ANNUAL REPORT

2020

EspeRare

"By establishing EspeRare, we fulfill our dream of dedicating our pharma expertise to children battling orphan diseases".

Leaving no one behind

At EspeRare we are committed with our hearts and collective expertise to transform the lives of children battling with life-threatening rare diseases.

Every minute, a child is born with a rare disease that has no cure and ONE out of FOUR of these children will not live to celebrate their 5th birthday. Approved treatments exist for only 5% of these conditions and where they exist, they are generally not well adapted for use in children and access can be challenging.

This is why EspeRare focuses on bringing to life and accelerating the development of innovative and accessible treatments to children affected by these underserved diseases. We put the patient and their families at the center of everything we do. The patient community guides how we tackle diseases, informing our approach: from therapeutic product selection to supporting clinical testing and help develop new strategies for therapeutic distribution.

EspeRare

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

Message from the Founders

> **"The future belongs to those who believe in the beauty of their dreams".**
>
> **Eleanor Roosevelt**

Dear Friends,

For more than a year now a devastating virus has completely turned our lives upside down. In addition to the terrible loss of human life, the pandemic has caused unbearable hardship to many, led entire families into extremely difficult situations and transformed significantly our perception of life. However, this Covid-19 crisis has also forced us to take time to observe, to refocus on essential elements, to remember that solidarity and kindness are at the core of our humanity. Alongside environmental issues, this crisis has allowed to put public health back at the center of human concerns.

Punctuated by the pandemic, this year has been challenging for EspeRare in many ways. With hospitals and research centers under siege, most of the foundation's R&D activities had to be adapted or delayed.
At the team level, home office has challenged our communication effectiveness and our sense of togetherness.

Despite these circumstances, 2020 was a grounding year for EspeRare. Together we have grown, and we are stronger than ever. Our common engagement for patients, their families and to advancing medical research has been our glue. Notably, this year, we made a major step towards carrying out our mission as we have found the right pharmaceutical partner for our program in X-linked ectodermal dysplasia (page 15). With Pierre Fabre, we are now on track of starting the clinical development for this groundbreaking treatment, and we are also setting a new therapeutic pathway to treat life-threatening diseases before birth with a novel in-utero administration. With regards to the NeoCare device for children with Congenital Heart defect (page 23), with our partners at the School of Management and Engineering Vaud, we were able to design a new generation of functional prototypes of the first PAB system matching premature neonates' anatomy.

Our collaboration with key actors from the rare disease ecosystem, a committed and passionate team, a strong network of partners and donors has been the cornerstone of EspeRare' success. All this support and kindness has given us the courage to overcome our challenges and to strive for enhancing our impact even further. We thank you warmly for your contributions in taking EspeRare this far down the road. We feel inspired to carry on the task ahead and look forward to our future collaboration.

Sincerely,

Béatrice Greco
Béatrice Greco
Founder & Board Member

Caroline Kant
Caroline Kant
Founder & Executive Director

Florence Porte-Thomé
Florence Porte
Founder & Research & Development Director

2020 Highlights

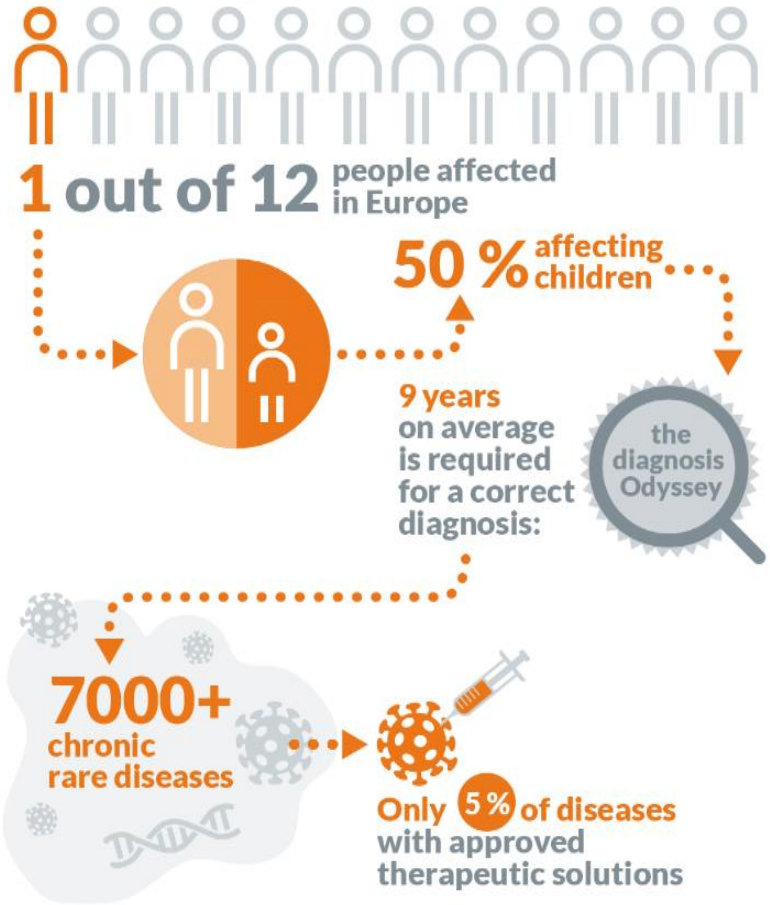
Addressing rare diseases

Why do only 5 % of rare diseases have approved treatments?

RARE DISEASES: A MAJOR GAP IN THE MEDICAL LANDSCAPE AFFECTING CHILDREN

In Europe, up to 30 million are impacted by a rare disease. It is considered as a rare disease, when it affects less than **1 person in 2,000.** In the United States, a disease or disorder is defined as rare when it affects less than 200,000 people*. Rare diseases are **chronic, progressive, degenerative and often life-threatening.** Because of their low prevalence and their 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, very lengthy and requires tight coordination between a large spectrum of research and development (R&D) activities and expertise. Recent reports estimated an average expenditure of at least one billion dollars and a time frame of ten to fifteen years to bring a drug to the market.

INSUFFICIENT EFFORTS IN DRUG DEVELOPMENT FOR RARE DISEASES

Despite significant progress made in scientific research and technologies, **drug development remains insufficient to address critical medical needs in rare diseases.** Therapeutic development suffers from the heterogeneity, complexity of these diseases, the limited number of patients, the fragmentation of medical expertise and the lack of pathophysiological understanding.

New hope for children with life-threatening rare diseases

ESPERARE DISEASE FOCUS

The aim of EspeRare is to uncover and rescue discontinued treatments with a high potential in rare diseases and by doing so address the unmet medical needs for these children.

The drugs selected by EspeRare are at different stages of development and have been discontinued because of several reasons that may include changes in therapeutic focus, lack of efficacy in the original indication or unwillingness to invest the necessary funds to pursue their development.

EspeRare focuses **on activities with a major impact for rare disease patients. Multiple criteria,** ranging from the severity of the unmet medical need are taken into account. The foundation has access to a strong disease community and to a ripe "drug development infrastructure" (e.g. scientific knowledge, patient registries, diagnostic test, etc.).

ESPERARE RESCUES AND REPOSITIONS DRUGS THUS ACCELERATES THE DEVELOPMENT OF ACCESSIBLE TREATMENTS FOR RARE DISEASES

Focusing on bringing to life discontinued treatments and transforming them into safe and life changing therapies.

There are some inherent incentives to this approach:

→ Existing drugs are already known to exert a biological response in humans and this response may become beneficial for other health conditions.

→ Many steps in the drug development process such as drug activity and good safety profile in humans have already been demonstrated during the initial development of the drug.

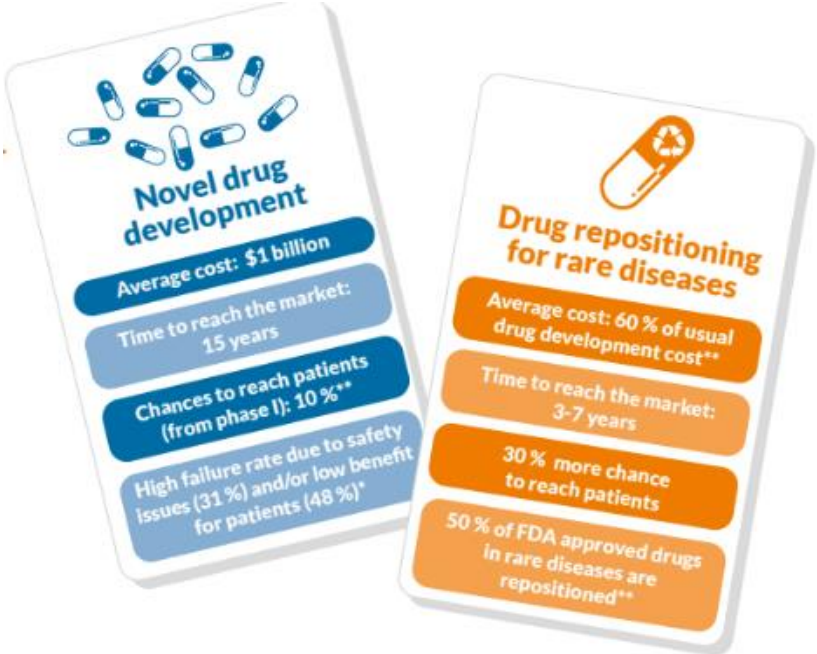
By focusing on these untapped and de-risked opportunities, **EspeRare identifies and develops existing therapeutic interventions that offer important prospects to improve the lives of patients with rare diseases.**

The foundation's model focuses on developing treatment opportunities that remain economically attractive for commercial partners as well as beneficial and accessible for patients and the healthcare system at large.

Repositioning drugs: A de-risked & cost contained approach to drug development:

→ **Faster, de-risked and cost contained approach to drug development***

→ **More accessible treatments & quicker access to medicine for rare disease patients**



** Ref: M. Hay et al., Nature Biotechnology 32, 40–51 (2014)*

*** Ref: Anne Pariser, Director at CDER*

EspeRare`s patient-centered approach

PATIENTS ARE AT THE CORE OF CURRENT PROGRESS IN RARE DISEASES

Patients are at the core of healthcare progress in rare diseases: Individuals affected by rare diseases, their families, communities and advocacy organisations have increasingly been recognised as critical partners in the drug development process.

EspeRare is exceptionally well positioned to work hand in hand with patient associations at each step of the development process.

Notably, because of the foundation's strategic alliance with Genetic Alliance, a network of more than 1,200 disease advocacy organisations.

A COLLABORATIVE AND ACCELERATED APPROACH

EspeRare combines pharmaceutical know-how and a mix of philanthropic and public investments to uncover and accelerate the development of treatments that have been discontinued. EspeRare focuses first and foremost on the therapeutic potential of these treatments, its well-characterised modes of action and well-established safety profiles in non-clinical and clinical studies. More specifically, EspeRare focuses on driving preclinical and clinical development activities that are required to demonstrate the therapeutic benefits of the drugs under investigation.

EspeRare works hand-in-hand with the patients' community at every step of their therapeutic development. Every effort is made to put the **patients' interests first, insuring the patient safety and maximizing the patient medical benefits, patients' access to treatment and enhanced care.**

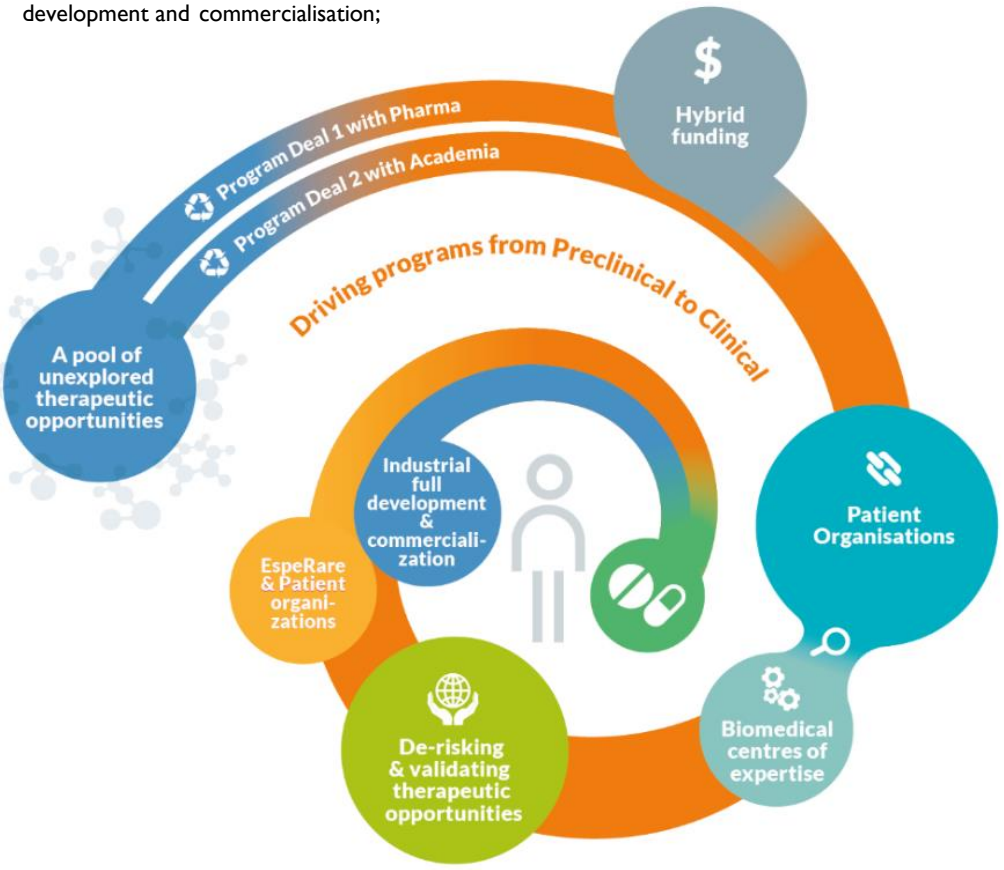
For each of its drug development programme, EspeRare develops Product Development Partnerships with the patients' community, medical experts and commercial partners that:

→ integrate "Patient voice" through working hand in hand with patient advocacy groups;

→ mobilize research and clinical experts and biomedical centers of excellence to conduct pre-clinical and clinical development activities,

→ 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 approval and patient access to treatment.



For each programme, we strive to develop trusted collaborations with patient organisations, to truly deliver patients-centered drug development.

EMPOWERED 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 have a strong influence on drug development.

→ Through support, research, fundraising and lobbying activities, they actively develop expert networks, manage disease related knowledge, engage in and support biomedical research.

With its unique patient-centered approach, EspeRare fully engages the patient community at each step of the drug development process.

THE PATIENT ADVISORY COUNCIL (PAC)

For each of our programmes, we strive to put in place a Patient Advisory Council (PAC)

The PAC serves as a patient advisory resource to EspeRare team members, senior management, and shared governance in the development and commercialization of a drug it develops. It offers a safe venue for patient groups representatives to:

→ Share views of 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 to co-development Partners;

→ Make recommendations to help plan, implement and refine efforts towards meaningful patient involvement.

A SNAPSHOT OF OUR STRONG AND ENGAGED NETWORK OF PARTNERS TO ADVANCE TREATMENTS FOR ORPHAN DISEASES

Pharma and Biotech Partners

MMV Medicines for Malaria Venture
National Institutes of Health
edimer Bringing Hope to XLHED
Pierre Fabre Médicament
Boehringer Ingelheim
MERIEUX EQUITY PARTNERS

Biomedical and R&D Partners

IQVIA
Johns Hopkins University
University of Bristol
Hospital de la Santa Creu i Sant Pau
Universitat Autònoma de Barcelona
HUG Hôpitaux Universitaires Genève
Université de Genève
CHUV
Institut de Myologie Innover pour guérir
Universitätsklinikum Erlangen
Great Ormond Street Hospital Charity
Centre de lutte contre le cancer Léon Bérard
Children's National

Patient Organisations

EURORDIS Rare Diseases Europe
Genetic Alliance
EDIN Ectodermal Dysplasias International Network
IRDiRC International Rare Diseases Research Consortium
Duchenne Parent Project
AFM Téléthon Cure through innovation
nfed Supporting you. Supporting each other. National Foundation for Ectodermal Dysplasias
Duchenne UK
Action Duchenne

Funders and Sponsors

Loterie Romande
McKinsey&Company
Pictet 1805 Fondation de bienfaisance du groupe Pictet
KTI/CTI Die Förderagentur für Innovation L'agence pour la promotion de l'innovation L'agenzia per la promozione dell'innovazione The innovation promotion agency
Fondation Prim'Enfance ...invest in infancy
Ashoka

Our alternative business model

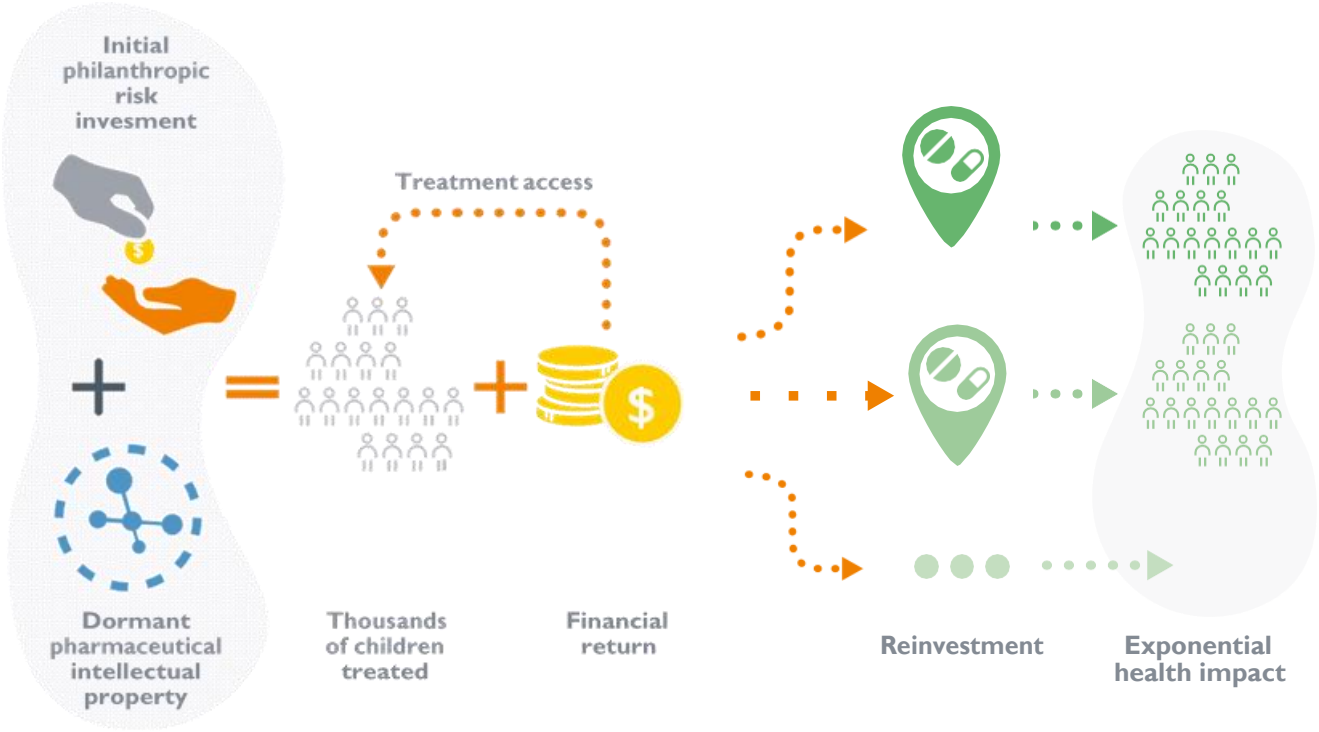
IMPACT OF ESPERARE'S BUSINESS MODEL ON THE RARE DISEASE COMMUNITY

OUR NOT-FOR-PROFIT 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

EspeRare combines pharmaceutical know-how and philanthropic investments to revive existing yet discontinued drugs to treat children with rare diseases, who are otherwise underserved due to the lack of current therapeutic options.

EspeRare is committed to using its funding resources in a socially responsible and not-for-profit manner. **It reinvests all of its profits to further achieve its mission,** which is to develop treatments for underserved rare disease patients, improve their quality of life and drive affordable access to medicine.

All financial returns that EspeRare receives are being used to strengthen EspeRare's organization and its portfolio of therapeutic programs and collaborative partnerships. These financial returns are enabling EspeRare to establish itself as a major drug development player within the paediatric rare disease space and confirm the viability of its novel not-for-profit model and its ability to accelerate accessible treatments for these underserved patients.



Innovative approach to advance treatments and care for patients

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

BIOMEDICAL INFORMATICS ENGINE

Our "*in silico*" approach enables to discover novel therapeutic opportunities for existing drugs. EspeRare is currently developing a **collaborative digital platform** to systematise the discovery and support the efficient development. It is constituted of different layers of:

Discontinued treatments database: compiling data on 2'000 existing drugs with the potential to be "redeveloped" in rare diseases. This database aggregates and structures data about these drugs such as their initial disease(s) of development, their safety and toxicity profile and their biological mechanism of action. A collaboration with the **National Institute of Health** (US) has enabled to have access to data on all drugs developed worldwide.

Rare disease analytics system: integrating biomedical data on the molecular pathophysiology of targeted rare diseases. The information is extracted from scientific literature and specialised databases. This understanding of the biological cascades involved in these diseases is validated and enhanced by integrating data and insights from EspeRare network of biomedical experts.

Patients' Vault: the platform integrates patients' insights. By working hand in hand with the patients' community, the identification of new therapeutic approaches and their development are powered by a patient-centered approach.

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

Sponsored by Loterie Romande

Our portfolio of treatments

With its first programme in Duchenne Muscular Dystrophy, EspeRare has proven its ability to give a chance to dormant therapeutic opportunities. After eight years, the foundation has now demonstrated the therapeutic potential of Rimeporide, a shelved drug that EspeRare has tested in children affected by Duchenne (see page 18).

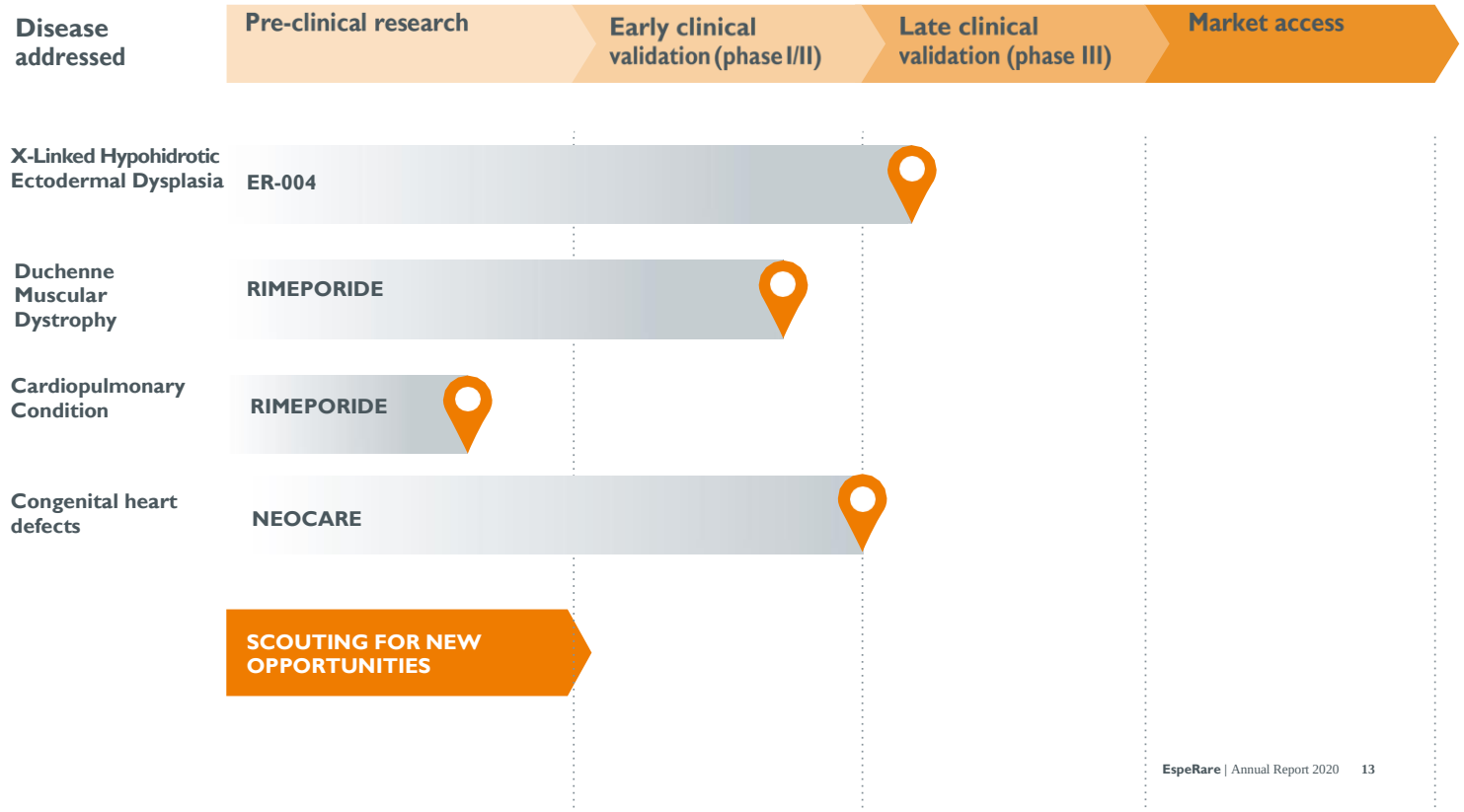
This first programme is also a validation of the strength of EspeRare's philanthropic model to drive and fund drug development in rare diseases.

Towards this goal, **with Pierre Fabre, EspeRare is now on track to bring ER-004 to the market as an antenatal treatment for XLHED** (see page 14). In 2020, ER-005 for paediatric cancers was discontinued due to unconclusive benefit-risk profile. Additionally, it is developing a new therapeutic device for infants affected by severe cardiac defects (see page 22).

EspeRare is diversifying its partners and developing its portfolio in rare diseases by:

- working with pharmaceutical companies, patient organisations and academic partners to evaluate opportunities that fit EspeRare's development model and address high unmet medical needs;
- developing its Platform, a biomedical informatics engine that systematically identifies and evaluates drug rescue and repositioning opportunities.

A PROGRAMME PORTFOLIO UNDER DEVELOPMENT WITH MULTIPLE PARTNERS



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 is 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, often persist into adulthood.

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

*N Engl J Med 2018 ; 378 : 1604-1610

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 a patient's lifespan can be expected. Consequences of brain damage, treatments related to hair, dentition issues as well as psychosocial challenges require important and costly medical care throughout the life of XLHED patients.

ER-004 PROGRAMME IN X-LINKED HYPOHIDROTIC ECTODERMAL DYSPLASIA

The development of ER004 (previously named EDI200) was stopped by Edimer Pharmaceutical, due to treatment's lack of efficacy when treating newborns with XLHED.

EspeRare has revived ER004 using a novel intra-amniotic administration route. It has also entered into partnership with Pierre Fabre with the aim of bringing this protein replacement therapy to the market.

BACKGROUND

2017

Edimer Pharmaceuticals closed down its operations because of the lack of positive results when administered ER004 to neonates. Then EspeRare was approached by Edimer Pharmaceuticals to revive ER004's clinical development of this programme in XLHED, then stalled.

EspeRare establishes a collaboration with Prof. Holm Schneider, the German paediatrician who worked closely with Edimer on the development of this therapy and pioneered the first intra-amniotic administrations of ER004 to 3 unborn XLHED foetuses.

The development of ER004 in XLHED using an intra-amniotic administration approach before birth was accepted in the European Medicines Agency's PRIority Medicines scheme. The "PRIME scheme" aims at accelerating the development of therapies for unmet needs. 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 through a Protocol Assistance meeting, seeks advice from the EMA to present all data collected and to understand whether this pioneering intra-amniotic administration route can be developed. The EMA has agreed with EspeRare's proposal that prenatal treatment of XLHED through intra-amniotic drug administration is the way forward to develop ER004 into a treatment for XLHED.

2019

A similar meeting was conducted with the FDA, who are also supportive of ER004 as an antenatal treatment for XLHED. This gives 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 to jointly develop ER004 towards commercialization as an antenatal treatment for XLHED. As partners, they sign up and commit to an Ethical Charter that governs their relationship and places the XLHED patient community at the heart of the development. Together EspeRare and Pierre Fabre are setting up a clinical trial that aims at bringing ER004 to the market in the EU and the US.

2021 and beyond

A worldwide clinical trial, probing the efficacy and safety of ER004 as a prenatal treatment for XLHED, will be conducted. If the trial meets its objectives, ER004 should be approved circa 2025 both in Europe and the USA. ER004 will not only be the first and only treatment for XLHED, it will also, in all likelihood, be the first approved prenatal treatment that corrects a genetic disease before birth.

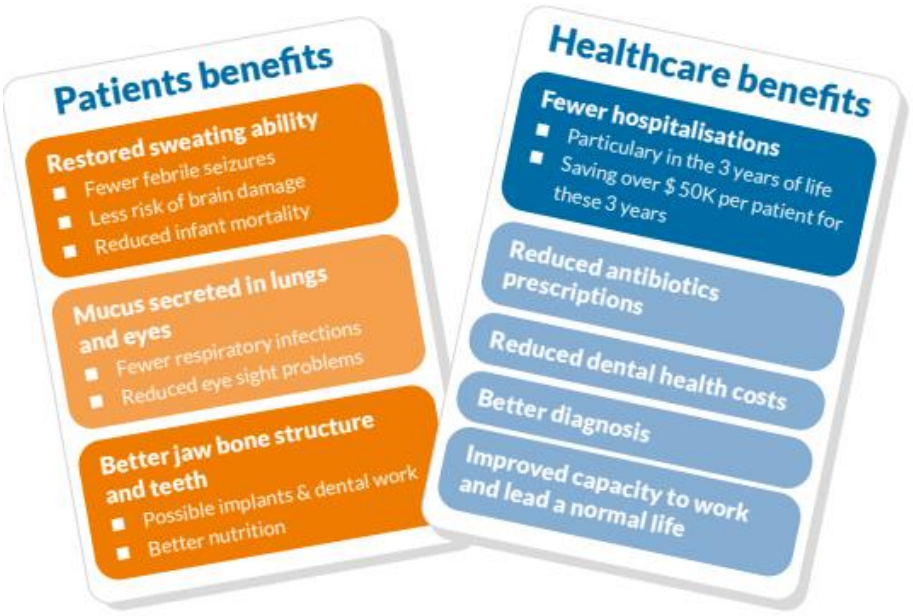
"Our hope is that this new treatment will change the life of XLHED patients, and that its innovative route of administration will pave the way to address other genetic diseases before birth".

Caroline Kant,
Founder & Executive Director

ER-004: A "SINGLE COURSE" THERAPY TO INDUCE NORMAL ECTODERMAL DEVELOPMENT

ER004 is a synthetic EDA protein engineered in Lausanne, Switzerland, and further developed by Edimer, a US-based biotech company. **This synthetic equivalent to EDA** acts as a substitute for the dysfunctional protein in XLHED patients to induce normal development of the key ectodermal structures such as glands, teeth and hair.

It is the first and only treatment for XLHED. Administered at the right time in development, it has the potential to become a "single course" treatment, effectively switching off symptoms of the disease throughout patients' lives.



OUR COMMITMENTS, PRINCIPLES AND VALUES

COMMITMENTS TO THE
XLHED PATIENT

EspeRare regards the continuing engagement of the patient community as critical for the success of the programme. They also acknowledge that the patient community has already greatly contributed to advance knowledge of the disease (e.g., through efforts of collecting natural history data and providing feedback on characterization of the disease and unmet medical needs). Therefore, in alignment with their shared values, EspeRare pledge to engaging the patient community to :

- ***Collect input all stages of the drug development process;***
- ***Share information and data, to support enhancement of patient knowledge and care;***
- ***Support market treatment access and equitable access to care.***

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.

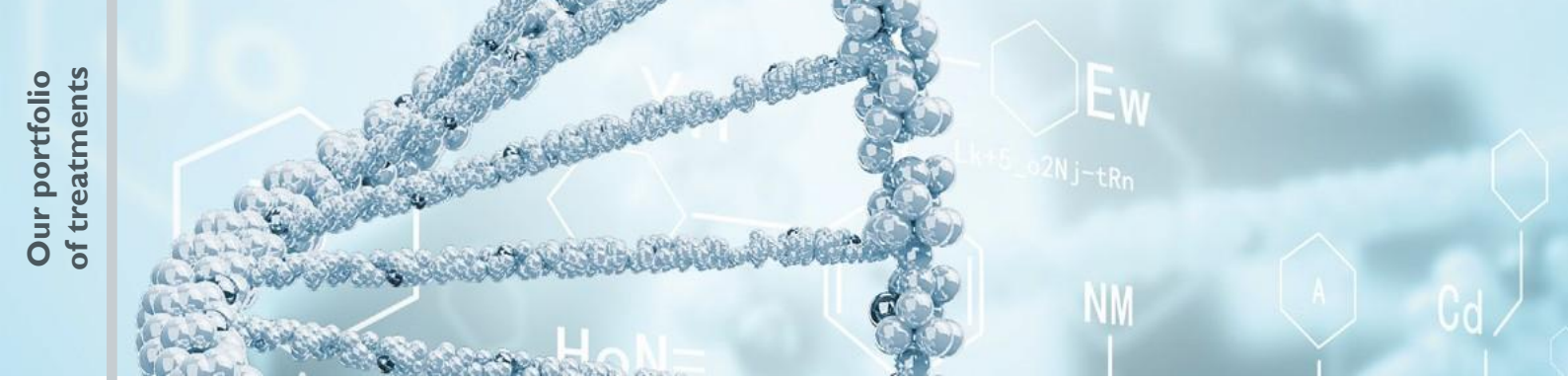
PATIENTS FIRST, including:
- Patient safety (comes first);
- Maximization of patient medical Benefits and patient access to treatment;
- Ensure patient engagement and continued information sharing with the patient community.

TRANSPARENCY about roles, responsibilities, constraints, potential conflicts of interest as well as the outcomes of the ER004 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 accountability.

EspeRare has also convened a **Patient Advisory Council** (PAC), composed of patient group representatives, whose mission is to serve as the primary interface between the XLHED patient community and EspeRare in order to streamline information sharing and collect input of the patient community into the development of ER004.



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 degeneresccence 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 around 10 years of age. It eventually spreads to the arms, neck and other areas.

Later in the twenties, this progresses to complete paralysis, increasing difficulty in breathing requiring ventilator due to respiratory muscle dysfunction, as well as cardiac muscle dysfunction leading to heart failure.

Cardiac dysfunction is present in most DMD patients and is the primary cause of premature death.

While there have been recent advances in the management of these patients, the heart failure in these patients related to the lack of dystrophin, is becoming the primary cause of premature death in these patients.

Because of the severity of the cardiac involvement in DMD patients, therapeutic interventions needed to prevent or stabilize the cardiac damages that will inevitably occur if left untreated.
It is essential to stop the progression of myocardial fibrosis prior to the onset of left ventricular dysfunction by acting on the direct mechanisms of DMD pathogenesis to try and prolong the life of patients with DMD.

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 on skeletal muscles, they do not alter the ultimate outcome of the disease.

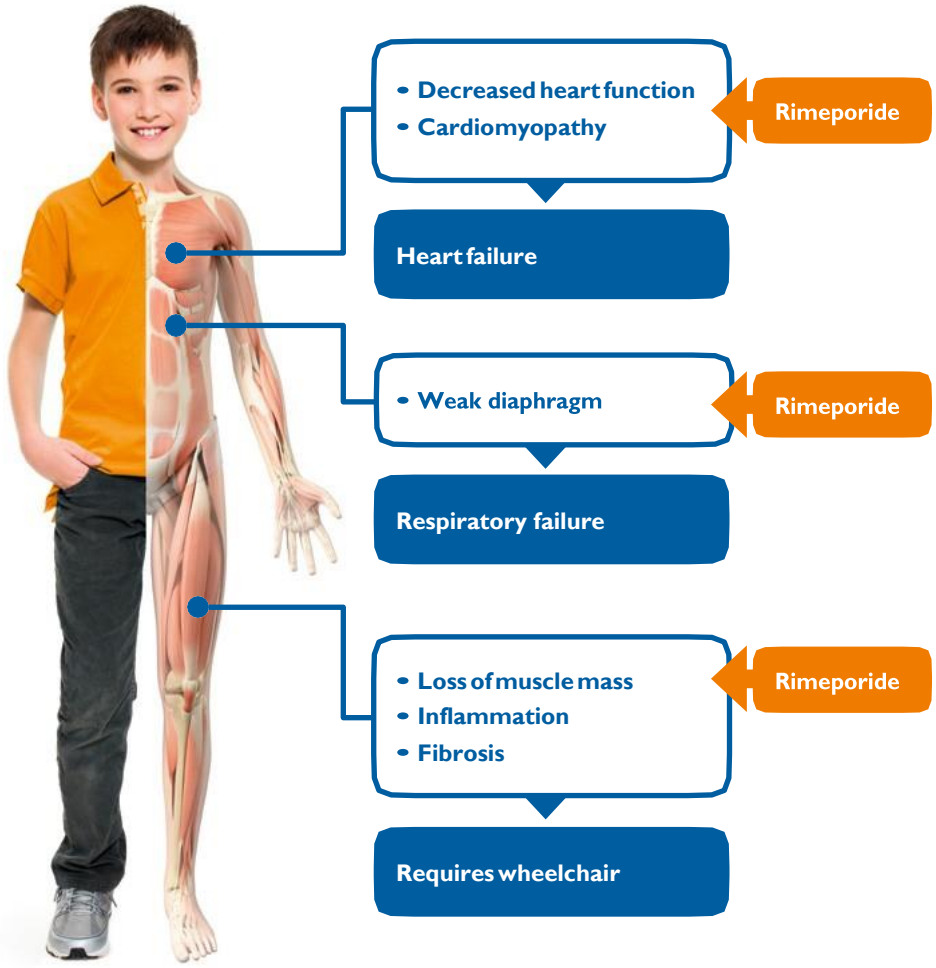
There is therefore an urgent need for new therapies to halt the progression of the disease and in particular the life-threatening cardiomyopathy for all Duchenne boys.

"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 effect profile."

Duchenne UK
DMD patient association

"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
Founder & 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

BACKGROUND

2013

EspeRare obtained the rights to develop Rimeporide in neuromuscular diseases.

2014

Two studies demonstrated Rimeporide's ability to significantly decrease levels of inflammation and fibrosis in a large panel of skeletal muscles, in the diaphragm and in the heart in a pre-clinical study.

2015

Orphan Drug Designation granted by the European Medicines Agency (EMA) for Rimeporide in DMD.

2016

A phase Ib clinical trial launched in young boys with DMD, to examine the safety, tolerability and pharmacokinetic and explore biomarkers of target engagement after an oral treatment of 4-weeks with Rimeporide.

2017

Phase Ib clinical trial enrollment completed, with 20 young patients with DMD. The study, coordinated by Prof. Muntoni was ongoing at leading neuromuscular centers: the Great Ormond Street Hospital (London, UK), the Armand Trousseau Hospital/ I-motion (Paris, France), the San Raffaele Hospital (Milan, Italy) and the Santa Creu i Sant Pau Hospital (Barcelona, Spain).

Large non-clinical translational study initiated at the École Nationale Vétérinaire d'Alfort (Paris, France). The objective of the study is to support the design of a phase II study, by guiding dose selection, primary/ secondary outcome measures, and by finding novel non-invasive biomarkers. Chronic oral administration prevented decline of left ventricular function and was shown to be cardioprotective.

US FDA grants Orphan Drug Designation for Rimeporide in DMD.

2018

Data from a safety study in DMD boys was analysed and report was completed. Good tolerability was shown in young DMD boys, confirming the safety and tolerability obtained previously seen in adult healthy subjects. In addition, there was preliminary evidence for biological efficacy on several serum biomarkers of inflammation and muscular function and injury, supporting the therapeutic potential of Rimeporide in patients.

2019

An extensive communication program was rolled out to share with the patients community and DMD experts the results of studies conducted with Rimeporide.

Results were presented at the World Muscle Society meeting in Copenhagen and at the Congress of Myology in Bordeaux.

EspeRare obtains the rights to develop Rimeporide in all indications.

EspeRare set up an international advisory board with Pr C. Spurney, Pr J. Soslow, Pr F. Muntoni, Pr P. Spitali to design the clinical plan for Rimeporide as the first treatment to specifically address the life-threatening cardiomyopathy in DMD boys.

2020

Sharing progress of development with the disease community is of key importance to EspeRare. Therefore, in 2020 two publications were released on Rimeporide key results:

→ The final analysis of a non-clinical study was published in the International Journal of Cardiology: Ghaleb B. et al. Int J Cardiol. S0167-5273(19), 35776-6(2020).

→ A peer reviewed paper presenting the safety, biomarkers and pharmacokinetic phase I results in Duchenne young boys were also published in Pharmacological Research Journal in September 2020.

In May 2020, the programme and its challenges were discussed with the patient community within the Duchenne Community Advisory Board (CAB), an annual meeting organised by the Duchenne Data Foundation (DDF).

In addition, the design of a phase II/III study was discussed with an Advisory Board composed of worldwide KOLs in cardiology, neurology and radiology. All experts acknowledged that Rimeporide uniquely addresses some of the key pathways that are likely major drivers of the DMD pathology. There is an undeniable potential for Rimeporide to provide a better early approach for these patients.

Additionally, in September 2020, Rimeporide was granted the Rare Paediatric Diseases Designation (RPDD) for cardiomyopathy in children with DMD by the US FDA. Rimeporide is the first drug to receive a RPDD for DMD related cardiomyopathy. Rimeporide will be eligible to receive a rare paediatric disease priority review voucher at the time of marketing approval.

2021 and beyond

EspeRare is seeking a partner to further develop Rimeporide as a major life changing treatment.

Continued discussions of the phase II/III study will occur with the International Scientific Advisory Board, Patients Groups and Health Authorities in order to pave the way for a specific targeted cardiac therapy.

Rimeporide is intended to be administered as a daily oral chronic treatment, in all patients with DMD, regardless of their mutation, and as soon as early signs of myocardial fibrosis are detected.

Rimeporide is a safe, potent and a first in class selective inhibitor of the NHE-1 receptor. It has been developed by Merck for congestive heart failure but was discontinued after phase I for strategic reasons.

Rimeporide represents a novel treatment that has the potential to delay the long-term accumulation of fibrosis and subsequent cardiac damages in patients with DMD. Rimeporide is also being tested for other cardiac related conditions.

Rimeporide has a significant potential to be a successful pharmacological intervention to address cardiac and respiratory dysfunction observed in DMD."

Prof. Francesco Muntoni,
Chair of Paediatric Neurology,
University College of London

" Rimeporide has the potential to transform Duchenne from a life threatening to a chronic disease"

Prof. Denis Duboc, Cardiologist,
Hôpital Cochin, Paris

Our hope is that Rimeporide becomes a major treatment option for patients suffering from DMD, alone or in combination with other available treatments. In particular, Rimeporide working through NHE1 inhibition is cardioprotective. Such important results have not been reported so far with other DMD compounds.

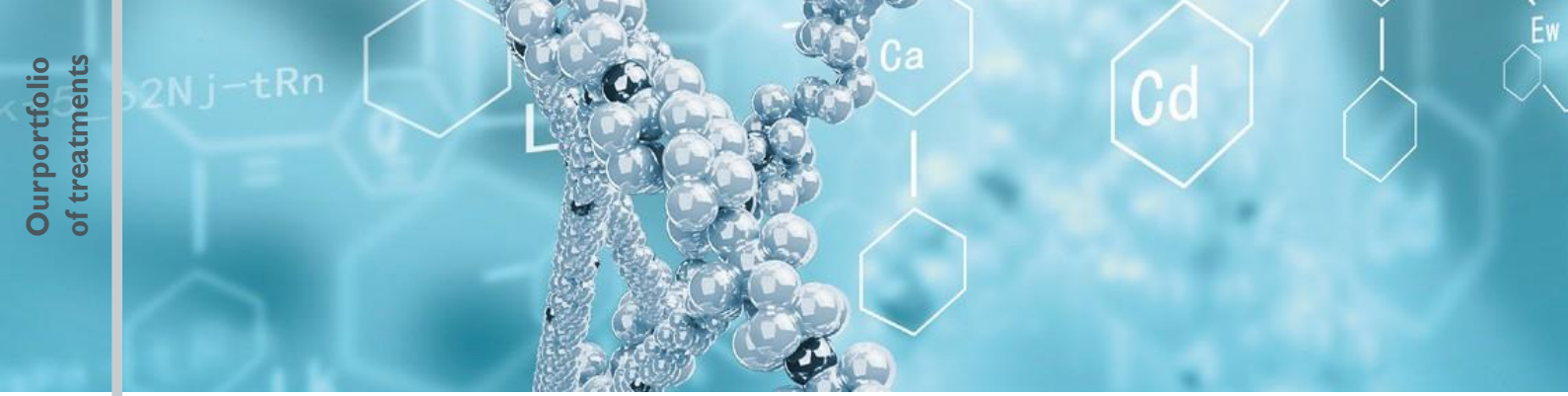
Rimeporide is the only clinical stage therapy intended to reduce inflammation and fibrosis both in the heart and skeletal muscles.

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

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

Key collaboration established with neuromuscular patient associations: AFM (France), PPMD (Spain and Italy), Altrodomani Onlus (Italy), Duchenne UK (United Kingdom). Duchenne Data Foundation

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).



Congenital Heart Defects (CHD)

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

Congenital heart disease (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 IS NEEDED TO OVERCOME CHALLENGES OF CONVENTIONAL PAB

Conventional PAB is far from being optimal. The implantation of the band is conducted under general anesthetic 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 therefore sometimes required. This situation is traumatic to newborn babies 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. **NeoCare is a remotely adjustable PAB medical device.** The technology comprises an implant coupled with an external control unit; the latter allows, post-implantation, the remote control and regulation of the blood flow without having to open the chest. It results in shorter stays in intensive care and no need for re-operations to adjust the banding and the flow in the pulmonary artery. In addition, the innovative adjustment capabilities of the system allow surgeons and cardiologists to develop new treatment possibilities tailored to their patients' needs.

NEOCARE

NeoCare is aiming to become the first life-saving device addressing key limitations of traditional pulmonary artery banding applicable to a broad population of patients suffering from Congenital Heart diseases.

NeoCare will be indicated for babies or young adolescents with life threatening heart defects such as single ventricles defects, one of the most serious forms of congenital heart diseases. The NeoCare device will enable to reach a broad number of patients in particular premature neonates who cannot tolerate an open chest surgery at birth.

A remotely adjustable pulmonary artery banding system is needed to alleviate the life-threatening condition of patients with severe CHDs.

NeoCare has been designed thanks to public and philanthropic funding as a miniature, implantable, wireless, battery-free device suited for banding small size arteries to perform non-invasive adjustments of pulmonary artery banding in paediatric patients, in particular premature newborns.

After implantation, banding of the pulmonary artery will be adjusted remotely through the chest avoiding repeated surgeries to adjust flow in the pulmonary artery and improve the quality of life of young babies born with heart abnormalities.

The first challenge for the NeoCare system was to miniature the banding device in order to make it match to the neonatal anatomy. The second challenge was to accurately, safely and efficiently regulate blow flow and pressure in the pulmonary artery of various diameters in order to prevent from irreversible damage of overflow to the lungs. Haute Ecole d'Ingenierie Vaudoise (HEIG-VD) were able to design such device.

The Advisory Board confirmed that the new geometry of the NeoCare system was also suited for premature neonates in terms of size and bulkiness.

The innovative control unit has also been designed and a software cybersecurity protection has been included. In parallel, EspeRare is looking for partners to externalise the manufacturing of the device.

HEIG-VD is using its expertise to develop prototypes to best achieve clinicians' requirements for an efficient and safe PAB in neonates born with congenital heart diseases.

EspeRare is also collaborating with Dr E. Kung from the University of Clemson (South Carolina, USA). Dr Kung has considerable experience in development of computational physiology simulation which will be essential to investigate NeoCare performance in new indications such as single ventricle patients.

Fulfilling EspeRare's Humanitarian Commitments, part of the NeoCare financial return will be used to enhance diagnostics of CHDs in pregnant women, improve care in those neonates born with CHDs in order to avoid irreversible injury caused by pulmonary overflow in these children.

KEY ACHIEVEMENTS FOR NEOCARE PAB DEVICE

MINIATURISATION

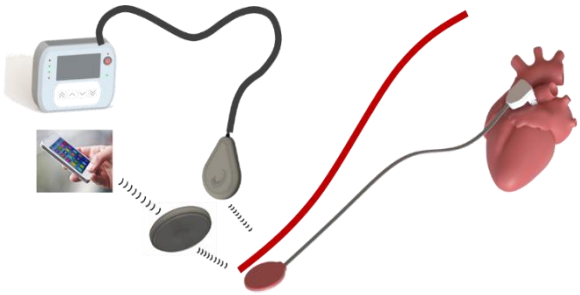
- → Premature babies – small diameter and size to better fit to neonates anatomy of premature babies
- → Variable size for PAB, according to the therapeutic indication
- → Deported antenna to improve energy transmission efficiency
- → Can be indicated for babies < 1kg and > 8 kg

LIFETIME (material and validation related)

- → Long term implantation

ADDITIONAL FEATURES AND UPDATED TECHNOLOGY (under development)

- → User interface, IT security, data protection



ER-005 Programme in Paediatric Cancers

ABOUT PAEDIATRIC CANCERS

Every paediatric cancer is a rare disease. There are about 60 different cancers affecting children. Each of them has to be studied and treated individually.

Each year, nearly 100'000 children under the age of 15 die from cancer worldwide – that is almost 250 children every day. In Europe alone 35'000 new cases occur per year.

In addition, many children who survive cancer suffer from long-term damages induced by surgery, cytotoxic chemotherapy, and radiotherapy, that includes mental disabilities, post-traumatic stress disorders, organ toxicities, amputation, organ removal and secondary cancers. Survivors will represent about half a million children in Europe by 2020.

Over the past 15 years most significant therapeutic innovations occurred in adult oncology, whereas their access and benefits to children are limited. Indeed, from 2011 to 2015, 70 new anti-cancer drugs were approved for adult cancers while only 2 were approved for paediatric malignancies.

Major breakthroughs that have been achieved during recent years in cancer care for adults have not been translated into benefits for children, mainly because:

- ***The process is more difficult, and paediatric cancer is by far rarer than adult cancer, which makes it less commercially attractive.***
- ***The etiology and biology of these cancers differ from those that occur in adults. A direct application of new cancer drugs to paediatric cancer indications is not possible.***

ESPERARE IS ADDRESSING THE PRESSING NEED FOR NOVEL TREATMENTS IN PAEDIATRIC CANCERS

EspeRare **is reviving the development of ER-005 as a first-in-class drug for the treatment of rare paediatric cancers.**

EspeRare has obtained from Merck the worldwide commercial rights for ER-005 following initial development in fibrotic and inflammatory conditions and has access to its legacy pre-clinical (including oncology data) and clinical safety and efficacy data package.

In addition, EspeRare has a strong pharmaceutical know-how within its team on the initial development of ER-005 in other indications up to clinical stage.

ER-005 selectively targets the JNK (c-Jun N-terminal kinase pathway), a cell signaling pathway that has been implicated not only in fibrotic and inflammatory diseases, but also in various cancers.

Future advances in paediatric cancer treatment will be centered on developing biology-driven new therapeutic strategies that build on current knowledge of oncogenic pathways.

ER-005 PROGRAMME IN PAEDIATRIC CANCERS

ER-005 is an oral, safe and selective JNK inhibitor. It has been clinically developed by Serono and Preglem for idiopathic pulmonary fibrosis and endometriosis, respectively, but was discontinued for strategic reasons.

ER-005 represents a first-in-class therapeutic strategy that has shown to be well tolerated in adults and has the potential to address paediatric cancers, alone or in combination with other therapies.

BACKGROUND

2016

A non-clinical study documented the anti-cancer effects of ER-005 in vitro.

2018

> EspeRare obtained the worldwide commercial rights for ER-005 following initial development in fibrotic and inflammatory conditions and obtained access to the compound's sizable legacy pre - clinical and clinical safety and efficacy data.

> EspeRare developed a strategic plan to reposition ER-005 in paediatric Oncology leveraging on robust and scientific literature.

> Non-clinical translational study in rare tumours performed at the Centre Léon Bérard (Lyon, France). ER-005 has shown to inhibit various rare and paediatric cancer cell growth. ER-005 was found to be non-toxictonormal healthy fibroblasts.

2019

Some additional analyzes were carried out in the same research center with the writing of a study report. The results were presented in October at the congress of the International Society for Pediatric Oncology.

2020

EspeRare explored the scientific rationale of redeveloping ER-005 in cancers affecting children. Upon thorough data analysis, the Foundation decided to discontinue the programme. The benefit-risk profile was not sufficiently convincing to justify progressing the drug into the clinic and testing it into young cancer patients

ER-005 IDENTITY CARD:

Name:	Bentamapimod
Target:	c-Jun N-terminal kinases (JNK) 1, 2, and 3
Originator:	Serono
Indications:	Rare pediatric cancers: Fibrolamellar hepatocellular carcinoma, hepatoblastoma, neuroblastoma, sarcoma, lymphoma; neuroendocrine tumor
Drug development phase:	Oral Treatment, Idiopathic pulmonary fibrosis and endometriosis development Administered to 87 adults (4 phase I trials) and 24 patients with endometriosis (phase II) for up to 5 months
Opportunity:	Excellent safety profile in humans, clinically relevant beneficial anti-inflammatory and anti-fibrotic effects Proven biological efficacy on JNK proteins which are involved in cancer development and progression

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. The President is Sharon Terry, a pioneer of patient empowerment and citizen health, and the CEO of Genetic Alliance, Washington DC, 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.

"As a not-for-profit organisation, our priorities are not determined by the size of a market. They are solely defined by the medical needs and great science. Above all, we strive to apply our patient-centric model and pharma know-how to advance new treatments for underserved patients."

Caroline Kant
Founder & Executive Director

THE FOUNDATION BOARD

SHARON F. TERRY

Sharon Terry is President 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 organisation 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 personalised medicine initiative, a member of the Board of Telethon-Italy and an Ashoka Fellow. Sharon links EspeRare with patients organisations and orphan disease advocacy.

Sharon F. Terry - President

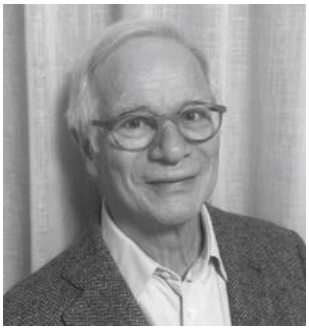
BÉATRICE GRECO

Béatrice Greco is a 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.

Béatrice Greco – Co-Founder

DENIS MORTIER

Denis Mortier is chairing EspeRare's Business Advory Committee. During his extensive carrier he served, among others, as a Partner of Coller Capital Ltd., on the Executive Committees of Credit National, as an Executive Officer in The World Bank Group and as the Chairman of the European and the French venture capital and private equity associations, as well as a Vice Chairman of NASDAQ Europe. He also took part in Advisory Boards and Investment Committees for multiple Venture Capital funds. Denis provides excellent counsel and guidance to support the growth of EspeRare's activities and business model.



Denis Mortier

PETER POTTER-LESAGE

Peter Potter-Lesage is the treasurer of the Foundation, a member of the Board of Trustees of the Malaria Consortium (UK) and Senior Advisor for fundraising, donor relations and strategy at Medicines for Malaria Venture (MMV) in Geneva, where he previously held the position of founding Chief Financial Officer for 12 years. Peter provides to EspeRare his expertise in financial representation and strategic business planning, in financial and fundraising analysis, and in support, risk identification and management.

Peter Potter-Lesage - Treasurer

EWEN SEDMAN

Ewen Sedman is SVP Strategy and Business Operations at Merck Healthcare. 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 leadership expertise across the whole pharmaceutical R&D value chain.

Ewen Sedman

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 is leading EspeRare since 2013. By driving forwards EspeRare, Caroline is realising her dream of dedicating herself to address rare diseases in honour of her daughter, and for all children suffering from orphan diseases. She is also advising leading NGOs to find new ways of applying venture philanthropy and social entrepreneurship to other pressing health challenges. Caroline was educated in Switzerland and the United States and holds degrees in neurobiology and product development. She is an ASHOKA fellow and was appointed "Swiss woman entrepreneur" of the year in 2015.

Caroline Kant

FLORENCE PORTE-THOMÉ

Founder & 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.

Florence Porte-Thomé

SYLVIE RYCKEBUSCH

Chief Business Officer

Sylvie Ryckebusch serves as EspeRare's Chief Business Officer, providing business development and licensing support to EspeRare. She has 12 years of business development experience within Serono International and Merck Serono where she occupied various senior roles within Business Development and Alliance Management. She has been involved in hundreds of product license discussions and has concluded dozens of transactions. Prior to establishing her consulting practice, Sylvie worked within the Index Ventures Life Sciences team and as a strategy consultant with Mckinsey and Company. While at Merck Serono, Sylvie supported the current EspeRare team to create the Foundation.

Sylvie Ryckebusch

MONIQUE A. CAILLAT

General Counsel

Monique A. Caillat is an Attorney at Law based in Geneva, Switzerland, specialised in the healthcare sector. During over 20 years, she has represented the private sector's interests in its relations with the authorities, international organisations, academia and NGO's. While specialised in the counsel to pharmaceutical companies, start-ups and not-for-profit organisations in the healthcare sector, Monique is also engaged in supporting interactions between patients and healthcare professionals, through medical mediation and through her membership on the Geneva Health Ethics Committee. Monique is the General Counsel of the Foundation.

Monique A. Caillat

JULIAN GRAY

Chief Medical Officer

Julian Gray supports EspeRare in all medical aspects related to programmes of EspeRare's portfolio. In addition, he advises on clinical development strategies and assists in the interactions with regulatory agencies. As a medical expert in Central Nervous System (CNS) and clinical research for the pharmaceutical industry, he led clinical studies on Parkinson's and Alzheimer's diseases. He has a strong track record in designing clinical and regulatory strategies for orphan drug, and obtaining subsequent approval in Europe and USA. Among others, he worked as medical advisor to Santhera Pharmaceuticals on the development of idebenone in Duchenne Muscular Dystrophy.

Julian Gray

TEAM

RESEARCH AND DEVELOPMENT

SAMEERA ALLIE
Medical Lead

After studying medicine at the University of Cape Town, Sameera specialized in global health and clinical research in infectious diseases such as HIV and TB. At EpseRare, Sameera provides medical support to the foundation programmes. In addition, Sameera is responsible for leading the development of EspeRare`s Biomedical Informatics Platform.

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.

STÉPHANIE CARNESECCHI
Biomaker Programme Manager

Stéphanie is pre-clinical project manager. She has deep experience in pre-clinical, biomarker and signaling discovery, spanning varied disease areas. At EspeRare, Stéphanie contributes to the development of the biomarkers programme in Duchenne Muscular Dystrophy.

ALEXIS COLETTE
Chemistry, Manufacturing & Control

Alexis is a senior CMC consultant with 15+ years of international experience at the cornerstone of science, regulatory and business aspects. Alexis is providing support to EspeRare on the Manufacturing and Commercialisation strategy for ER-004.

CAROLINE DURAND-AVALLONE
Clinical Programme Leader

Caroline was previously in charge of Pharmaceutical Affairs for a French biotech company. She has experience in the field of development and biomanufacturing and has held various positions in R&D, industrialization, and analytical development at Sanofi Pasteur (Lyon, France). She has also led and coordinated several pre-clinical and clinical studies. At EspeRare Caroline is leading the clinical aspect of the ER-004 programme.

OLIVIER FAVRE-BULLE
Chemistry, Manufacturing & Control

Olivier has over 25 years in the pharmaceutical industry, helping companies and clients in their pharmaceutical development for their biologicals. Olivier is advising EspeRare on the Manufacturing and Commercialisation strategy for the ER-004.

AGNÈS JAULENT
Programme 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, Patient engagement and Business Development.

DELPHINE LABOLLE
Clinical Project Manager

Delphine is a clinical research expert. She has many years of experience in clinical operations, mainly in Eastern and Western Europe. At EspeRare, she provides her clinical operational expertise to ER-004 as well as support the Quality System.

CAROLE PUGH
Regulatory Advice

Carole is Managing Director at EUDRAC Limited, a regulatory consultancy company (UK). She has worked with small start-up, medium and large global companies during her time at EUDRAC, and performed due diligence activities, undertaken agency scientific advice procedures and presented on current regulatory intelligence topics. She is EspeRare'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.

OLIVIER WARIDEL
NeoCare Programme Lead

Olivier has more than 20 years of experience in the design, development, production and sales of innovative and complex medical systems. During this career, he has been managing technology transfer, business mergers and team integration as well as leading commercial medtech initiatives internationally. Enriched by those experiments, he moved into a consulting role, supporting different medical device and healthcare related programmes. Within EspeRare, Olivier is leading the NeoCare project including coordination of various partners.

PATIENT ADVOCACY

CAMILLE PREZIOSO
Programme Leader

Her several positions at NGO`s and foundations have led her to travel and collaborate with local groups worldwide, allowing her to gain expertise in leveraging their strengths and managing their organizational constraints to maximise their impact. Camille is responsible for developing EspeRare`s "patient-centered" approach, the implementation of its patient engagement strategy and its interface with patient organisations.

FINANCE & 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 organisations for various humanitarian causes engaged in creating a better world. At EspeRare, Sarah links ledger accounting to reporting and auditing activities, as well as support Human Resources Management.

IT & BIOINFORMATICS

CÉDRIC MERLOT
BioInformatics 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. 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. STÉPHANE BLOT

Prof. Blot is heading the neurobiology laboratory of the Veterinary School of Alfort (ENVA), France. He participates among others to the instruction of students preparing the myopathology diploma of the French Institute of Myology. He provides EspeRare with his expertise in conducting animal models of Duchenne Muscular Dystrophy.

PROF. ANNA DAVID

Prof. David is 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.

PROF. PEDRO DEL NIDO

Prof. Del Nido is a thoracic surgeon in Boston, Massachusetts and is affiliated with Boston Children's Hospital. He has been in practice for more than 20 years. As one of the world's leading paediatric cardiac surgeons, he is the Chief of Cardiac Surgery at Boston Children's Hospital. Prof. Del Nido is particularly renowned for performing cardiac chirurgical procedures in the womb.

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.

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. RUDOLF KORINTHERBERG

Prof. Korintherberg, MD, is Professor of Paediatrics and Child Neurology at the Department of Paediatrics and Adolescent Medicine (Freiburg, Germany), and the Dean of the Medical Faculty. He is an active member of several German scientific societies involved in neurology.

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 cardiovascular 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 registration 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

Tippi is a pediatric and fetal surgeon focused on developing better ways to diagnose and treat genetic diseases before birth. She advises EspeRare and collaborates with the foundation on prenatal treatment modalities.

PROF. JIRI MAREDA

After obtaining a PhD in physical organic chemistry at the University of Geneva, Prof. Mareda worked as the research associate at the University of Pittsburgh, where he fully specialised in computational and theoretical chemistry. He has then taught organic chemistry for more than 28 years at the University of Geneva. He now provides EspeRare with an helpful insight at the molecular and chemical levels.

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.

PROF. RENÉ PRÊTRE

Prof. Prêtre is the Head of the Paediatric Cardio-Vascular surgery unit at Lausanne University. He is recognised as one of the world's leading paediatric surgeons, 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 Medecine 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. 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. 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 the creation of several biotech start-up companies. Alexandra advices EspeRare in Intellectual Propriety and Business Development topics.

REGI AALSTAD

Mrs. Aalstad is an experienced board member, Private Equity adviser and a former General Manager in Fast Moving Consumer Goods in Asia, Europe and Middle East & Africa. She has served women and children globally for over 25 years with innovation and health education in Feminine and Baby Care at Procter & Gamble. Regi is committed to voluntary humanitarian board and adviser work to continue to improve people's lives.

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 neuromuscular, cardiovascular, and dermatological diseases. In partnership with patient organisations, 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 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, two senior managers, with 4 employees, and 25 contractors. EspeRare as an organisation is exempt from cantonal and federal taxes and is the equivalent of an exempt organisation 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 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 2020

The year was characterized by a number of factors, in particular R&D activities were negatively impacted by the COVID-19 pandemic. During the year 2020 the Foundation focused mainly on maintaining its R&D portfolio and on the development of the ER-004 project. Staff were maintained, planning had to be adapted. At the end of the year the portfolio was composed of 4 ongoing projects. 2020 R&D expenditure amounted to CHF 1'343'155 with a 36% reduction in expenses as compared to 2019. Income from Research & Development Project funding amounted to CHF 367'367 (7b) while income from R&D Donations amounted to CHF 843'620 (note 7). A Credit Note of CHF 345'453 granted to Espoir XLHED Sàrl, the Foundation daughter company, reduced the total Income to CHF 886'885 (note 7).

Overall this year, the foundation generated a loss (more expenses than income) of CHF 661'289.

Founding Capital

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

Donations

Total donations recognised in 2020 amounted to CHF 843'620, including an amount of CHF 616'245 deferred from 2019, EUR 15'000 from the Dioraphte Stitching was also received for the ER-004 program. CHF 200'000 from a Private Geneva Foundation and USD 6'000 from ASHOKA were received as COVID-19 relief donations and fully recognized in 2020. Ashoka has also donated EUR 21'500 as a COVID-19 dedicated grant (note 7a).

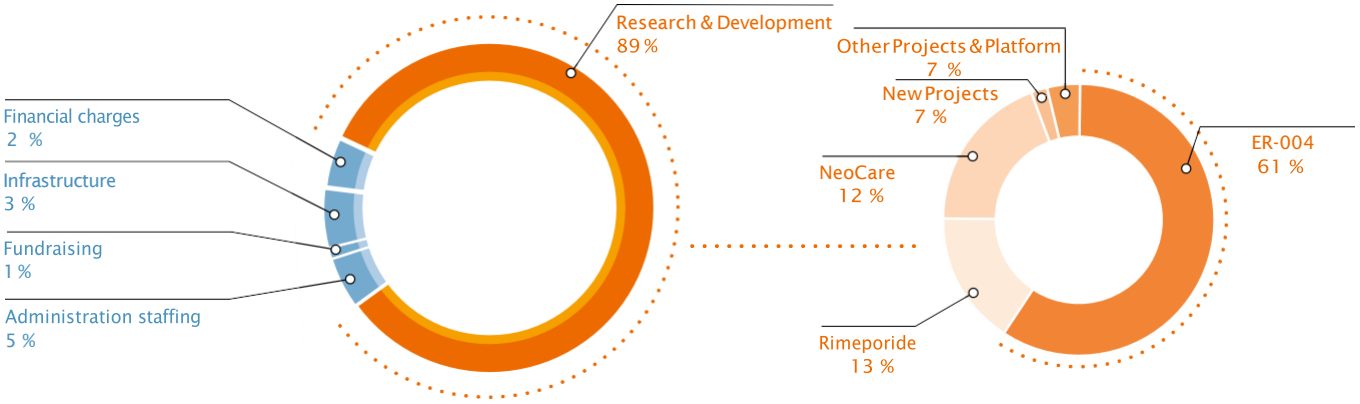
Staff

At end-year the senior management team consisted of an Executive Director and a R&D Director. Furthermore, EspeRare has a team of 4 Program Managers, a Senior Medical advisor, 25 contractors and counts as well on the support of many other people including Board Members, Senior Scientific Advisors and Volunteers.

General Administration

The total 2020 general and administration expenses amounted CHF 161'894 amounting to a 30% reduction in spending as compared to 2019. Expenses here reflect general foundation expenses in overall support of R&D activities (note 8g).

SNAPSHOT OF ESPERARE EXPENDITURE 2020



THE FINANCIAL YEAR AHEAD TO DECEMBER 2021

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, EUR as per the various agreements signed between Pierre Fabre Médicament and Espoir XLHED Sàrl, clinical activities expenses for ER-004 started to increase significantly at the end of the 2020. Those expenses will be recharged to Espoir XLHED Sàrl in EUR. The resulting exposure of exchange risk is evaluated at budget time 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.

Moreover, to better reflect increasing scientific activity the analytical accounting has been implemented since 2019 in agreement with KPMG Switzerland our auditors.

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 moving into these later stages of development, the foundation's need for financial support is increasing. Given the global COVID-19 context, 2020 has been a challenging year for fundraising efforts, this trend is expected to continue in 2021. However, in alignment with its fundraising strategy, EspeRare will actively seek new funding sources to enable EspeRare increase R&D activities and its impact, thus diminishing the burden on those patients suffering from rare diseases.

Conclusion

The detailed financial tables that follow – Balance Sheet and Statement of Income & Expenditure – represent EspeRare in its eight year of operation where all the various basic financial components of the organisation have been established step by step to create a prudent, transparent financial management framework. The scale-up of EspeRare activities has been dampened by the COVID-19 pandemic. Despite these external challenges, the Foundation is striving in the most efficient way, to reach its major goal: the discovery and development of new medicines for the treatment of rare diseases.

ESPERARE BALANCE SHEET

ASSETS	NOTES	2020 CHF	2019 CHF
Current Assets			
Cash & Cash Equivalents		813 680	1 637 192
Prepaid & Receivables			
Trade Accounts Receivable	11	329 020	623 409
Other Current Receivables		28 567	6 407
Witholding Tax		-	254
Prepaid Expenses from accrued income	12b	22 419	37 798
TOTAL CURRENT ASSETS		**1193 686**	**2 305 060**
Non-Current Assets			
Financial assets		13 638	14 258
Investments	4	20 000	20 000
Tangible Fixed Assets (Equipment)	2d	56 875	54 786
(less depreciation)		(44 334)	(30 431)
TOTAL NON-CURRENT ASSETS		**46 178**	**58 613**
TOTAL ASSETS		**1 239 864**	**2363 673**

LIABILITIES	NOTES	2020 CHF	2019 CHF
Short Term Liabilities			
Trade Accounts Payable		47 480	12 644
Employees Accounts		-	-
Other Short Term Liabilities		46 622	16 509
VTA Payable		-	64 900
Short Term Provisions	2f	-	-
Accrued Expenses	2g	21 197	77 601
Deferred Income	7a	17 954	616 245
Long Term Liabilities			
Covid Loan	16	192 128	-
TOTAL LIABILITIES		**325 380**	**787 899**
Capital & Reserves			
Foundation Capital	10	50 000	50 000
Operations Reserve	3	1 525 774	1 735 311
Net excess of (Expenditure)/Income		(661 290)	(209 538)
TOTAL CAPITAL & RESERVES		**914 484**	**1 575 774**
TOTAL LIABILITIES AND CAPITAL		**1 239 864**	**2 363 673**

ESPERARE STATEMENT OF PROFIT AND LOSS

	NOTES	2020 CHF	2019 CHF
TOTAL INCOME	7	**886 885**	**2 150 711**
Research & Development Expenses	8		
Espoir 004 Project	8a	(813 533)	(1 594 271)
Rimeporide Project	8b	(170 450)	(167 539)
Flowatch Project	8c	(167 300)	(68 373)
New Projects	8d	(95 803)	(202 035)
Other Projets	8e	(8 991)	(36 397)
Repositioning Platfrom	8f	(87 078)	(29 370)
TOTAL RESEARCH & DEVELOPMENT EXPENSES		**(1 343 155)**	**(2 097 985)**
General Foundation Administration	8g	(161 894)	(234 615)
Operating Result (Expenditure)/Income		**(618 163)**	**(181 899)**
Financial Income & Expenses	9	(43 126)	(68 358)
Non-operating & Extraordinary Income & Expenses	12	-	40 709
NET EXCESS OF (EXPENDITURE) / INCOME		**(661 289)**	**(209 538)**

NOTES TO FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2020

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 accelerating the cost-effective development of unexplored (re)positioning opportunities for rare neurological and immunological diseases. 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.

b) Recognition of donations

Contributions from donors (both public, private and philanthropic sources) are recognised 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 date of the transaction.

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 recognised in the profit and loss statement. 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:
1 EUR = CHF 1.081550
1 USD = CHF 0.883944
1 GBP = CHF 1.208300

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:

- office furniture (second hand and low cost) 3 years
- office furniture (new) 5 years
- fixtures and installations 3 years
- computers and equipment 3 years

Assets	2019 CHF	Acquisitions	Disposals	2020 CHF
IT Equipment	24 771		-	24 771
Furniture	30 015	2 089	-	32 104
TOTAL	**54 786**	**2 089**	**-**	**56 875**

Depreciation	2019 CHF	Depreciation	Disposals	2020 CHF
IT Equipment	16 279	3 885	-	20 164
Furniture	14 151	10 019	-	24 170
TOTAL	**30 431**		**-**	**44 334**
TOTAL NET VALUE	**24 355**			**12 540**

e) Research and Development

Expenditure and grants allocated for research activities are undertaken with the prospect of gaining new scientific or technical knowledge and understanding for 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 capitalising development costs.

f) Provisions

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

g) Accruals

An accrual is recognised 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) Employee Benefits - Pension Plan

EspeRare's pension plan is classified as a defined contribution plan. Contributions to the defined contribution pension plan are recognised as an expense in the statement of income and expenditure as incurred.

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

j) Impairment
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.

k) Financial Income
Interest income is recognized in the income statement as earned.

l) Income Tax
EspeRare has received exoneration from income tax from the Geneva cantonal and Swiss federal authorities from the year 2013 for 10 years.

3. RESERVES

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

4. INVESTMENTS

The Esperare Foundation owned 100% of the capital of EspoirXLHED Sàrl. EspoirXLHED is a limited liability company incorporated on March 28, 2018 and based at avenue Sécheron 15, 1202 Geneva, Switzerland. The purpose of the company is the Research and Development of treatments modulating to the Ectodysplasin Pathway.

5. COMMITMENTS

As at 31 December 2020, there were no significant capital expenditure commitments.

6. SUBSEQUENT EVENTS

No events occurred subsequent to 31st December 2020 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 follow

Income	2020	2019	
Income from R&D Donations	843 620	206 468	(a)
Direct Income from R&D Activities	367 399	1 921 282	(b)
Other Operating Income	21 320	22 962	(c)
Less allowance	(345 453)	-	(d)
Total	**886 885**	**2 150 711**	

a) Income from R&D Donations and differed income

During 2020 the following donations were granted:

Donors	Notes	Currency	Exch. rate	Total Grant	Deferred from 2019 CHF	Received during 2020 CHF	Recognised during 2020 CHF	Deferred to 2021 CHF	Notes
EspoirXLHED Sàrl	3	CHF		1 950 000	616 245		616 245		Grant – R&D program & foundation
Ashoka Covid-19 relief		USD	0,979	6 000		5 872	5 872		Grant – R&D program & foundation
Stitching Dioraphte		EUR	1,067	15 000		16 001	16 001		Grant – EspoiR-004
Private Geneva Foundation		CHF		200 000		200 000	200 000		Grant – R&D program & foundation
Ashoka Covid-19 grant		EUR	1,091	21 500		23 455	5 502	17 953	Grant – New Prospect/Rim in COVID
TOTAL					**616 245**	**245 328**	**843 620**	**17 953**	

As a comparison 2019 the following donations were granted:

Donors	Currency	Exch. rate	Total Grant	Deferred from 2018 CHF	Received during 2019 CHF	Recognised during 2019 CHF	Deferred to 2020 CHF	Notes
Prim'Enfance	CHF		20 000	20 000		20 000	0	Grant – FloWatch/NeoCare
Private Donor	CHF		200 000	171 468		171 468	0	Grant - EspoiR-004
EspoirXLHED Sàrl	CHF	1.151	1 950 000	616 246			616 246	Grant – R&D program & foundation
Fondation Tell et un Tel	CHF		15 000		15 000	15 000	0	Grant - Platform
TOTAL				**807 713**	**15 000**	**206 468**	**616 246**	

b) Direct Income from R&D activities consisted of CRO services to Espoir XLHED Sàrl for the development of EspoiR-04 in X-linked Ectodermal Dysplasia for an amount of CHF 332'900 and consulting services to Pro Clara for the development of NPT189 for an amount of CHF 34'499.

c) Other Operating Income consists of the subletting of part of Esperare offices to a partner.

d) In 2020, EspeRare issued a credit note to EspoirXLHED Sàrl related to invoices raised in 2019.

8. EXPENSES

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

R&D Expenditures	2020	2019	
Espoir 004 Direct Costs	278 498	697 513	
Espoir 004 Support Costs	535 035	896 757	
Total Espoir 004	**813 533**	**1 594 271**	(a)
Rimeporide Direct Costs	23 160	93 533	
Rimeporide Support Costs	147 289	74 007	
Total Rimeporide	**170 450**	**167 539**	(b)
NeoCare (Flowatch) Direct Costs	81 318	26 253	
NeoCare (FloWatch) Support Costs	85 982	42 119	
Total NeoCare (FloWatch)	**167 300**	**68 373**	(c)
New projects prospect Direct Costs	5 928	35 153	
New projects prospect Support Costs	89 876	166 882	
Total New Pojects	**95 803**	**202 035**	(d)
JNK Direct Costs	-	15 821	
JNK Support Costs	8 991	20 576	
Cilengitide Direct Costs	-	-	
Cilengitide Support Costs	-	-	
Total Other Projects	**8 991**	**36 397**	(e)
Repositioning Platform Direct Costs	5 778	-	
Repositioning Platform Support Costs	81 300	29 370	
Total Repositioning Platform	**87 078**	**29 370**	(f)
Total	**1 343 155**	**2 097 985**	

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 (as evolution of the FloWatch project that was stopped).
d) Prospection & generation of new drug development projects for rare diseases, including Rimeporide for COVID-19.
e) Other projects: Development of JNK-inh in Duchenne Muscular Dystrophy and in Paediatric Cancer.
f) Repositioning platform development to support the systematic discovery and evaluation of new projects.

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 project including the Foundation.

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

General Foundation	2020	2019
Administration staffing	84 357	143 631
Patient Association Consultancy	-	-
Office Rental	5 080	6 340
Audit Expenses and accounting	12 460	13 253
General Insurance	21 106	7 573
IT Expenses	-	233
Communications	-	119
General Legal Fees	8 440	18 037
Fundraising direct costs	2 549	13 874
Advertising Costs	10 017	11 184
Board meeting	3 981	6 089
Other Operating Expenses	-	-
Depreciation	13 904	14 282
Total	**161 894**	**234 615**

9. FINANCIAL INCOME AND EXPENSES

The financial income and expenses are split as follow:

Financial Income and Expenses	2020	2019
Financial Income	-	1 041
Financial Charges	(1 736)	(2 087)
Exchange Differences (loss) gain	(41 390)	(67 312)
Total	**(43 126)**	**(68 358)**

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 329'020 from Espoir XLHED Sàrl (2019: CHF 582'529). This inter-company receivable includes a receivable of CHF 358'534 and a payable of CHF 29'514.

12. NON-OPERATING EXCEPTIONAL INCOME AND EXPENSES

A settlement agreement with Phast AG on disputed invoices for a total amount of EURO 39'995 was concluded on 22nd January 2020. These costs were already in the income statements of 2017 and 2018. The settlement agreement was booed as an exceptional income for the amount of CHF 40'709 in the year 2019 (2020:nil).

13. PERSONNEL EXPENSES

Total staff benefits for 2020 amount to CHF 892'405 in comparison of a total of CHF 871'564 for 2019.

14. GOUVERNANCE

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

Corresponds to a bridging loan granted in the context of the COVID-2019 crisis amounting to CHF 192'128. This loan is guaranteed by the Swiss Federal Council and is without interest and to be repaid on free terms, however at the latest within a period to be determined by the Swiss Federal Parliament, currently 5 years. This loan is contracted on honour and assorted by special conditions of the Swiss Federal Government, EspeRare is compliant with these conditions.

17. CONTINGENT LIABILITIES

EspeRare has 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 December 31st 2020, a total of 687 hours were incurred, representing a total of CHF 206'100 amount that stayed unchanged since 2019. EspeRare has not accrued nor provisioned these costs (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, Genève

As statutory auditors, we have examined the financial statements (balance sheet, profit and loss statement, cash flow and notes) of the Foundation EspeRare for the year ended 31 December 2020.

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 and regulations.

KPMG SA

Cédric Rigoli
Licensed Audit Expert
Auditor in Charge

Pierre Henri Pingeon
Licensed Audit Expert

Geneva, 23 March 2021

Enclosure:
- Financial statements (balance sheet, profit and loss statement, cash flow and notes)

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 Baudoin Foundation** which allows **European and USA citizens** to make cross-border donations while still benefiting from the tax advantages of their country of residence.

AS AN INDIVIDUAL OR AS 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 the impact 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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