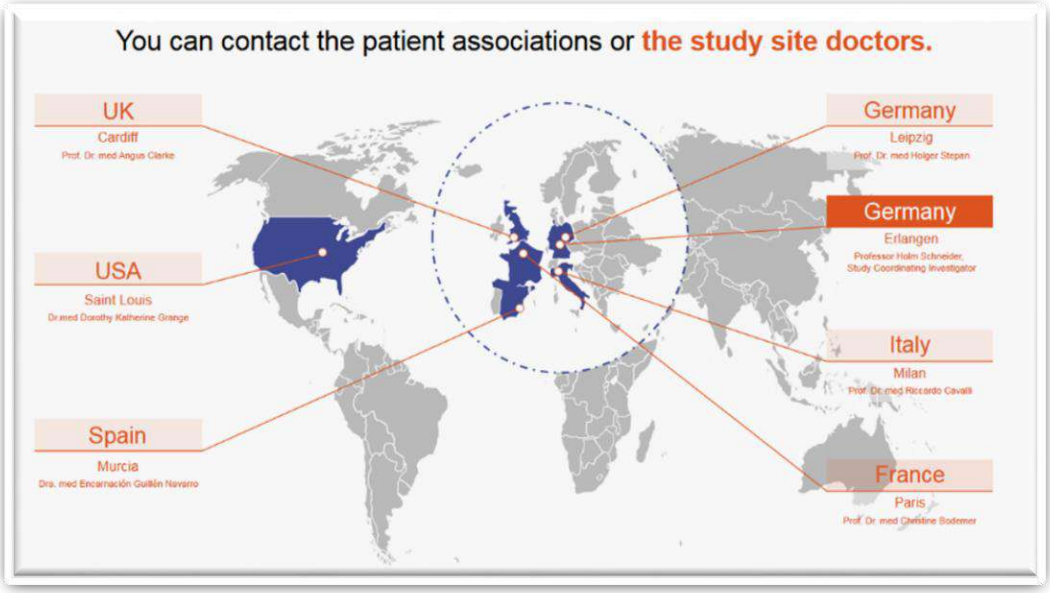


Thank you to the NFED for everything that you're doing. It is super helpful to have everything and to have been able to track it all of these years. I would not be in this seat right now had it not been for all the countless hours. I can't even imagine everything that has gone into the research to get to this point. Thank you for everything. Bennett is the most amazing, amazing little guy ever!" - Laura Reiser.

At EspeRare we are very grateful to the NFED for sharing this inspiring story on its blog. Together with other Ectodermal Dysplasia patient groups, the NFED has been at the forefront of advancing research and healthcare for individuals affected with XLHED, for the best part of three decades.

THE EDELIFE CLINICAL STUDY FOR XLHED CONTINUES RECRUITING PREGNANT WOMEN

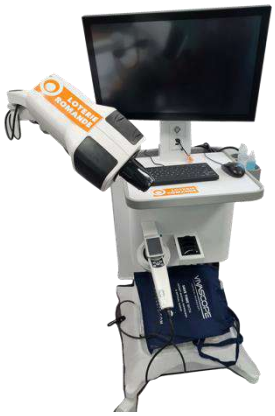
EDELIFE is a pivotal clinical study for the prenatal treatment of XLHED-affected boys. It has been set up to offer to all interested XLHED-affected families that meet certain criteria, the treatment Laura and a handful of other families benefited from. Indeed, these fetuses were treated by Prof Schneider under a "named patient use" scheme, and not within a clinical study yet.



The first investigational site opened for recruitment in Germany in November 2021, followed by the sites in France, Italy, Spain, the UK, and finally the US in August 2022 to offer to as many eligible patients as possible, the chance to participate in the clinical study.
In 2022, the first fetal patients were recruited in the EDELIFE clinical study and received three injections of the ER-004 treatment as planned. Since opening in 2022, the trial has recruited a total of 10 subjects, with more than 80 interested pregnant women contacting the clinical sites. This experimental treatment (not approved for commercial use yet) is administered through the mother's abdomen into the amniotic fluid surrounding the baby. The pivotal study aims to treat approximately 15 to 20 unborn baby boys across 8 investigational centers in Europe and the US to assess the safety and efficacy of the ER-004.

The efficacy will be measured after birth by assessing the restoration of the sweating function. Studying the development of sweat glands, which are visible as pores on the skin surface is achieved by using high-resolution imaging devices, the VivaScopes®.

Thanks to the generous support of the Swiss Lottery (Loterie Romande), EspeRare was able to fully equip the clinical sites with these devices, specific to dermatological diagnosis and essential to the successful conduct and approval of the EDELIFE clinical study.



LOTERIE ROMANDE

Interested participants are encouraged to get in touch with the Investigators or their ED Patient Associations, even if they do not live in the countries where the study is conducted, as travelling from abroad to the investigational site is allowed and expenses are covered by the study.

Based upon EspeRare's patient-centered approach, a dedicated website for interested families was co-written with patient groups, and enhanced in 2023 providing more information on the trial in 6 languages, including who can take part in the study, what taking part in the study will involve and who to get in touch with for further information. To raise awareness for the Edelife trial, the online communication campaign was launched in 2023.

Additional details are also available on www.clinicaltrials.gov.
Study NCT04980638

edelife

An open-label phase 2 trial to investigate efficacy and safety of intra-amniotic administrations of ER004 in male subjects with X-linked hypohidrotic ectodermal dysplasia (XLHED)

espeRare Pierre Fabre

OUR COMMITMENTS, PRINCIPLES AND VALUES

COMMITMENTS TO THE

XLHED PATIENT COMMUNITY

EspeRare regards the continuing engagement of the patient community as critical for the success of the programme. With its unique patient-centered approach, we fully engage the patient community at each step of the drug development process.

JOINT PRINCIPLES AND VALUES

These principles and values guide all interactions with any other stakeholders involved in the programme. Every effort is made to extend their largest application possible.

PATIENTS FIRST, including:

- Patient safety (comes first);
- Maximization of patient medical benefits and patient access to treatment;
- Ensure patient engagement and continued information sharing with the patient community.

TRANSPARENCY about roles, responsibilities, constraints, potential conflicts of interest as well as the outcomes of the ER-004 programme.

RESPECT, including:

- Fairness in all situations;
- Consultation and accessibility;
- Ability to hear and take into account diverging views;
- Equal partnership, co-learning with mutual added-values.

INTEGRITY of behaviors, processes, use of funds, as well as being driven by moral soundness and account-ability.

MAINTAINING A PATIENT-CENTERED APPROACH

EspeRare has convened a **Patient Advisory Council** (PAC), composed of patient groups representatives, whose mission is to serve as the primary interface between the XLHED patient community and the Foundation to streamline information-sharing and collect insights from the patient community for the development of ER-004. Within the framework of joint principles and values, PAC promotes patient-centeredness in the conduct of activities at different stages of the therapy development process.

Since the early development of ER-004, the patient groups representatives played invaluable role in providing the disease expertise, identifying unmet needs, participating in the discussions with authorities, and facilitating the design and recruitment process of the EDELIFE clinical study.

Clinical study design:

- Synopsis review
- Protocol feasibility
- Site selection feedback
- Glossary review for the clinical study documents

Clinical study recruitment:

- Review of study guide
- Review of study leaflet to advertise research
- Leverage on their communication channels to help recruiting families
- Advocate for EDELIFE clinical study at family conferences

ER-008

ADVANCING PRENATAL INTERVENTIONS FOR TRISOMY 21 AND PRE-ECLAMPSIA/FETAL GROWTH RESTRICTION

As part of its growing prenatal biotech pipeline, EspeRare is advancing the development of ER-008, an investigational small molecule therapy. Originally studied for cardiovascular indications, its properties make it a promising candidate for use in prenatal conditions where no effective therapies currently exist.

In Trisomy 21 (Down syndrome), which affects approximately 1 in 700 live births, cognitive impairments and neurodevelopmental alterations begin in utero. Despite decades of research, no approved therapies are available to prevent or reduce the intellectual disability associated with this genetic condition. ER-008 is being explored for its potential to modulate key mechanisms of early neuroinflammation, a major driver of the neurological damage seen in Trisomy 21. A preclinical proof-of-concept study launched in 2024 in partnership with the University of Bologna demonstrated that the compound can cross the blood-brain barrier and interact with its intended target in the central nervous system. A second phase of the research study, focused on the prenatal therapeutic window, is now underway with results expected in 2025.

In parallel, EspeRare is exploring ER-008 for the treatment of fetal growth restriction (FGR) associated with early-onset preeclampsia (EOPE), a severe pregnancy complication that can lead to life-threatening outcomes for both mother and child. EOPE is responsible for a significant proportion of preterm births and neonatal complications globally. It is characterized by poor placental development, inflammation, and systemic vascular dysfunction and impaired fetal growth.

Current treatments are limited, and early delivery remains the only effective intervention, often at great cost to neonatal health. With its novel mechanism of action, ER-008 may offer a unique therapeutic avenue to support placental function and fetal development, extending pregnancy safely and improving outcomes. In 2024, EspeRare initiated a feasibility study in partnership with Professor Anna David at University College London to define a development path for this second prenatal indication.

Together, these programmes reflect EspeRare's commitment to pioneering therapies that address severe prenatal conditions at their root, opening new possibilities to improve lifelong outcomes starting before birth.

Pediatric Care

CONTINUING OUR WORK ON INNOVATIVE THERAPIES FOR CHILDREN

In 2024, EspeRare has continued to drive forward our commitment to transforming the lives of children affected by severe and underserved pediatric diseases. This year, we continued our work on two major programmes: Rimeporide as a treatment for Duchenne Muscular Dystrophy (DMD); and the advancement of Neocare, a device for infants with life-threatening Congenital Heart Defects (CHDs).

With both programmes reaching important milestones in 2024, EspeRare is now seeking commercial partnerships that will enable bringing these life-saving innovations to the children and families who need them most.

Duchenne Muscular Dystrophy

EspeRare's DMD programme focuses on the development of Rimeporide, a novel oral therapy targeting the multi-systemic nature of Duchenne, including skeletal, respiratory, and cardiac deterioration.

In 2024, we have continued to refine our clinical strategy with international experts and regulatory bodies, while actively seeking a commercial partner to carry Rimeporide through pivotal trials and ultimately to market. The goal remains clear: to develop a therapy that meaningfully slows disease progression and improves long-term outcomes for all boys living with DMD, regardless of their genetic mutation.

Our key work in 2024 on our DMD programme includes:

- Continuing strategic engagement with the FDA and Key Opinion Leaders (KOLs) to refine trial design and positioning.
- Continuing our efforts to optimise regulatory and clinical pathways for potential accelerated approval.

Congenital Heard Defects CHD

NeoCare was developed as an adjustable, transcatheter pulmonary-artery banding system to improve survival and shorten intensive-care stays for neonates and infants with complex congenital heart disease (CHD).

Our efforts included:

- Global IP reinforced: Patent-Cooperation-Treaty (PCT) application published in December 2023, expanding international protection and freedom to operate.
- Extreme prematurity validated: Advisory testing confirmed safe deployment in neonates weighing < 1 kg.
- Route-to-market mapped: An extensive search was unsuccessful at securing a MedTech partners for scale-up and commercialisation.

Strategic reassessment of NeoCare

A combined internal review and external expert consultation found that:

- Minimally invasive surgical and fully transcatheter techniques have replaced banding as first-line care
- Rapid advances in fetal and neonatal cardiology further limit NeoCare's future clinical relevance

On expert recommendation, EspeRare has ceased all NeoCare R&D and investment on 31 December 2024. Released resources will be redirected to our rare-disease and prenatal-therapy portfolio, where patient-access pathways are clearer.

We remain deeply grateful to the clinicians, engineers, funders and families who brought NeoCare this far. EspeRare will continue to explore external avenues that might still deliver the technology's benefits to CHD patients, while concentrating our own efforts on areas with the greatest unmet need and impact potential

Duchenne Muscular Dystrophy (DMD)

ABOUT DUCHENNE MUSCULAR DYSTROPHY (DMD)

Duchenne Muscular Dystrophy (DMD) is a severe genetic paediatric disease that affects 1 in 3,500 boys worldwide.

Patients affected by DMD have progressive weakness and loss of muscle function in their early childhood. The degeneration of muscle cells is accompanied by an immune reaction (inflammation) and scarring of the muscle (fibrosis). This progressive muscle wasting typically leads to loss of ambulation (ability to walk) around 10 years of age. It eventually spreads to the arms, neck and other areas of the body.

Later in the twenties, increasing difficulty in breathing requires using a ventilator at night, while cardiac muscle dysfunction progressively leads to heart failure.

Cardiac dysfunction is present in most DMD patients and is the primary cause of premature death. While there has been recent progress in the management of these patients, heart failure is becoming the primary cause of premature death.

The use of corticosteroid is the main pharmacological intervention, but it has limited efficacy and induces severe side effects upon chronic use.

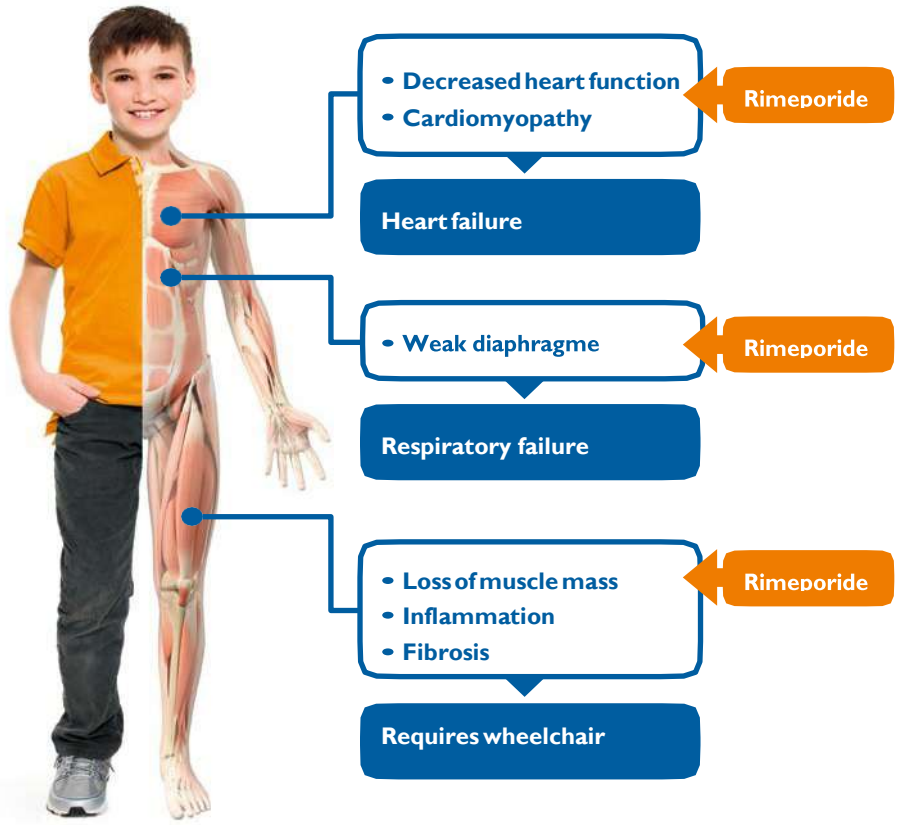
While additional therapies and treatments exist to alleviate symptoms associated with skeletal muscle pathology, they do not alter the ultimate outcome of the disease.

There is therefore an urgent need for new therapies to halt the progression of the disease and in particular treatments that help preserve heart and respiratory functions for all Duchenne boys, e.g., regardless of their mutation.

> “Treatment for Duchenne is currently largely limited to glucocorticoids that have been shown to prolong ambulation and also help to prevent scoliosis. More satisfactory treatments are urgently needed. Efforts are focused on identifying drugs or biological agents that have the potential to maintain long term muscle function alongside an acceptable side effects profile” -
>
> **Duchenne UK**
> DMD Patient Association

> “He was walking quite early but when he would come to any kind of step, he would look for something to hold on to” –
>
> **Mother of Jenson, 2023**

> “Duchenne is a heartbreaking disease. Children like Laurent, my cousin, affected with this disease are bright and engaged but as they grow up, they inexorably get weaker and experience the loss of the few abilities they had acquired. I have in my genes the eagerness to find treatments for this disease and I am committed to giving them the strength to fight their disease”
>
> **Florence Porte-Thomé**
> Founder and R&D Director



300 000 boys affected worldwide

Affects the longest gene in the body: the dystrophin gene

Symptoms appear between the ages of 2 and 5 years

Described by Dr. Duchenne in 1861

A SOLID NETWORK OF PATIENT GROUPS AND DISEASE EXPERTS TO ADVISE AND STRENGTHEN RIMEPORIDE DEVELOPMENT STRATEGY

R&D funding and collaboration with patient groups: French Telethon (AFM) & Swiss Technology & Innovation (CTI) supported research in non-clinical studies; AltroDomani Onlus, Duchenne Parent Project Onlus (PPMD) and Merck Serono support the clinical development.

Strategic partnership with clinical centers of Excellence: Great Ormond Street Hospital (London, UK), Armand Trousseau Hospital (Paris, France), Santa Creu i Sant Pau Hospital (Barcelona, Spain) and San Raffaele Hospital (Milan, Italy).

RIMEPORIDE PROGRAMME IN DUCHENNE MUSCULAR DYSTROPHY (DMD)

BACKGROUND

2013

EspeRare obtained the rights to Rimeporide from Merck KGaA.

2014 to 2018

Repositioning of Rimeporide for Duchenne Muscular Dystrophy (DMD)

Repositioning program launched to confirm the scientific hypothesis and the therapeutic benefit of using Rimeporide to prevent skeletal and respiratory damage related to the loss of dystrophin in DMD. Short- and long-term studies confirmed that chronic oral administration of Rimeporide is anti-inflammatory, anti-fibrotic, and provides a clinically relevant effect to protect the skeletal muscles, the respiratory muscle (diaphragm), and is cardioprotective.

Phase Ib clinical trial treating 20 young patients with DMD has been completed. The study showed that the administration of Rimeporide to young DMD boys (aged from 6 to 11 years old) was well tolerated. That was a significant achievement opening the way for Rimeporide to be used as a treatment to prevent muscles wasting due to the lack of dystrophin.

Orphan Drug Designation granted by the European Medicines Agency (EMA) for Rimeporide in DMD in 2015, and by the US FDA in 2017.

2019 to 2022

Designing of the next phase of clinical development for Rimeporide in DMD

EspeRare launched a large biomarker study in order to identify noninvasive biomarkers to be measured in clinical phase.

An International Scientific Advisory Board with Pr C. Spurney, Pr J. Soslow, Pr F. Muntoni, Pr P. Spitali was set up to support the designing of the clinical plan for Rimeporide as the first treatment to specifically address the life-threatening cardiomyopathy in DMD boys.

Biomarkers study results were presented at the World Muscle Society meeting in Copenhagen, DK and at the Congress of Myology in Bordeaux, FR.

In May 2020, Rimeporide programme received advice from the Duchenne Community Advisory Board (CAB), organized by the Duchenne Data Foundation (DDF). This meeting helped to integrate the patients' voice in the clinical plan.

In September 2020, Rimeporide was granted Rare Paediatric Disease Designation (RPDD) for cardio-myopathy in children with DMD by the FDA in the United States. Rimeporide is the first drug to receive a RPDD for DMD related cardiomyopathy. Rimeporide will be eligible to receive a Priority Review Voucher at the time of marketing approval.

A sound clinical plan has been developed with the Scientific Advisory Board and expert statisticians at Precision for Medicine, an organization with significant experience in rare disease clinical design, including DMD studies. A phase II efficacy study of Rimeporide in DMD boys was designed using recent natural history data (to understand the progression of the disease and the variability among patients) from DMD boys generated by key stakeholders from the community. With this new strategy, the clinical development path is de-risked and timelines to reach the market are optimized. Potential conditional approval could be achieved within 3 years of starting the phase II trial.

Late 2021 and early 2022, a new Rimeporide Business Development campaign was kicked off, aimed at finding a commercial partner to take over the next phase of development.

2023

Discussions of the phase II/III study design took place with the International Scientific Advisory Board, Patient Groups and Health Authorities to pave the way for a therapy that specifically targets DMD boys who have lost ambulation.

EspeRare has been seeking advice from the US FDA on the clinical phase II protocol as well as key aspects of the development.

FDA feedback was highly supportive of Rimeporide's further development.

In addition, EspeRare has received positive feedback from patient groups emphasizing the unique and distinctive positioning of Rimeporide. By targeting the skeletal, respiratory, and cardiac muscles, Rimeporide may offer patients the potential to prolong ambulation and ultimately shield their fragile heart from additional fibrosis.

Rimeporide is intended to be administered as an oral daily, and chronic treatment in combination with dystrophin replacement therapies and other approved treatments, in all patients with DMD, regardless of their mutation, and as soon as early signs of myocardial fibrosis are detected.

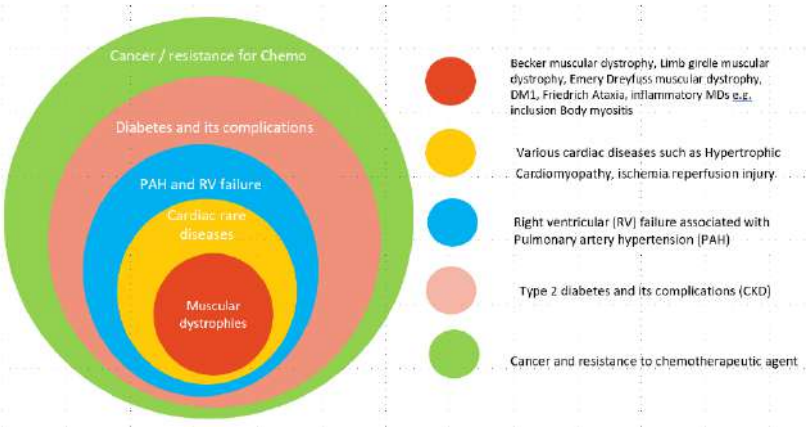
2024 and beyond

Finding the partner for the pivotal development

EspeRare received FDA feedback on the clinical study design for its upcoming Phase 2 trial in boys with DMD. Following preliminary input on data prerequisites and study design, the next regulatory step is a formal Type D meeting. Proposed cardiac clinical endpoints for this pivotal Phase 2 trial are aligned with those used in a recently submitted Biologics License Application, opening a potential path toward accelerated approval.

Separately, new preclinical data have demonstrated that Rimeporide confers significant protection against Pulmonary Arterial Hypertension (PAH), preventing functional, structural, and biochemical deterioration of the right heart and lungs. These findings position Rimeporide as a promising candidate for PAH and have been published in the *Journal of the American Heart Association*.

A pipeline in a product



Rimeporide is an NHE-1 inhibitor. NHE-1 is a Na/H exchanger that participates in the maintenance of the pH balance inside and outside the cell and the prevention of intracellular acidification. It is moreover involved in several other critical cell processes such as cell migration, proliferation control, adhesion, and apoptosis, as well as expression and function changes (that influence inflammation) and that are closely associated with a number of diseases (including cardiovascular disease and diabetes). The inhibition of NHE-1 by Rimeporide is therefore expected to bring benefit in multiple indications.

From 2020 onwards, Rimeporide has been tested in other disease indications, in addition to Duchenne Muscular Dystrophy:

Rimeporide for Pulmonary Arterial Hypertension

Pulmonary Arterial Hypertension (PAH) is one form of a broader condition known as pulmonary hypertension, which relates to high blood pressure in the blood vessels of the lungs.

PAH is a rare, progressive disorder characterized by high blood pressure (hypertension) in the arteries of the lungs (pulmonary artery) leading to right ventricular failure and premature death. Symptoms of PAH include shortness of breath (dyspnea) especially during exercise, chest pain, and fainting episodes. Although treatable, there is no known cure for the disease. It is important to treat PAH because without treatment, high blood pressure in the lungs causes the right heart to work much harder, and over time, this heart muscle may fail.

- EspeRare has collaborated with the Lausanne University Hospital (CHUV) to confirm the utility of Rimeporide for patients suffering from pulmonary hypertension, addressing both the pulmonary vascular resistance and the maladaptive right ventricular failure.
- During that collaboration, the efficacy of Rimeporide in PAH models was confirmed. Chronic curative treatment with Rimeporide was shown to partially reverse PAH, with results not seen with available PAH drugs. Rimeporide elicited a decrease in right ventricle fibrosis and pulmonary vascular fibrosis.

Rimeporide Patent filing for coronavirus infections

While knowledge around the COVID-19 multifaceted illness has progressed, EspeRare has been looking into the potential of Rimeporide to address the cardiovascular life-threatening complications occurring after virus infection, with potential for application in the setting of long-term COVID-19 cardiovascular complication prevention and treatment. In August 2020, EspeRare co-filed with Merck KGaA a priority patient application. Data on the potential benefit of Rimeporide were generated and confirmed the utility of adding Rimeporide to the arsenal of multiple drugs that work in different ways to prevent life threatening complications related to Coronavirus infections. This data was added to the patent and a European PCT was filed in 2021 and subsequently published in March 2022 (International Publication Number WO 2022/043343 AI). The national phase of this patent application started in February 2023. Due to limited funds, the geographic focus of this invention was limited to the US, EU (including the UK and Switzerland), Canada and Japan. EspeRare has collaborated with the European Patent Office to refine the patent claims, including the likelihood of approval.

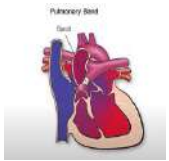
Congenital Heart Defects (CHD)

SEVERE CONGENITAL HEART DEFECTS IN NEWBORNS AND PULMONARY ARTERY BANDING (PAB)

Congenital heart defect (CHD) affects 1 in 100 newborns each year. In 5% of cases the severity of CHD is life-threatening and is responsible for the largest proportion of mortality caused by birth defects. Severe cases are treated by cardiac surgery at birth; when this is not possible, because the health status of the neonates, in particular premature neonates, does not allow open heart surgery at birth, pulmonary artery banding (PAB) is used as a palliative technique to control blood flow in the pulmonary artery (PA) and avoid subsequent development of life-threatening issues known as a pulmonary vascular resistance. With standard PAB, additional surgeries are often required to adjust the PAB and the blood flow in the pulmonary artery. This impacts survival, complications, and the quality of life of newborns and their families and implies prolonged hospital stays.

A REMOTELY ADJUSTABLE DEVICE DESIGNED TO OVERCOME CHALLENGES OF CONVENTIONAL PAB

Conventional Pulmonary Artery Banding (PAB) which consists of a simple GORE-TEX band is far from being optimal for newborns and infants with severe congenital heart defects. The band is placed under general anesthesia and artificial respiration which makes the adjustment of the device very difficult. Long stays in intensive care and further operations to readjust the band tightness are sometimes required. Moreover, GORE-TEX band often leads to scarring and fibrosis of the Pulmonary Artery (PA) vascular walls and requires PA's reconstruction at the time of PAB removal. This situation is traumatic to newborns and their parents, and results in increased mortality and morbidity.



This problem is even more acute in developing countries where surgery and post-operative care are often basic at best.

To address this high unmet medical need, EspeRare had initiated the development of **NeoCare: a new generation of remotely adjustable medical device** that aims to regulate the blood flow to overcome challenges of a conventional PAB.

NeoCare was intended as an innovative and a life-changing device addressing the healthcare needs of patients with severe Congenital Heart Defects (CHDs). The technology which applies a Swiss watch-making precision allows to perform non-invasive adjustments of the Pulmonary Artery flow and pressure in patients with CHD.

In addition, the innovative adjustment capabilities of NeoCare would allow surgeons and cardiologists to develop new treatment possibilities tailored to the needs of their patients.

NEOCARE

NeoCare aimed to become the first life-saving device addressing key limitations of traditional Pulmonary Artery Banding (PAB) applicable to a broad population of patients suffering from Congenital Heart Defects.

PAB is a palliative approach to open heart cardiac repair used in patients with CHDs to prevent irreversible damage to the lungs and the heart due to over circulation.

The NeoCare device was indicated for newborns, infants, and children up to adults born with life threatening Congenital Heart Defects. This device was designed to reach a broad number of patients, in particular premature neonates who cannot tolerate an open-heart surgery at birth.

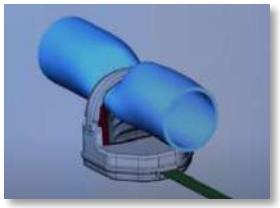
THE DEVICE

NeoCare has been developed by leveraging on public and philanthropic funding. It was designed as a miniature, implantable and battery-free device suited for banding arteries.

The technology that applies a Swiss watch-making precision, allows to perform non-invasive adjustments of Pulmonary Artery flow, especially in premature newborns.

NeoCare is composed of an implant that is placed around the pulmonary artery and controls the flow with an external control unit. Once implanted, the banding of the pulmonary artery can be adjusted remotely through the chest avoiding repeated surgeries to adapt its tightness.

NeoCare regulates the blood flow whilst preserving the circumference and anatomical properties of the PA. As a result, no reduction in elasticity of the PA tissue occurs and crucially, fibrosis is avoided.



At the time of cardiac repair, the device aims to be simply removed, and the PA spontaneously expands back to its original anatomy.

A CONSORTIUM TO SET THE GOLD STANDARD FOR SAFE AND EFFICIENT PAB DEVICE WITH ACADEMIC ENGINEERING PARTNERS:

The first challenge for the NeoCare system was to miniature the banding device to make it match to the neonatal anatomy. The second challenge was to accurately, safely and efficiently regulate blood flow and pressure in the pulmonary artery of various diameters in order to prevent irreversible damage of overflow to the lungs.

At end of 2-year collaboration with the School of Engineering and Management (HEIG-VD) funded by the Innosuisse Confederation first NeoCare prototypes were successfully produced.

Thanks to its unique geometry, design and precision the device aims to be fully applicable to a broad population of patients suffering from multiple Congenital Heart Defects, including premature or small babies of less than 1kg, as confirmed by the Advisory Board.

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra
Swiss Confederation
Innosuisse – Swiss Innovation Agency

HEIG VD

COMMUNITY IMPACT

NeoCare as an innovative and potentially life-saving device, was designed to bring many therapeutic benefits for CHD community members and the healthcare actors. It sought to avoids re-operations, reduces hospitalization stays in the intensive care unit and releases some of the financial burden on the healthcare system at large. Ultimately aiming at a safer and quicker management of heart conditions with higher survival chances in severe cases.

LONG-TERM VISION

After a detailed internal review and external expert consultation, we concluded that NeoCare no longer meets an unmet clinical need. Less-invasive surgical and transcatheter solutions have become the preferred standard for pulmonary-artery banding, and recent advances in neonatal and fetal cardiac care further limit the device's relevance. On our advisers' recommendation, EspeRare will halt development and end all investment in NeoCare on 31 December 2024.

Resources released by this decision will be redirected to rare-disease and prenatal projects with clearer patient-access pathways, in line with our mission. We remain grateful deeply to the clinicians, engineers, funders and families who brought NeoCare this far, and we will continue to explore external avenues that might still deliver its benefits to patients.

Organisation

The Board and the management team constitute EspeRare's statutory structure.

The Board is the supreme body that ratifies all decisions. In line with EspeRare's not-for-profit status, Board members act on a voluntary basis. They are key opinion leaders in the healthcare and rare disease space. Sharon Terry, an innovator in patient advocacy and rare diseases, holds the position of President. She is also named orphan diseases hero by the US congress, and the CEO of Genetic Alliance and the iHope Genetic Health program, USA.

The strategic and day-to-day activities are managed by the management team, appointed by the Board. Ad-hoc committees such as the Scientific Advisory Committee and the Business Advisory Committee have also been constituted to support the development of the Foundation.

The Management Team drives a number of employees, part-time consultants and volunteers to deliver on EspeRare's objectives.

EspeRare has significantly scaled up its workforce to support its growing portfolio of therapeutic programmes.

> "Fostering access to health for patients that are the most in need is what this Foundation is about, and is what I am about" –
>
> **Béatrice Greco**
> Founder and Board Member

THE FOUNDATION BOARD

SHARON F. TERRY

Sharon Terry is President of EspeRare and CEO of Genetic Alliance, a network of more than 10,000 organisations, including 1,200 disease advocacy organisations. Genetic Alliance enables individuals, families, and communities to become full participants in the medical research process. She is the founding CEO of PXE International, a research advocacy organization for the rare genetic condition pseudoxanthoma elasticum. She is, among others, a member of the Executive Committee of the International Rare Disease Research Consortium and the US personalized medicine initiative, a member of the Board of Telethon-Italy and an Ashoka Fellow. Sharon links EspeRare with patient organisations and orphan disease advocacy.

BÉATRICE GRECO

Béatrice Greco is a co-founder of EspeRare. She is a Board member and plays an active role in the Executive Committee. Béatrice has a strong background in neurosciences. In the Serono pharmacology department, she led a number of drug discovery projects while heading the translational testing of investigational drugs. Since 2009, within the Platform of Global Health she has led novel and integrated translational research programs in neglected diseases. Béatrice's passion for innovation and her particular interest in applying science to address vulnerable patients naturally drove her to co-develop this Foundation.

EWEN SEDMAN

Ewen Sedman was appointed a SVP Strategy and Business Operations at Merck Healthcare until the end of 2021. He has led key projects and functions from early discovery research to late-stage clinical development in a variety of different therapeutic areas. Previously he was responsible for the successful build-up of the Neurodegenerative Disease Research unit at Merck Serono. Ewen brings to EspeRare a wide range of leadership expertise across the whole pharmaceutical R&D value chain.

ERIN GAINER

Erin Gainer is a Board member of EspeRare. She has a pharmaceutical industry and not-for-profit experience spanning from drug development , chief executive, board member, and philanthropist roles. In 2017, Erin created the Ella fund, a venture philanthropy fund devoted to backing social entrepreneurs working to empower women worldwide through education, health, and entrepreneurship. Erin provides her expertise in R&D, fundraising and business development to support the growth of EspeRare's therapeutic pipeline, patient engagement, and innovative health management approaches.

BERTRAND KIEFER

Bertrand Kiefer is a distinguished member of the Geneva and Swiss scientific community and a newly appointed Board member of EspeRare. He served for 12 years as a member of the Swiss National Commission for Ethics in the Human Domain. After receiving his medical degree in infectious diseases from the University of Geneva, Dr. Kiefer studied theology and philosophy of science at the University of Fribourg and then in Rome, before engaging in bioethics research. Bertrand is the editor-in-chief of the Swiss Medical Journal and the author of over 600 articles, columns, and editorials. He brings to EspeRare a wealth of experience in medicine and ethics to help guide the Foundation through the next stages of its development.

MANAGEMENT TEAM

CAROLINE KANT

Founder & Executive Director

After supporting the build-up of an IT start-up in Silicon Valley and a successful career in the pharmaceutical industry, Caroline Kant co-founded and has led EspeRare since 2013. A formal Vice-Chair of the Geneva University Hospitals and alumna of the Swiss Board School, she is a recognized leader in patient-centered drug development, pioneering innovative paths in pharma and tech. As such, Caroline is realizing her dream of tackling rare diseases in honor of her daughter and for all children affected by orphan conditions. An award-winning entrepreneur and an ASHOKA fellow, she also advises leading NGOs on applying venture philanthropy and social entrepreneurship to pressing global health challenges. Educated in Switzerland and the United States, she holds degrees in neurobiology and product development.

FLORENCE PORTE-THOMÉ

Founder and R&D Director

Florence Porte is in charge of leading and developing EspeRare's R&D portfolio and platform, selecting new programmes and driving them until proof of concept in patients. After a successful carrier of 20 years of experience in pharmaceutical R&D, in particular leading translational research and managing clinical studies within the pharmaceutical industry, Florence co-founded EspeRare. Growing up with a cousin affected with Duchenne Muscular Dystrophy and seeing him gradually decline, Florence has an unconditional motivation to drive this EspeRare forward.

ALEXANDRA CARREL

Outside Legal Council

Alexandra Carrel is an attorney with over twenty years of experience in international legal practice, specializing in technology transfer and the development of innovative products, including drugs, medical devices, digital platforms. Former General Counsel and Secretary General of Inserm Transfert, she is now a partner at MCE LEGAL in Switzerland and founder of Cabinet CARREL with offices in Paris and Lyon. Her expertise spans French, Swiss, and U.S. law, and she brings deep proficiency in managing international operations and strategic alliances. Alexandra serves as external legal counsel to the Foundation, advising on intellectual property, partnership agreements, regulatory compliance, corporate governance, and risk management, thereby safeguarding EspeRare's legal interests in all its activities.

SEBASTIEN MAZZURI

Prenatal Platform Development Director

Sébastien brings to EspeRare two decades of international experience spanning clinical medicine, strategy consulting, biotech innovation, and global health. After training as a medical doctor at the University of Geneva and earning an MBA with distinction from INSEAD, he held senior roles at McKinsey & Company, Apax Partners, and the global impact advisory firm FSG, where he led the Europe office and spearheaded health innovation strategies for leading life sciences companies, foundations, and public-private partnerships. At EspeRare, Sébastien leads the Prenatal Therapy Initiative, providing strategic and operational leadership to advance cutting-edge treatments for neglected conditions before birth. His work integrates scientific foresight, cross-sector collaboration, and ethics-driven governance to shape the future of prenatal medicine.

URSULA VOGEL

Chief Business Officer

Ursula works with EspeRare in an advisory capacity for various development projects. She has over 25 years of global Biopharma industry experience, having started her career at Merck Sharp & Dohme and Sanofi, followed by a pivotal leadership role at pioneering US biotech Genetics Institute where she set up and managed the European affiliate until its acquisition by Wyeth (now Pfizer). She has been a major contributor to the success of 2 marketed products (*Infuse®/InductOs, BeneFIX®*). Since 2000 she has worked as an independent consultant helping conclude a multitude of licensing transactions and bring biopharmas to successful exits. Her main focus areas are Business & Corporate Development, and C-level or Board level representation. She holds a PhD from Cambridge University, and an MBA from INSEAD.

TEAM

RESEARCH AND DEVELOPMENT

ISABELLE AELBRECHT
Translational Project Leader
Isabelle is a PharmD and brings over 25 years of experience in the pharmaceutical industry, with strong expertise in clinical project management and strategic program leadership across both large and small biopharma companies. At EspeRare, she leads the translational development of ER-008 in Down syndrome and fetal growth restriction, providing strategic, technical, and operational oversight.

CHRISTOPHE BARCELLA
Quality Management Advice
Christophe is President of Montrium GXP Consulting and auditor. He brings EspeRare over 27 years of international experience in GxP regulatory compliance as per ICH, EMA, FDA regulations & directives, and in quality management.

ANNE-SOPHIE CLERMONT
Translational Project Leader
Anne-Sophie has 15 years of experience in pharmaceutical and biotechnology laboratories. She specializes in Quality Assurance, Clinical project management and operations from phase 1 to pivotal phase 3. At EspeRare Anne-Sophie is responsible for the development of the ER-004 project and the maintenance of its quality system.

DR. ALICIA DAEDEN
Prenatal Research and Technology Innovation
Alicia brings over a decade of experience in biomedical research from leading institutions including the University of Geneva, University College London, and the London Centre for Nanotechnology and holds a Ph.D. in biophysics, and engineering from the Ecole Supérieure de Biotechnologie de Strasbourg, and a Master's degree in health and drug discovery. Alicia is a Scientific Associate at EspeRare, where she contributes to the exploration of innovative opportunities in the prenatal therapy space.

OLIVIER FAVRE-BULLE
Chemistry, Manufacturing & Control
Olivier brings over 25 years of experience in the pharmaceutical industry, supporting companies and clients in the development of biologics. He is currently advising EspeRare on the manufacturing and commercialization strategy for ER-004, a protein replacement therapy.

AGNÈS JAULENT
Project Leader & Alliance Manager
Agnès studied for her PhD in chemistry at Imperial College London. She is an expert in all fields pertaining to peptide chemistry and brings academic and industrial experience in developing New Biologics Entities to EspeRare as a clinical programme leader for ER-004, for the CMC and Business Development. Agnès is also responsible for developing patient-centered approach and implementing patient engagement strategy.

PIERRE-AXEL MONTERNIER
Non-clinical development
Pierre-Axel Monternier holds a PhD in biology and brings over 10 years of experience in scientific research, including 6 years dedicated to advancing pharmaceutical development for rare and metabolic diseases. His expertise covers preclinical pharmacology, drug repositioning, and regulatory strategy. After experiences in both biotech companies and academic research centers in France and the U.S., he is supporting EspeRare as a consultant in non-clinical development focusing on bridging early-stage research with clinical translation for innovative therapies (Down syndrome and Foetal Growth restriction)

ANNA CHIARA NASCIMBENI
Discovery and Biomarker Expert
Anna Chiara holds a PhD in Neurosciences and a postgraduate specialization in Medical Genetics. She was previously involved in research and diagnosis on rare neuromuscular diseases and cell biology research, mainly on autophagy. At EspeRare, she is responsible for new therapeutic discovery in drug repositioning.

CAROLE PUGH
Regulatory Affairs
Carole is Managing Director at EUDRAC Limited, a regulatory consultancy company (UK). She has worked with small start-up, mediumand large global companies during her time at EUDRAC, and performed due diligence activities, undertaken agency scientific advice procedures and presented oncurrent regulatory intelligence topics. She oneofEspeRare's regulatory affairs consultant.

ERIC TEILLAUD
Chemistry, Manufacturing & Control
Eric has over 30 years of experience in pharmaceutical R&D and quality. Now he runs his own consultancy firm that offers services in drug development strategies and pharmaceutical quality management. He brings to EspeRare his experience in Quality and Chemistry, Manufacturing and Control.

FINANCE AND ADMINISTRATION

SARAH DELACOSTE
Accounting & Human Resources
Sarah is an accounting and controlling specialist. In addition, she combines Human Resources and IT expertise. She is active in not-for-profit organizations for various humanitarian causes engaged in creating a better world. At EspeRare, Sarah links ledger accounting to reporting and auditing activities, as well as supports Human Resources Management.

ANNA HEITZMANN
Internal Processes Compliance and Communication Manager
Anna has more than 15 years of experience in managing relations within the private and public sector, in various countries and cultures. She brings to the Foundation an excellent track record in managing communication and fundraising activities. Anna supports the Head Office in enhancing and sustaining a robust and compliant Quality Assurance framework by developing, documenting, and maintaining processes tailored to EspeRare's needs.

IT & BIOINFORMATICS

CÉDRIC MERLOT
BioInformatics & IT Consultant
Cédric is the CEO of Drugdesigntech which he founded in 2007. He has vast experience in Management and Bioinformatics and Data Management. He applies his expertise to support the development of the foundation's data Platform and provides IT support.

GENIX SECURITY GROUP
Cyber Security Support
The Swiss company specializes in the installation and maintenance of corporate surveillance and security systems. As a trusted partner, Genix ensures EspeRare`s digital security and applies innovative technologies which increase security. Thus, providing the Foundation with data safety and integrity and its employees with data protection.

SCIENTIFIC ADVISORS

PROF. RENATA BARTESAGHI
Renata Bartesaghi is a former Member of the Executive Committee of the Trisomy 21 Research Society and Deputy Director of the Department of Physiology at the University of Bologna, Member of the Department Board of the Department of Biomedical and Neuromotor Sciences. She is advising EspeRare in evaluating the preclinical feasibility of prenatal therapy in Down Syndrome.

PROF. MAURICE BEGHETTI
Prof. Beghetti is the medical chair of the Paediatric Cardiology and Orphan Diseases Units for the Western Swiss Hospitals. He is a European Medicines Agency expert advisor for paediatric pulmonary hypertension and congenital heart defects and has taken part in multiple paediatric drug development efforts as a medical strategic advisor for key pharmaceutical companies in the orphan space.

PROF. CHRISTINE BODMER
Prof. Bodmer is the head of the department of dermatology at Hôpital Necker-Enfants Malades in Paris, and a professor in dermatology at the Paris University. Her vast experience and know-how in paediatric dermatology, particularly rare skin disorders are invaluable for the ER-004 treatment in XHLHED.

PROF. ANNA DAVID
Prof. David is a consultant in Obstetrics and Maternal / Fetal Medicine at UCLH. Her team is developing new treatments for fetal growth restriction using maternal gene therapy and is pioneering the first clinical trial of in utero stem cell transplantation for brittle bone disease. She supports the development of the ER-004 antenatal treatment in XLHED and advise EspeRare on its prenatal strategy .

PROF. JOEL DUDLEY
Prof. Dudley was the Director of Genomic Sciences and Biomedical Informatics at Icahn School of Medicine at Mount Sinai, New York. Prof. Dudley is a world leader in computational drug repositioning and molecular profiling. In 2014, he was named one of the 100 Most Creative People in Business by Fast Company magazine.

DARIA GHIDONI
Daria Ghidoni is an Italian lawyer who has worked as Group General Counsel at Recordati for over 23 year and now acts as Of Counsel at BonelliErede. She has served as legal counsel to EspeRare and assisted in finalising contract with the University in Bologna for the Proof of Concept study with ER-008 in a trisomic mice model.

PROF. ARIANE GIACOBINO
The Former Head of the Integrated Genetics and Psychiatry Consultation Service at HUG, Down Syndrome Unit, Ariane Giacobino is now Medical Director at Hirslanden Precise, Specialist in Medical Genetics and Member of the National Consultative Ethics Committee (France) advised on neurodevelopment evolution in Down Syndrome newborns.

DR. DOROTHY KATHERINE GRANGE
Dr. Grange is a professor of Paediatrics, Genetics and Genomic Medicine at the Washington University School of Medicine in St.Louis, USA. Her areas of interest include genetic diseases, inherited disorders, birth defects, peadiatric pathology among others. Dr. Grange advises EspeRare on prenatal development programme.

DR. NEIL KIRBY
Neil is a seasoned biotech veteran and ex-CEO of Edimer Pharmaceuticals, the company from which EspeRare acquired the rights of ER-004. Neil is still involved in the ER-004 programme, providing EspeRare with strategic advice.

PROF. BARTHA MARIA KNOPPERS
Prof. Bartha Maria Knoppers is a Distinguished James McGill Professor Emerita and the Founding Director of the Centre of Genomics and Policy at McGill University. Internationally recognized for her pioneering contributions to the ethical, legal, and social implications of genomics and biotechnology, she has played a central role in shaping global policy frameworks in these domains. Prof. Knoppers is instrumental in EspeRare's Prenatal Ethics Initiative, contributing her expertise to the development of a structured guidance framework for the responsible advancement of prenatal therapies.

DR. ETHAN KUNG
Dr. Kung is an assistant Professor at the University of Clemson (USA). Dr. Kung's research integrates experimental, computational, and clinical aspects of cardio-vascular biomechanics. Dr. Kung obtained his PhD in Bioengineering from Stanford University and in Electrical Engineering from Queen's University. He is contributing to the development of NeoCare.

DR. CHRISTIAN LAVEILLE
Dr. Laveille is Director of Cavalgone and has more than 25 years of drug development experience within the pharmaceutical industry and has also contributed to several registrations for new drug applications. He is EspeRare's advisor in pharmacology and toxicology.

ELIZABETH LUNDINGTON
Elizabeth holds a PhD in Biostatistics from the University of Iowa and a MA in Mathematics/ Statistics from Boston University. Elizabeth Lundington has approximately 20 years of experience in providing statistical, technical, and strategic expertise for pre-clinical studies, INDs, Phase 1-Phase 4 clinical studies, eCTDs, and post-marketing requirements.

PROF. TIPPI MACKENZIE
Prof. Mackenzie is a world renowned paediatric and fetal surgeon as UC San Francisco, focused on developing better ways to diagnose and treat genetic diseases before birth. She advises EspeRare on prenatal treatment modalities.

DR. ERIC M. MESLIN
Dr. Eric M. Meslin is a Senior Fellow at the PHG Foundation (University of Cambridge), Distinguished Research Scholar at the University of Miami, and Adjunct Professor at the Dalla Lana School of Public Health, University of Toronto. With a career spanning over three decades, he has held prominent roles including President and CEO of the Council of Canadian Academies, Founding Director of the Indiana University Center for Bioethics, and Executive Director of the U.S. National Bioethics Advisory Commission. Dr. Meslin brings his extensive experience in bioethics and science policy to EspeRare's Prenatal Ethics Initiative, aiding in the formulation of governance models that underpin ethical innovation in prenatal medicine.

PROF. FRANCESCO MUNTONI
Prof. Muntoni is a Paediatric Neurologist at University College London. He is one of the world's leading clinical experts of the pathological and molecular aspects of neuromuscular disorders. Prof. Muntoni is key in driving Duchenne Muscular Dystrophy medical research and drug development globally. He is the principal investigator of EspeRare's Rimeporide project in that indication.

ELIAS NYBERG
Elias Nyberg is a US Consultant in Regulatory Affairs with a strong experience and knowledge in the DMD and rare disease fields. He has been supportive in developing feedback to FDA in 2024 following EspeRare's request of advice before conducting the next phase 2 study.

VANN PARKER
Vann Parker, PhD, is a highly experienced biopharmaceutical developer with over 25 years of experience in the industry. He specializes in providing strategic advice for clinical development of drugs, preparing IND, NDA and BLA documentation and facilitates interactions with the FDA. In addition to pre-IND activities, Vann is well-versed in the application process, including Orphan Drug Designation, Fast Track, Breakthrough and Paediatric Plans.

DR. WILLIAM HUGHES PERANTEAU
Dr. Peranteau is an attending surgeon in the Division of General, Thoracic and Fetal Surgery at Children's Hospital of Philadelphia, USA (CHOP). He specializes in fetal biology, fetal and neonatal surgery, and general paediatric surgery.

PROF. RENÉ PRÊTRE
Prof. Prêtre is the Head of the Paediatric Cardio- Vascular surgery unit at Lausanne University. He is recognized as one of the world's leading paediatric surgeons, an

international leader in congenital heart defects repair. He was elected "Swiss of the year" in 2009. He advices EspeRare for the NeoCare programme.

PROF. HOLM SCHNEIDER

Prof. Schneider is a professor of Paediatrics at the University Hospital in Erlangen (Germany) and has been focusing for many years on treating children with genetic diseases. He has worked closely on the development of ER-004 for Edimer and pioneered the first intra-amniotic administrations of ER-004 to 3 unborn XLHED children. Prof. Schneider is the Principal Investigator for the upcoming clinical intra-amniotic study of ER-004 in XLHED.

DR. PASCAL SCHNEIDER

Dr. Pascal Schneider is a tenured senior lecturer and researcher at the University of Lausanne. He is a biochemist with long-standing experience and interest in the TNF family ligands, including EDA. ER-004 was originally developed in his laboratory and Pascal still lends EspeRare his expertise for this programme.

DR. TONY SCIALLI

Dr. Scialli is a specialist in reproductive and developmental toxicology and in obstetrics and gynecology. In addition to his consulting services, he is Clinical Professor of Obstetrics and Gynecology at George Washington University School of Medicine and Adjunct Professor of Obstetrics and Gynecology and of Pharmacology and Physiology at Georgetown University Medical Center.

PROF. UMBERTO SIMEONI

Prof. Simeoni is Professor of Paediatrics at the Faculty of Biology and of Medicine at University of Lausanne and Director of the Division of Paediatrics and of the Developmental Origins of Health and Disease (DOHaD) Research Unit at CHUV University Hospital in Lausanne, Switzerland. His research is oriented towards the Developmental Origins of Health and Disease. He is also highly interested in perinatal bioethics. For EspeRare, he advices the development of ER-004 antenatal treatment in XLHED.

DR. AGNÈS SAINT-RAYMOND

Dr. Agnès Saint-Raymond is a pediatrician and former Head of International Affairs at the European Medicines Agency (EMA). Throughout her career, she has significantly contributed to the development of regulatory frameworks for pediatric and orphan medicines. In her collaboration with EspeRare, Dr. Saint-Raymond provides independent expertise on the ethical and regulatory dimensions of prenatal therapy development, with a disease- and product-agnostic perspective to help shape standards applicable across the field.

DR. ELIA STUPKA

Dr. Stupka is a bioinformatics leading expert who started his genomics career in the Human Genome Project. He also led the development of the first Translational Genomics and Bioinformatics Center in Italy at San Raffaele Hospital in Milan. He is currently a strategic Advisor for many ventures in the bioinformatics space. He provides his computational biomedical expertise to develop EspeRare's proprietary data analysis platform.

BUSINESS AND STRATEGIC ADVISORS

DR. DIEGO BRAGUGLIA

Dr. Braguglia is General Partner at VI Partners AG focusing on life-science and biotech investments. He held various managerial positions in the pharmaceuticals and medical devices sectors as well as in biotech start-ups in Europe and United States. He also serves or has served on the Board of various biotech and MedTech companies and as Director of Swiss Private Equity & Corporate Finance Association. He brings Business Development advice to EspeRare.

DR. DJORDJE FILIPOVIC

Dr. Filipovic is Chief Executive Officer of AB2 Bio Ltd. and a seasoned pharmaceutical executive with over 20 years of experience in R&D, marketing, strategic leadership, and general management across global markets. Formerly a senior leader at Novartis, he oversaw late-stage development and commercialization of key assets in oncology and immunology. He brings Business Development and Commercial Strategy expertise to EspeRare, particularly in the field of pediatric and ultra-rare diseases.

DR. ALEXANDRA RICHARDSON

Dr. Richardson heads marketing and business development for Clayton Biotechnologies, Inc. She has over 15 years of experience in licensing and managing intellectual property portfolios. She has assisted in the creation of several biotech start-up companies. Alexandra advices EspeRare in Intellectual Propriety and Business Development topics.

DR. TIMOTHY WELLS

Dr Timothy Wells is the Distinguished Scientist at Medicines for Malaria Venture (MMV). He was the Chief Scientific Officer from 2007-24, and led the team which launched 13 new products and co-created a pipeline of over 30 new medicines. Prior to MMV he was Head of Research for the Swiss biotech company Serono, and has advised a number of companies and investments, including being a non-executive director at Kymab. He has a PhD in Chemistry from Imperial College, UK, and an ScD in Biology on cytokine biology from Cambridge UK. As Strategic R&D Advisor to EspeRare, he brings deep portfolio-crafting expertise, alliance leadership and a decades-long record of translating breakthrough science into first-in-class therapies for vulnerable and under-resourced populations.

Financial view

NB : For ease of reading, all the amounts are rounded

EspeRare receives funding from project partners, patient associations, private foundations and donors as well as international, governmental and public bodies. These funds are used to finance EspeRare's diverse activities geared towards accelerating the cost-effective development of unexplored therapeutic opportunities for rare neuro-muscular, cardiovascular, and dermatological diseases. In partnership with patient organizations, EspeRare addresses the drug development gaps as well as ethical and clinical development challenges in rare and prenatal therapies, acting as trusted partner for pharmaceutical companies, academic centres, and regulatory agencies to drive effective development and foster affordable access to new treatments for rare disease patients. Established as a not-for-profit Swiss foundation under statutes dated 28 March 2013, EspeRare is managed by a Foundation Board, 3 directors managing 5 employees, and 28 contractors.

EspeRare as an organisation is exempt from cantonal and federal taxes and is the equivalent of an exempt organization within the meaning of Section 501(c)(3) of the United States Internal Revenue Code. Accounting is outsourced to a local accounting firm, D-Fox Sàrl while KPMG Switzerland acts as an external auditor.

A global banking relationship was created with a major Swiss bank for current accounts and cash-management facilities in multiple currencies.

THE FINANCIAL YEAR TO 31 DECEMBER 2024

Throughout 2024, several notable factors shaped the year. The Foundation directed the efforts towards enhancing its prenatal R&D portfolio, notably prioritizing the ER-004 (p. 14) and Trisomy 21 (p. 23) programmes. Additionally, the focus was given, to the development of the prenatal platform, including laying the foundation for the Ethics and Oversight Observatory to provide an ethical and regulatory framework in this emerging therapeutic field.

A prenatal medical director was onboarded, the overall staff was maintained, and contractors were recruited to address the growing focus on prenatal activities and its programs. By the end, the portfolio consisted of 5 active R&D programs and the development of a Prenatal enabling Platform.

R&D expenditures in 2024 amounted to CHF 1'893'921. Income from R&D activities amounted to CHF 744'249 while income from Donations amounted to CHF 1'287'275 (note 7).

Overall, this year, the Foundation generated a deficit of CHF 11'659.

Founding Capital

The Capital Fund of CHF 50,000 contributed by the three founders, was already fully subscribed on 31 December 2013.

Donations

Donations recognized in 2024 amounted to CHF 1'287'274 and consisted of CHF 328'736 received from Espoir XLHED Sàrl for R&D program activities and CHF 900'000 donation from a Private foundation for the Prenatal prenatal platform and the Trisomy 21 program. In addition, two CHF 150'000 grants were received in 2022 from the Loterie Romande (GE and VD).

Both grants were used to buy two medical devices needed for the EDELIFE clinical study (p. 21) and have been accounted as fixed assets.

In 2024, from these Loterie Romande grants CHF 29'914 were recognized, and the remaining portions of these grants were distributed as short-term and long-term differed income. Donations received to cover future activities are deferred to the balance sheet for a total amount of CHF 168'074. From this amount CHF 58'538 is allocated to short-term activities and CHF 109'536 to long-term activities and CHF 168'074 (note 7).

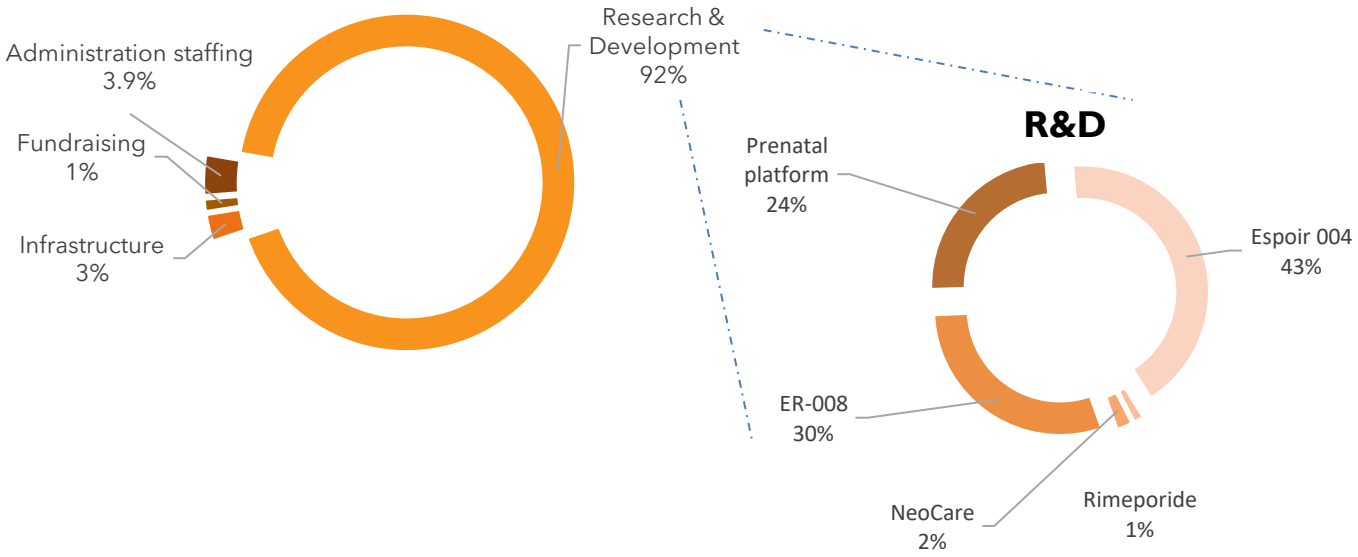
Staff

At end-year the C-level management team consisted of an Executive Director, an R&D Director and a Prenatal Director. The administrative, fundraising and program management activities were run by 5 employees, and 28 contractors and with the support of many other people including Board Members, Senior Scientific Advisors and Volunteers.

General Administration

The total 2024 general and administration expenses amounted to CHF 224'452 as compared to CHF 310'794 in 2023. Expenses here reflect the Foundation's general expenses in overall support of R&D activities (note 8g).

SNAPSHOT OF ESPERARE EXPENDITURE 2024



THE FINANCIAL YEAR AHEAD TO DECEMBER 2025

EspeRare operates in a complex multi-currency environment in Geneva, Switzerland. The bulk of donations are currently received in CHF, although other currencies such as EUR and USD are also involved. Outflows for projects are mainly in CHF and EUR as per the agreements signed between Pierre Fabre Médicament and Espoir XLHED Sàrl. Clinical activities expenses for ER-004 decreased in 2024 as the project entered a steady development phase. The expenses continue to be cross-charged to Espoir XLHED Sàrl in EUR. The resulting exposure of exchange risk is evaluated at the beginning of each calendar year, to provide a realistic fixed EUR/CHF budget rate for the year. The accounts are kept in CHF.

A well-developed treasury management and accounting approach, matching inflows to outflows by currency and taking timely multi-currency investment and foreign exchange decisions is now in place.

The philosophy underlining EspeRare's financial management is that of prudent, conservative control, including appropriate return on interim treasury investments, coupled with the use of the latest IT solutions for bank information, transfers and accounting requirements. As the EspeRare portfolio of therapeutic programmes is maturing and strategic investments in prenatal R&D activities expend, the foundation's need for financial support needs are intensifying.

EspeRare's fundraising efforts are being challenged by growing global geopolitical uncertainty. In line with its fundraising strategy and organizational maturation, EspeRare—internationally recognized as a frontrunner in prenatal therapeutic innovation—is intensifying funding efforts to scale its activities, with a strategic focus on its pioneering prenatal initiatives. This strategic acceleration aims to address the pressing needs of children with rare diseases that cannot be treated postnatally.

Conclusion

The detailed financial tables that follow - Balance Sheet and Statement of Income and Expenditure – represent EspeRare in its twelve years of operation where all the various basic financial components of the organization have been established step by step to create a prudent, transparent financial management framework. The rapid expansion of EspeRare's operations has been hindered by inflation, economic and geopolitical challenges arising from the ongoing global instability. Despite these external challenges, the ER-004 partnership with Pierre Fabre shall secure organisational continuity for the upcoming years.

In addition, funding received in 2024 to expand its prenatal activities is enabling the Foundation to extend the reach of its mission. Furthermore, the Foundation is striving in the most efficient way to reach its major goal: the discovery and development of new therapeutic interventions for the treatment of rare diseases and drive progress in the space of prenatal treatments.

ESPERARE BALANCE SHEET

ASSETS		NOTES	2024 CHF	2023 CHF
Current Assets				
	Cash & Cash Equivalents		960 460	2 290 847
Prepaid & Receivables				
	Trade Accounts Receivable	11	167 387	7 018
	Other Current Receivables		12 394	10 555
	Prepaid Expenses and Accrued Income		64 572	79 428
TOTAL CURRENT ASSETS			**1 204 813**	**2 387 848**
Non-Current Assets				
	Financial Assets	4a	11 382	11 156
	Investments	4b	20 000	20 000
	Tangible Fixed Assets (Equipment)	2d	351 574	363 358
	(less depreciation)		(185 452)	(137 866)
TOTAL NON-CURRENT ASSETS			**197 504**	**256 648**
TOTAL ASSETS			**1 402 317**	**2 644 495**

LIABILITIES		NOTES	2024 CHF	2023 CHF
Short Term Liabilities				
	Trade Accounts Payable	2h	167 158	84 852
	Other Short Term int. Bearing Liabilities (COVID)	16	33 416	33 416
	Accrued Expenses	2g	224 201	216 324
	Short Term Deferred Income	7a	58 538	1 287 274
			483 313	**1 621 866**
Long Term Liabilities				
	Covid Loan	16	58 464	91 880
	Long Term Deferred Income	7a	109 536	168 074
TOTAL LIABILITIES			**651 313**	**1 881 820**
Capital & Reserves				
	Foundation Capital	10	50 000	50 000
	Operations Reserve	3	713 663	665 509
	Net Excess of (Expenditures)/Income		(11 659)	47 166
TOTAL CAPITAL AND RESERVES			**751 004**	**762 675**
TOTAL LIABILITIES AND CAPITAL			**1 402 317**	**2 644 495**

ESPERARE STATEMENT OF PROFIT AND LOSS

	NOTES	2024 CHF	2023 CHF
TOTAL INCOME	7	**2 034 611**	**1 892 841**
Research & Development Expenses	8		
Espoir-004 Project	8a	(803 586)	(868 093)
Rimeporide Project	8b	(26 729)	(169 788)
NeoCare Project	8c	(40 393)	(122 908)
Espoir-008 Project	8d	(563 352)	
New Projects	8e	(3 928)	(96 339)
Prenatal Platform	8f	(455 933)	(245 209)
TOTAL RESEARCH & DEVELOPMENT EXPENSES		**(1 893 921)**	**(1 502 337)**
General Foundation Administration	8g	(224 452)	(310 794)
Operating Result (Expenditure)/Income		**83 762**	**79 710**
Financial Income & Expenses	9	22 244	(32 544)
Non-operating & Extraordinary Income & Expenses	12	49 859	-
NET EXCESS OF (EXPENDITURE) / INCOME		**(11 659)**	**47 166**

NOTES TO FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2024

1. ORGANISATION

The EspeRare Foundation ("EspeRare") is a Swiss Foundation, established as a not-for-profit legal entity, registered in Geneva under statutes dated 27th March 2013 and in accordance with article 80 and those that follow of the Swiss Civil Code. It is managed by a foundation board, an executive director, R&D director and 2 senior managers.

With its head office in Geneva, the aim of EspeRare is to bring public and private sector partners together to both fund and provide managerial and logistical support to drive the identification and development of treatments for rare diseases. The Foundation focuses on selecting deprioritized therapies and technologies assets with high therapeutic potential in rare diseases and accelerating their cost-effective therapeutic development. In partnership with patient organizations, EspeRare addresses the key translational gaps and clinical development challenges, acting as a trusted partner for pharmaceutical companies, academic centers and regulatory agencies to drive effective development and foster accessible access to new treatments for rare disease patients.

As with all Swiss foundations recognized for international public good, EspeRare is oversighted by the Swiss Federal Supervisory Board for Foundations.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

The significant accounting policies adopted by EspeRare in the preparation of the financial statements are set out below.

a. Accounting principles

The accounting principles followed are those of the Swiss Code of Obligations, specifically the 32nd Title.

b. Recognition of donations

Contributions from donors (both public, private and philanthropic sources) are recognized in the financial statements when they have been received or confirmed in writing by pledges. Contributions which are subject to donor-imposed stipulations for a specific purpose or use in future years may be deferred or attributed to a restricted reserve according to the particular nature of the specified conditions.

c. Foreign Currency Transactions

Transactions in foreign currencies are translated at the foreign exchange rate ruling at the monthly average rate.

Monetary assets and liabilities denominated in foreign currencies at the balance sheet date are translated to CHF at the foreign exchange rate ruling at that date. Foreign exchange differences arising on translation are recognized in the profit and loss statement except for unrealized gains taken to the Balance sheet according to the imparity principle. Non-monetary assets and liabilities that are measured in terms of historical cost in a foreign currency are translated using the exchange rate at the date of the transaction.

The following exchange rates were used at year-end:

2023	2024
1 EUR = CHF 0.929700	1 EUR = CHF 0.938450
1 USD = CHF 0.841624	1 USD = CHF 0.906250
1 GBP = CHF 1.072875	1 GBP = CHF 1.135038

d. Fixed assets

Fixed assets are stated at cost less accumulated depreciation. Depreciation is charged to the statement of income and expenditure on a straight-line basis over the estimated useful lives of the assets. The estimated useful lives of assets are as follows:

i. office furniture (second hand and low cost) 3 years
ii. office furniture (new) 5 years
iii. special imaging equipment 5 years
iv. fixtures and installations 3 years
v. computer and equipment 3 years
vi. special medical equipment (Vivascopes) 5 years

Assets	2023	Acquisitions	Disposals	2024
IT Equipment	38'614	3 ;206	15'040	26'780
Furniture	32'104		-	32'104
Special equipment (Vivascopes)	292'640	50		292'690
Total	**363'358**	**3'256**	**15'040**	**351'574**

Depreciation	2023	Depreciation	Disposals	2024
IT Equipment	32'424	3'898	14'899	21'422
Furniture	32'104			32'104
Special equipment (Vivascopes)	73'338	58'587		131'925
Total	**137'866**	**62'485**	**14'899**	**166'123**

Total net value	**225'492**			**166'123**

e. Research and Development

Expenditure and grants are allocated for research activities with the prospect of gaining new scientific or technical knowledge and understanding in order to progress the development of therapeutic assets in rare diseases. They are recorded on a contract or letter of understanding basis, the expense being accounted by EspeRare at the moment of allocation and initial payment. In the case of any portion remaining unpaid at the year-end, it is included under current provisions and accruals.
Regulatory and other uncertainties inherent in the development of new products in this sector preclude EspeRare from capitalizing development costs.

f. Provisions

A provision is recognized in the balance sheet when EspeRare has a present legal or constructive obligation as a result of a past event, and in EspeRare's opinion it is probable that an outflow of economic benefits will be required to settle the obligation.

g. Accrued Expenses

An accrual is recognized in the balance sheet when EspeRare has a fair certitude of the outflow of economic benefits that will be required to settle the expense.

h. Accounts Payable

In 2023, EspeRare has been contacted by INSERM requesting an amount of 62'500 EUR from a research collaboration in 2016 to 2018. The Foundation does not agree on the open amount and is currently supported by the Legal department. In order to respect the caution principle, The Foundation has recognized the full amount in payable.

i. Employee Benefits

Pension Plan

EspeRare's pension plan is classified as a defined contribution plan. Contributions to the pension plan are recognised as an expense in the statement of income and expenditure as incurred. No amount was recognized as payable to the CIEPP in 2024 (2023: nil) and an accrued expense of CHF 9'229 to the FER CIAM for the old age insurance in 2024 (2023: CHF 6'677).

j. Cash and Cash Equivalents

Cash and cash equivalents comprise cash balances of current accounts and are valued at nominal value.

k. Impairement

The carrying amounts of the EspeRare's assets are reviewed at each balance sheet date to determine whether there is an indication of impairment. If any such indication exists, the asset's recoverable amount is estimated. An impairment loss is recognised whenever the carrying amount of an asset exceeds its recoverable amount.

l. Financial Income

Interest income is recognized in the income statement as earned.

m) Income Tax

EspeRare has received exoneration from income tax from the Geneva cantonal and Swiss federal authorities from the year 2013 for 10 years and a renewal for an indefinite period in 2022.

3. RESERVES

a. Operations Reserve

The Operations Reserve represents an excess of donations over expenditure for the period and is freely available to be utilized for future operation and project funding costs as the evolving research and development project pipeline dictates.

4. FINANCIAL ASSETS & INVESTMENTS

a. A rental warranty of CHF 11'382 towards EPFL is kept for office facilities.

b. The Esperare Foundation owns 100% of the capital and rights of EspoirXLHED Sàrl in 2024 with no change compared to 2023. EspoirXLHED is a limited liability company incorporated on 28th March 2018 and based at Avenue de Sécheron 15, 1202 Geneva, Switzerland. The company's purpose is the Research and Development of treatments modulating to the Ectodysplasin Pathway.

5. COMMITMENTS

As of 31 December 2024, and 2023, there were no significant capital expenditure commitments.

6. SUBSEQUENT EVENTS

No events occurred subsequent to 31st December 2024 and prior to the approval of the financial statements that would require modification of or disclosure in the financial statements.

7. INCOME

The income is split as follows

Income in CHF	2024	2023	
Income from R&D Donations	1'287'275	1'062'538	(a)
Direct Income from R&D Activities	744'249	824'543	(b)
Other Operating Income	3'087	5'760	(c)
Total	**2'034'611**	**1'892'841**	

a. Income from R&D Donations and differed income

During 2024 the following donations were granted:

Donors	Notes	Currency	Total Grant	Deferred from 2023 CHF	Received during 2024 CHF	Recognised during 2024 CHF	Deferred short term 2025 CHF	Deferred long term (>2025) CHF	Notes
EspoirXLHED Sàrl	3a	CHF	2 400 000	328 736	0	328 736	0	0	R&D program & foundation
Loterie Romande Genève	3a i)	CHF	150 000	107 621	0	29 914	29 914	47 793	Vivascope 1)
Loterie Romande Vaud	3a i)	CHF	150 000	118 991	0	28 624	28 624	61 743	Vivascope 2)
Fondation Privée		CHF	900 000	900 000	0	900 000	0	0	Prenatal
TOTAL			**3 600 000**	**1 455 438**	**0**	**1 287 274**	**58 538**	**109 536**	

i) Two CHF 150'000 Grants from Loterie Romande Genève and from Loterie Romande Vaud were received in 2022, each to fund the acquisition and maintenance of one imaging instrument (VivaScope) for the EspoiR004 program. The value of these instruments is reported in note 2d) (fixed assets). The equipment depreciation was recognized in 2023 and their remaining value deferred.

ii) As a comparison during 2023 the following donations were granted:

Donors	Notes	Currency	Total Grant	Deferred from 2022 CHF	Received during 2023 CHF	Recognised during 2023 CHF	Deferred to 2024 CHF	Deferred short term (2024) CHF	Deferred long term (>2025) CHF	Notes
EspoirXLHED Sàrl	3a	CHF	2 400 000	1 328 736	0	1 000 000	328 736	328 736	0	Grant – R&D program & foundation
Loterie Romande Genève	3a i)	CHF	150 000	137 536	0	29 914	107 621	29 914	77 707	Grant – EspoiR004 (Vivascope #1)
Loterie Romande Vaud	3a i)	CHF	150 000	147 614	0	28 624	118 991	28 624	90 367	Grant – EspoiR004 (Vivascope #2)
Alps Automation		CHF	3 000	0	3 000	3 000	0	0	0	Grant - NeoCare
Kiwanis Monthes		CHF	1 000	0	1 000	1 000	0	0	0	Grant - Foundation
Fondation Privée		CHF	900 000	0	900 000	0	900 000	900 000	0	Grant - Prenatal
TOTAL			**3 604 000**	**1 613 886**	**904 000**	**1 062 538**	**1 455 348**	**1 287 274**	**168 4**	

b. Direct Income from R&D activities consisted of Contract Research Organization (CRO) services to Espoir XLHED Sàrl for the development of EspoirR-004 in X-linked Ectodermal Dysplasia for an amount of CHF 744'249.

c. Other Operating Income consists of the subletting of part of EspeRare offices to a partner until the end of April 2024.

8. EXPENSES

The R&D expenses are allocated by project as follow:

R&D expenses	2024	2023	
Espoir-004 Direct Costs	285 623,25	234 726,72	
Espoir-004 Support Costs	517 963,24	633 366,09	
Total Espoir-004	**803 586,49**	**868 092,81**	**(a)**
Rimeporide Direct Costs	5 938,34	78 252,31	
Rimeporide Support Costs	20 791,04	91 535,51	
Total Rimeporide	**26 729,38**	**169 787,82**	**(b)**
NeoCare (Flowatch) Direct Costs	2 304,40	63 191,97	
NeoCare (Flowatch) Support Costs	38 089,21	59 715,85	
Total NeoCare	**40 392,61**	**122 907,82**	**(c)**
Espoir-008 Direct Costs	76 277,46	-	
Espoir-008 Support Costs	487 075,16	-	
Total Espoir-008	**563 351,62**	**-**	**(d)**
New projects prospect Direct Costs	3 300,00	2 428,69	
New projects prospect Support Costs	627,60	93 909,87	
Total New Prospects	**3 927,60**	**96 338,56**	**(e)**
Prenatal Platform Direct Costs	104 000,29	73 120,39	
Prenatal Platform Support Costs	351 933,47	172 088,67	
Total Prenatal Platform	**455 932,76**	**245 209,06**	**(f)**
Total	**1 893 921,47**	**1 502 337,08**	

a) Development of Espoir-04 in X-linked Ectodermal Dysplasia.
b) Development of Rimeporide in Duchenne muscular dystrophy.
c) Development of the NeoCare technology for infants with Cardiac defects.
d) Development of Espoir-008 a previously deprioritized therapeutic asset, targeting both prenatal and postnatal administration for patients with Trisomy 21 and Pre-eclampsia/Fetal Growth Restriction.
e) Prospection & generation of new drug development projects for rare diseases.
f) Platform development to support the systematic discovery and evaluation of new projects and prenatal therapeutic development.

The support costs are allocated to each project based on the following rules:

- Salaries and social charges are allocated according to the percentage of the time spent by employees on each project;
- Rental charges are allocated according to the percentage of surface used by the Administration and used by the R&D organisation, then according to the percentage of the time spent by employees on each project for the R&D part of the rental charges;
- Accounting expenses, office supplies, telephone and IT expenses are allocated according to a percentage of the direct activities by projects, including the activities of the Foundation's administration.

g) General Foundation expenses in overall support of R&D activities are split as follow:

General Foundation	2024	2023
Administration staffing	81 262	155 924
Office Rental	4'856	5 172
Audit Expenses	16 765	15 478
General Insurance	17 773	17 773
IT Expenses	-	-
Communications	-	-
General Legal Fees	13 069	21 159
Fundraising direct costs	24 951	13 313
Advertising Costs	1 128	18 845
Board meeting	2 212	983
Depreciation	62 436	62 146
Total	**224 452**	**310 794**

i) Advertising expenses increased significantly from CHF1'909 in 2022 to CHF 18'845 in 2023, attributed to the 10th Anniversary Celebration of the Foundation.

9. FINANCIAL INCOME AND EXPENSES

The financial income and expenses are split as follow:

Financial Income and Expenses	2024	2023
Financial Income	12 707	10 427
Financial Charges	(2 725)	(2 239)
Exchange Differences (loss) gain	12 262	(40 732)
Total	**22 244**	**(32 544)**

10. FOUNDATION CAPITAL

The Capital Fund is fully subscribed at CHF 50'000.- as stipulated under the original legal statutes of EspeRare dated 27 March 2013.
This founding capital was donated by the three initial individual founders.

11. TRADE ACCOUNTS RECEIVABLES

There is a receivable amount of CHF 167'387 from Espoir XLHED Sàrl.

12. EXTRAORDINARY INCOME

This amount originates from the reversal of accrual for CHF 50'000 to FONGIT, along with proceeds from the disposal of certain miscellaneous fixed assets.

13. PERSONNEL EXPENSES

Total staff benefits for 2024 amount to CHF 1'374'525 in comparison of a total of CHF 1'084'068 for 2023.

14. GOVERNANCE

The Foundation Board is the Foundation's supreme body. It takes all decisions necessary or effective for the achievement of the Foundation's aims. It has general responsibility for the affairs of the Foundation and supervises all activities carried out under its authority by the Foundation's other bodies to which power and authority have been delegated.
Members of the Board act on a voluntary basis and may not claim any financial compensation other than expenses incurred such as travel and accommodation. For activities over and above the normal requirements of the position, each Member may receive appropriate reimbursement and compensation. Payment of any such reimbursement or compensation is only permissible where it corresponds to a service carried out for the benefit of the Foundation.

Employees paid by the Foundation such as the Executive Director and the R&D Director serve on the Board only in an advisory capacity and have no voting rights.

15. RISKS AND UNCERTAINTIES

EspeRare encounters certain risks and uncertainties in conducting its affairs. These risks and uncertainties have financial statement implications. In all instances, these have been considered in the financial statements, despite the fact that the outcomes of these uncertainties cannot be predicted with absolute certainty. Management has concluded that provisions for these risks are appropriate, and any adverse resolution of these uncertainties will not have a material impact on the financial position or results of the Foundation.

16. LONG TERM LIABILITIES

This loan corresponds to a bridging loan granted during the COVID-19 crisis, initially amounting to CHF 125'296 in 2020. The loan has been repaid in installments, and as of 2024, the remaining balance stands at CHF 91'880, divided into CHF 33'416 as short-term debt and CHF 58'464 as long-term debt. The loan was granted on an honor basis under special conditions set by the Swiss Federal Government, with which EspeRare remains fully compliant. It is guaranteed by the Swiss Federal Council and accrues interest. Repayments have been made through quarterly installments of CHF 8'354 since January 2022.

17. CONTINGENT LIABILITIES

EspeRare has a potential liability that may occur, depending on the outcome of an uncertain future event. The contingent liability relates to work performed by a consultant who agreed to be paid only if an out-licencing deal for Rimeporide is achieved. As of 31st December 2024, a total of 687 hours were incurred, representing a total of CHF 206'100 amount that has stayed unchanged since 2019. EspeRare has not accrued nor provisioned these costs since no licensing deal has been signed (off balance sheet).

18. FULL-TIME EQUIVALENTS

The annual average number of full-time equivalents for the reporting year, as well as the previous year, is less than 10.

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Report of the Statutory Auditor on the Limited Statutory Examination to the Board of Trustees of Fondation EspeRare, Geneva

As statutory auditor, we have examined the financial statements (balance sheet, profit and loss statement and notes) of Fondation EspeRare for the year ended 31 December 2024.

These financial statements are the responsibility of the Board of Trustees. Our responsibility is to perform a limited statutory examination on these financial statements. We confirm that we meet the licensing and independence requirements as stipulated by Swiss law.

We conducted our examination in accordance with the Swiss Standard on the Limited Statutory Examination. This standard requires that we plan and perform a limited statutory examination to identify material misstatements in the financial statements. A limited statutory examination consists primarily of inquiries of personnel and analytical procedures as well as detailed tests of documents of the unit as considered necessary in the circumstances. However, the testing of operational processes and the internal control system, as well as inquiries and further testing procedures to detect fraud or other legal violations, are not within the scope of this examination.

Based on our limited statutory examination, nothing has come to our attention that causes us to believe that the financial statements do not comply with Swiss law and the Foundation's charter.

KPMG SA

Elodie Elloy
Licensed Audit Expert
Auditor in Charge

Arthur Duterme

Geneva, 6 March 2025

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How can I support EspeRare?

EspeRare is a Foundation recognised by the Swiss authorities to be operating for the international public benefit. As such, it is fully tax exempt and eligible for **Swiss and international subventions** as well as non-financial support.

The Foundation is also a member of the **Transnational Giving Europe (TGE) network**, and has created the **American Friends of EspeRare fund, hosted by the King Baudouin Foundation** which allows **European and USA citizens** to make cross-border donations while still benefiting from the tax advantages of their country of residence.

WHETHER YOU'RE INDIVIDUAL OR A CORPORATE ORGANISATION, THERE ARE MANY WAYS TO SUPPORT ESPERARE

I WANT TO SUPPORT THE FOUNDATION FINANCIALLY

Supporting us financially, you will help us to further secure theimpact of EspeRare and the identification of new treatments for children with rare diseases.

I WANT TO DONATE TO A SPECIFIC R&D PROGRAMME

Our financial structure is composed of several sub-funds, each of them dedicated to a specific R&D programme. Your donation will support and accelerate the development of a new treatment for the disease of your choice.

I WANT TO ESTABLISH A CORPORATE PARTNERSHIP

If you would like to engage in fund-raising activities or in a corporate donation to EspeRare, we would be happy to discuss the modalities that best fit your aims.

WE ARE HAPPY TO GIVE YOU FURTHER INFORMATION AND ANSWER YOUR QUESTIONS :

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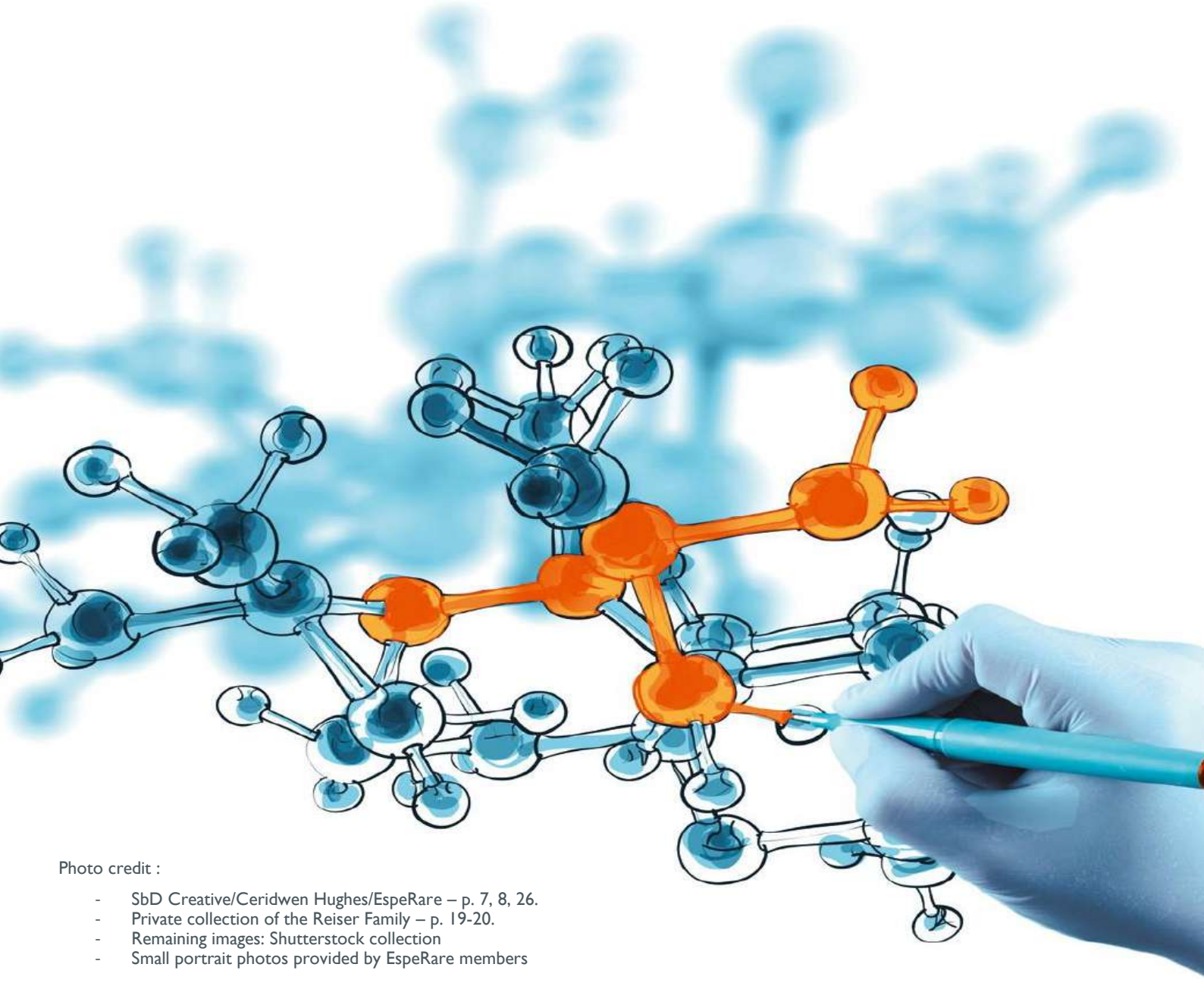

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