



# ANNUAL REPORT 2018





Picture of EspeRare founders:  
Florence Porte-Thomé,  
Caroline Kant & Béatrice Greco

# Mission & vision

## MISSION

At EspeRare we are committed to improve the lives of children with life-threatening rare diseases. EspeRare addresses the unmet medical needs of these children by uncovering the potential of existing treatments.

As a not-for-profit organization, we achieve this through a collaborative approach centered on patient engagement with the aim of giving children and their families fair access to these therapies and a new hope for the future.

## VISION

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



For further information on EspeRare, please visit [www.esperare.org](http://www.esperare.org)

<b>Message from the Chief Executive Officer</b>	<b>4</b>
Highlights	6
<b>Addressing rare diseases</b>	<b>8</b>
A new hope for children with life-threatening rare diseases	10
EspeRare uncovers and develops new therapeutic potential of discontinued treatments	11
Our alternative business model	13
A collaborative system to advance treatment and care for patients	14
<b>Our portfolio of treatments</b>	<b>15</b>
X-Linked Hypohidrotic Ectodermal Dysplasia (XLHED)	16
DMX-101 Programme in X-Linked Hypohidrotic Ectodermal Dysplasia	17
Duchenne Muscular Dystrophy (DMD)	20
Rimeporide Programme in Duchenne Muscular Dystrophy (DMD)	22
Congenital Heart Defects (CHD)	24
Development of the NeoCare FloWatch	25
ER-005 Programme in paediatric cancers	26
<b>Organisation</b>	<b>28</b>
<b>Financial view</b>	<b>34</b>
<b>How can I support EspeRare?</b>	<b>42</b>





## Message from the Chief Executive Officer

*At EspeRare we are committed with our heart 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 1 out of 4 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. Patient organisations guide how we tackle diseases, informing our approach from therapeutic product selection to supporting clinical testing and help develop new strategies for therapeutic distribution.*

**“Let us make our future now, and let us make our dreams, tomorrow’s reality”**

**Malala Yousafzai**

Dear Friends,

Since the start of its journey and its launch in April 2013, EspeRare has much to be proud of. Our organization has evolved from a small start-up to a well-established biotech. Our growth and success are a reflection of EspeRare’s ability to attract the best and the brightest, including senior leaders from the pharmaceutical industry, top medical experts, and regulatory professionals.

In such a short time, we are proud to have provided a new **hope to millions of children affected with life-threatening rare diseases** like Duchenne ([page 20](#)), congenital heart diseases ([page 24](#)) and cancers affecting children ([page 26](#)). Additionally, with DMX-101 we are not only in the latest phase of development for this therapy that has the potential to **correct the most debilitating symptoms of a rare form of ectodermal dysplasia**, but moreover, we are also **setting a new path for treating life-threatening diseases before birth with a novel in-utero administration approach** ([page 16](#)).

Given the magnitude of healthcare challenges today, working hand in hand with the patient community and integrating solidarity commitments early in the drug development process, represents an ethical way forward for developing new medicines

in the future. In many ways, **EspeRare serves as a philanthropic venture that revives the therapeutic and financial value of existing, yet unexplored treatments**. In 2018, we have been able to demonstrate that its not-for-profit biotech model is a viable and impactful business model that not only **delivers promising therapeutic programmes but also generates financial returns that are reinvested into its mission as well as shared with initial programme contributors**.

Looking ahead, in addition to delivering on our current portfolio of programmes, it is now the time to envision how to further grow and advance the EspeRare model and realize its potential of sustainably and systematically uncovering therapies for rare diseases. In order to do this, we anticipate the need and plan for the development of a digitally-enabled collaborative system where scientific experts, medical professionals, pharma groups, patients’ communities and health authorities will interact and ensure a continuous flow of data and insights. **Our vision is a platform that will always put the patient first and will aim to methodically leverage all layers of intelligence to efficiently develop treatments and drive real-life improvement for these children and their families.**

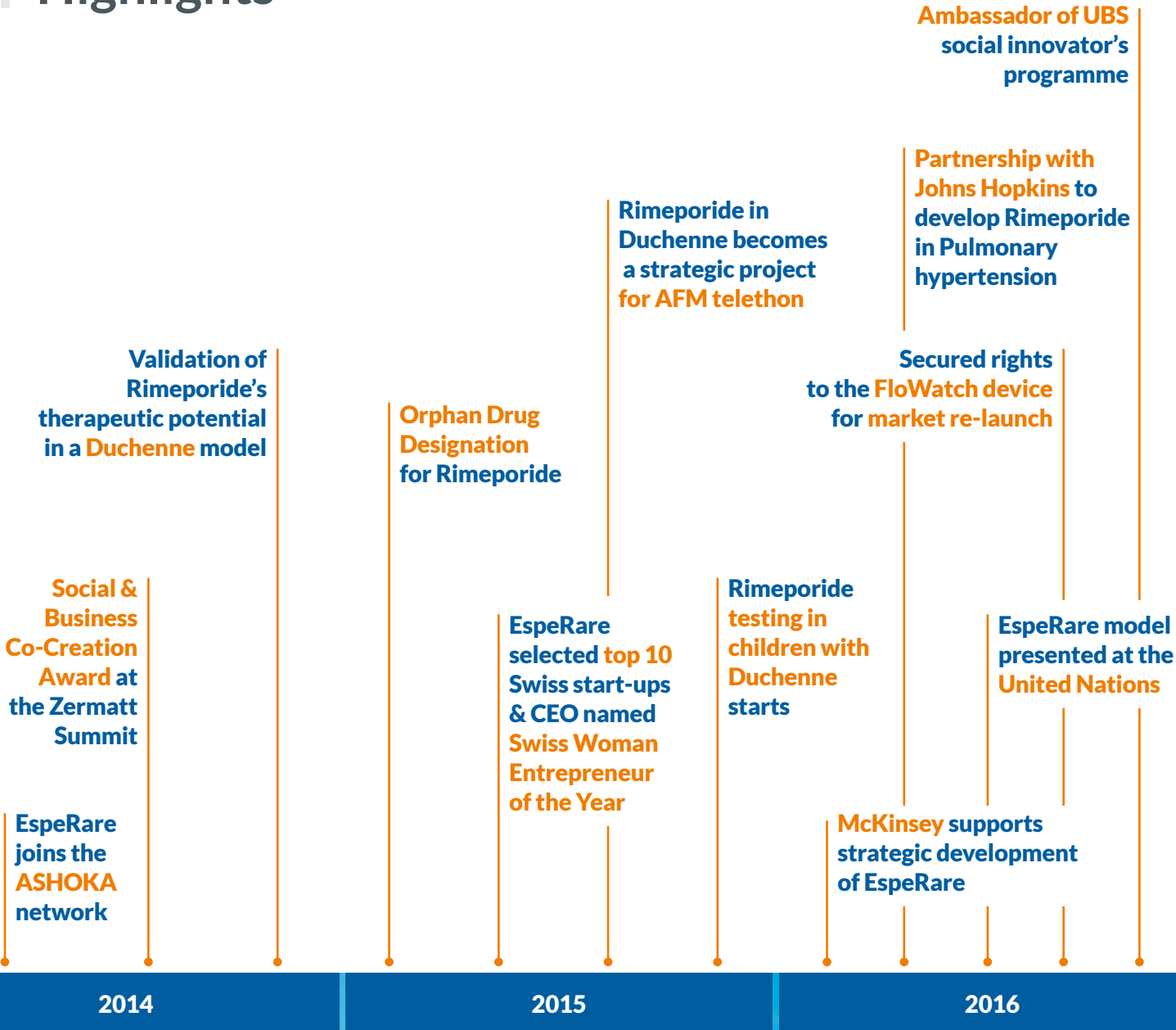
Collaborations with key actors from the rare disease ecosystem, a committed and passionate team, a strong network of partners and donors has been the cornerstone of EspeRare’s growing success over these past 5 years. All this support has been instrumental in our achievements and has given us the courage 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 energized to carry on the task ahead and look forward to your extended support throughout the years.**

Sincerely,

**Caroline Kant**  
Founder & CEO

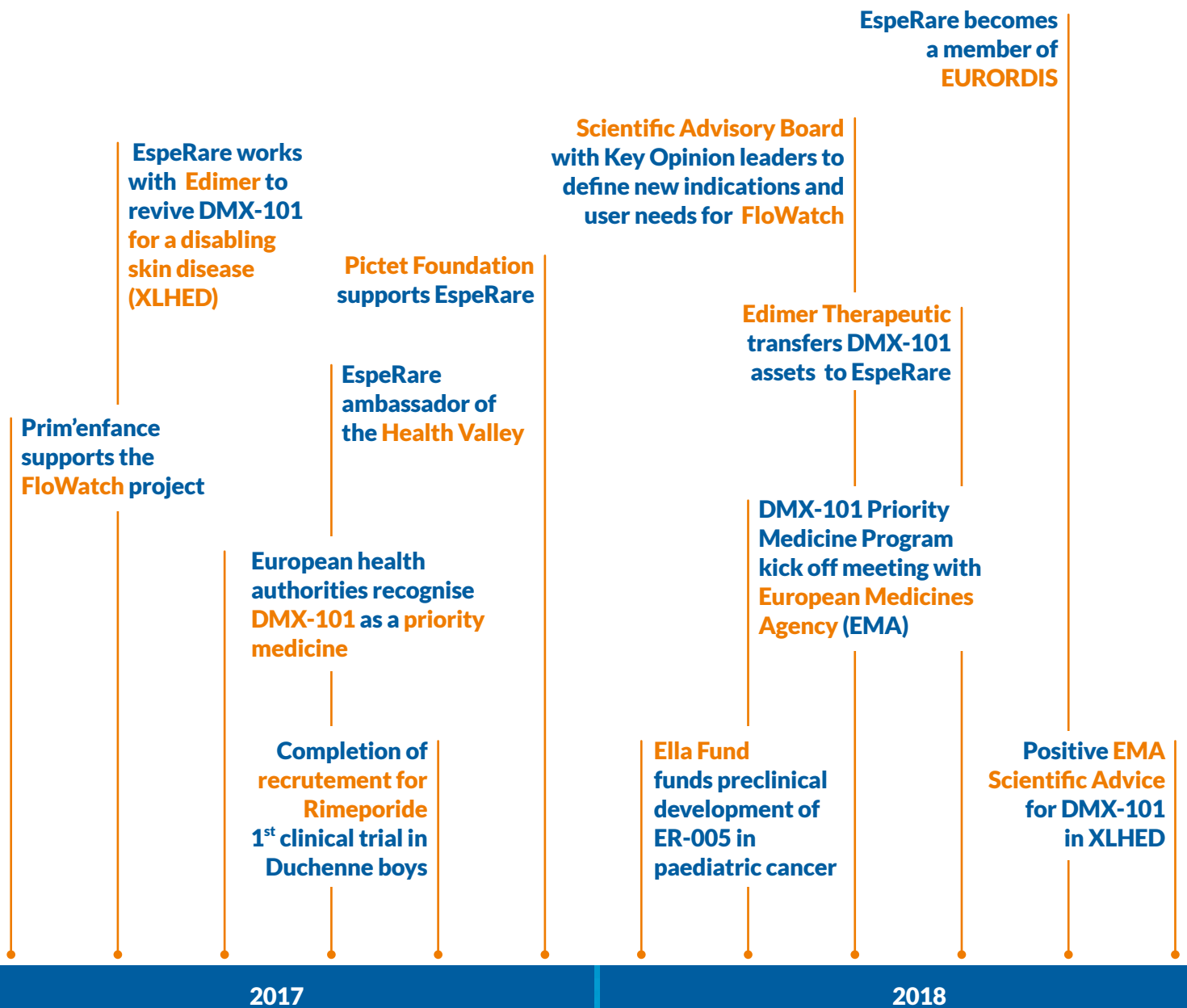


# Highlights



“Everyone has some inner power that awaits discovery.”

Chard Paul Evans



2018





# Addressing rare diseases

## WHAT IS A RARE DISEASE?

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.

## EMPOWERED PATIENT ADVOCACY ORGANISATIONS IN RARE DISEASES

Particularly in rare conditions, patient advocacy organisations are key partners 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.

\* Source: Orphanet and the US Orphan Drug Act



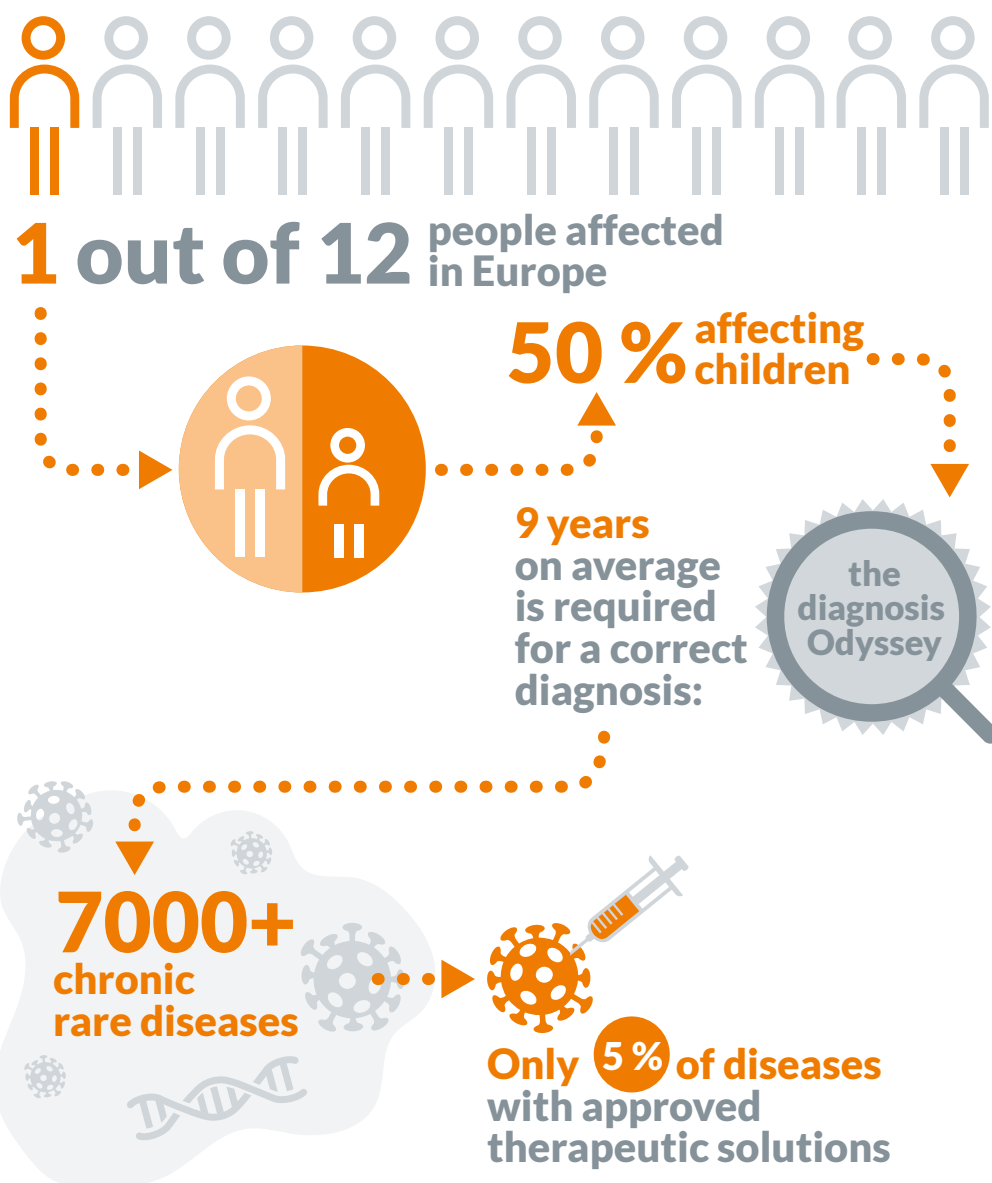
#### PATIENTS ARE AT THE CORE OF CURRENT PROGRESS IN RARE DISEASES:

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.

### RARE DISEASES: A MAJOR GAP IN THE MEDICAL LANDSCAPE



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

# A new hope for children with life-threatening rare diseases

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

### 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.

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

### 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.

### ESPERARE DISEASE FOCUS

EspeRare opted to **concentrate most of its activities on rare children diseases that represent nearly 50 % of rare diseases.** EspeRare has selected approximately **thirty diseases to focus its efforts on.** These diseases have been selected thanks to multiple criteria, ranging from the severity of the unmet medical need, the foundation's access to a strong disease community and the presence of a ripe "drug development infrastructure" (e.g. scientific knowledge, patient registries, diagnostic test, etc.).

**With a unique patient-centered approach with full engagement of the patient community at each step of the drug development process. ■**

## ESPERARE RESCUES AND REPOSITIONS DRUGS TO ACCELERATE THE DEVELOPMENT OF TREATMENTS FOR RARE DISEASES

Bringing to life discontinued treatments into safe and life changing therapies for children with severe rare diseases.

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 and beneficial for patients and the healthcare system at large. ■**



# EspeRare uncovers and develops new therapeutic potential of discontinued treatments

## 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 pre-clinical 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 that:

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

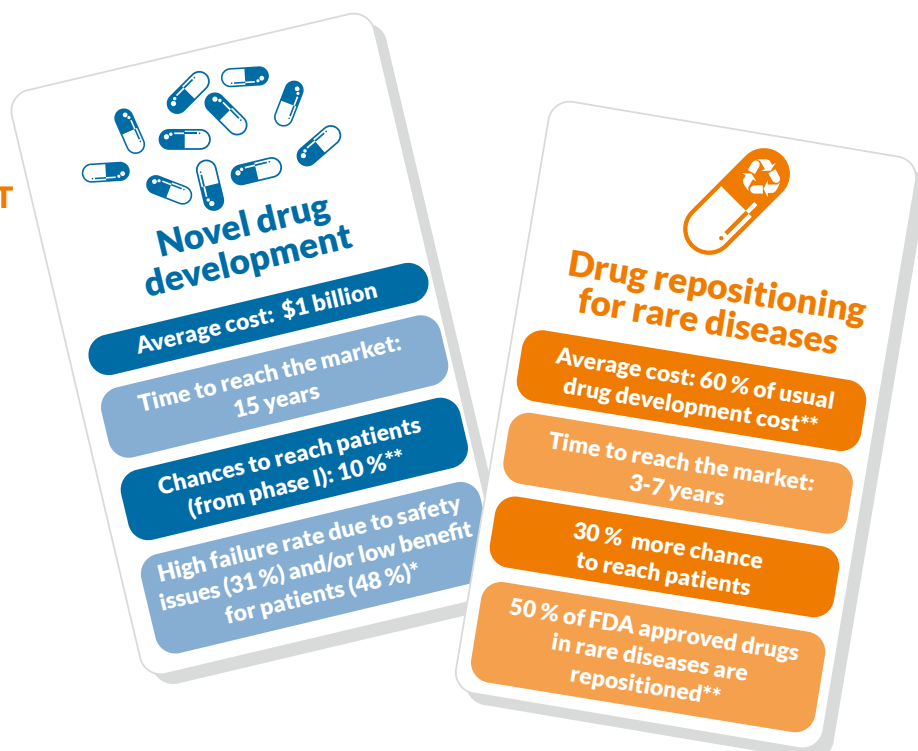
→ interact directly with regulatory agencies and health authorities to best pave the way to drug approval and patient access to treatment.

***EspeRare bridges the patient's medical and commercial interests into a system that accelerates drug development with the goal of bringing new treatments to underserved patients. ■***

## REPOSITIONING DRUGS: A DE-RISKED & COST-CONTAINED APPROACH TO DRUG DEVELOPMENT

### EspeRare's strategy drug development in rare diseases:

- **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 ACTION: BRIDGING PATIENT AND COMMERCIAL INTERESTS TO ACCELERATE AND "DE-RISK" DRUG DEVELOPMENT



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 a number of 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.

*At the heart of EspeRare's novel model lays the development of a network of highly collaborative, patient-centered, public/private partnerships that drive the development of accessible drugs for rare diseases. ■*





## Our alternative business model

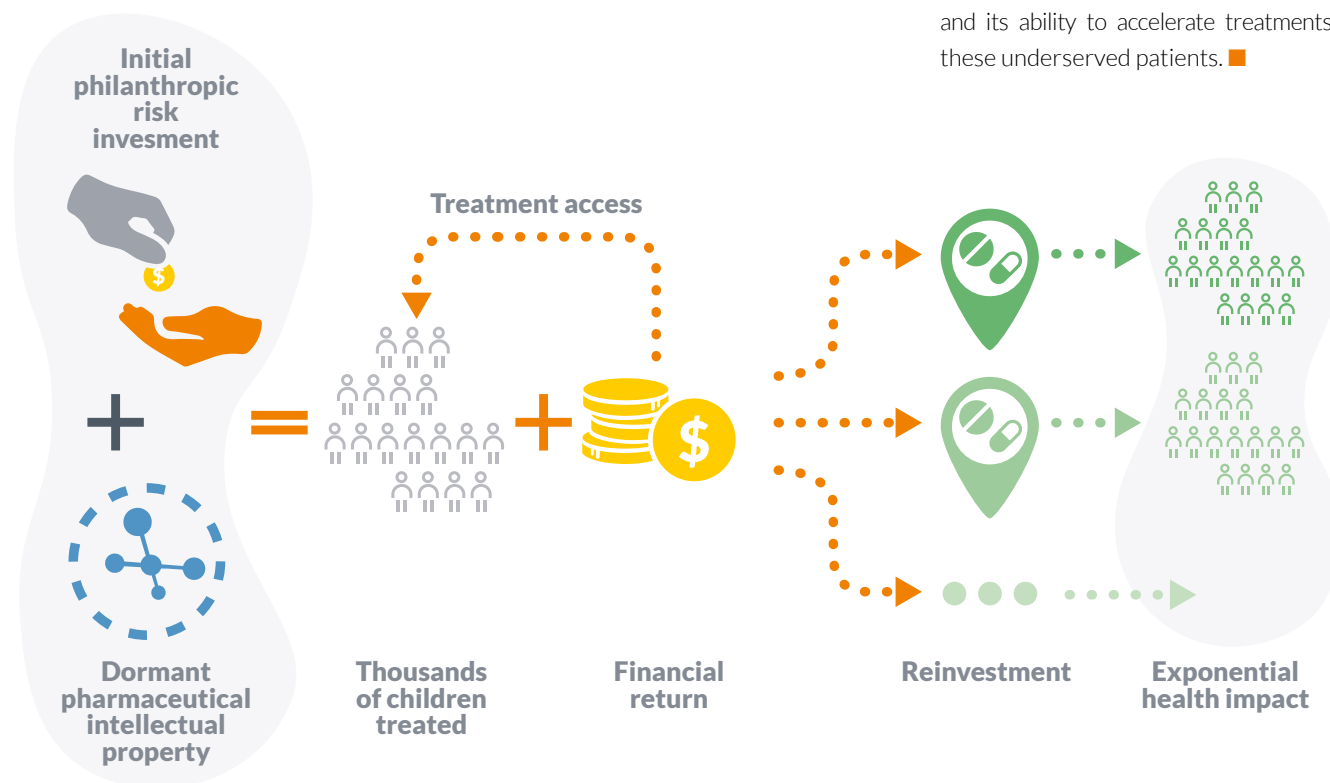
### IMPACT OF ESPERARE'S BUSINESS MODEL ON THE RARE DISEASE COMMUNITY

**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 programmes 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 treatments for these underserved patients. ■





## A collaborative system to advance treatment and care for patients

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

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)** enables 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. ■*



# 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 five 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 20](#)).

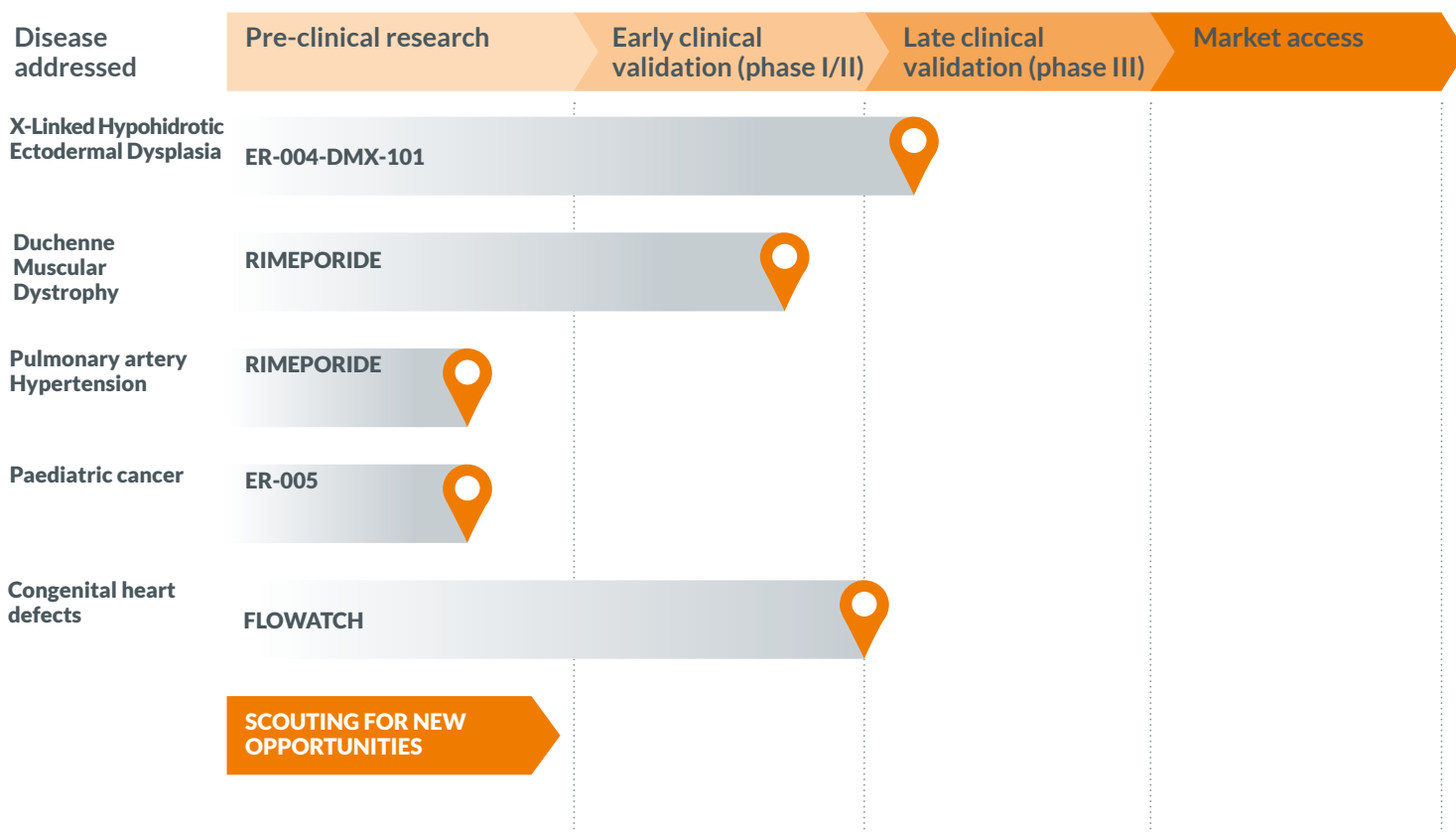
This first programme is also a validation of the strength of EspeRare's philanthropic model to drive and fund drug development in rare diseases.

Towards this goal, **EspeRare is also reviving DMX-101 using a novel intra-amniotic administration route in XLHED** (see [page 16](#)). Additionally, it is developing a new therapeutic device for infants affected by severe cardiac defects (see [page 24](#)), and is repositioning ER-005 as a first-in-class drug for the treatment of rare paediatric cancers (see [page 26](#)).

EspeRare is trying to diversify its partners and develop 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).

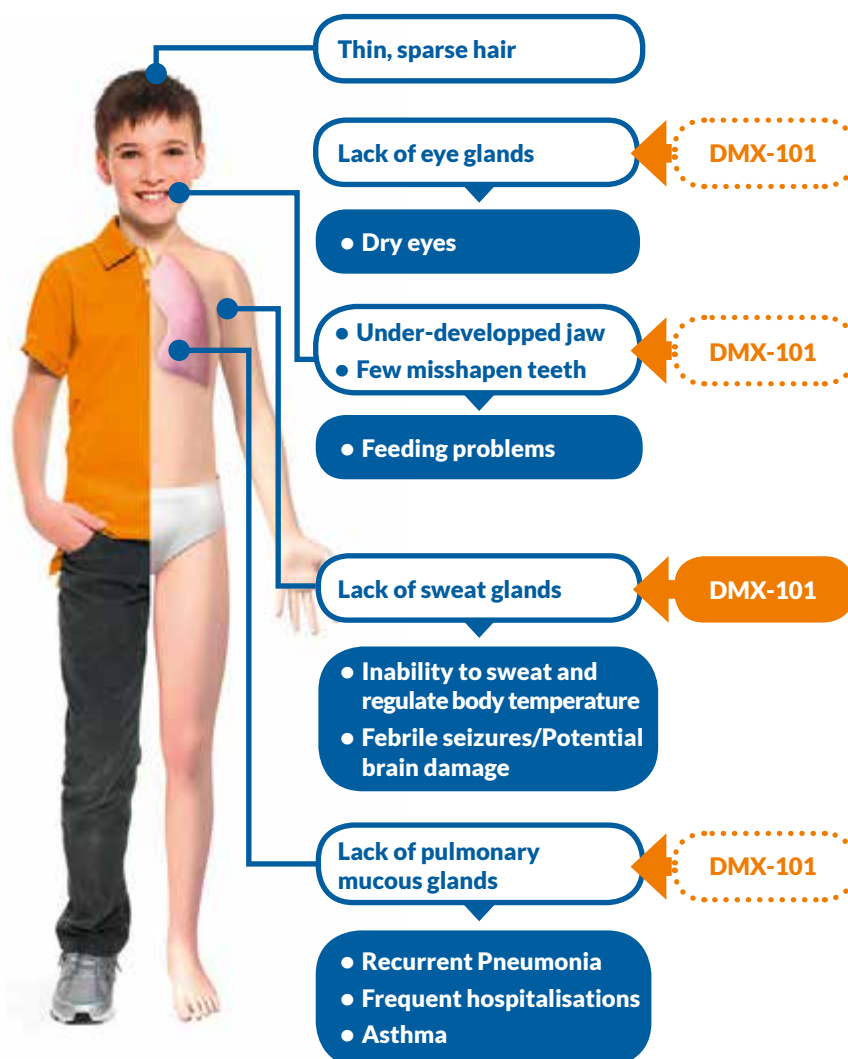
Consequently, the development of ectodermal structures such as skin, teeth, glands and hair is impaired. As boys have one single copy of this gene on their X-chromosome, they usually display the full spectrum of the syndrome as opposed to girls that are in general less affected.

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.*

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. ■



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



# DMX-101 PROGRAMME IN X-LINKED HYPOHIDROTIC ECTODERMAL DYSPLASIA

The development of DMX-101 (previously named EDI200 or ER-004) was stopped by Edimer Pharmaceutical, due to treatment's lack of efficacy when treating newborns with XLHED.



EspeRare has revived DMX-101 using a novel intra-amniotic administration route. It has also entered into partnership with Dermelix 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 DMX-101 to neonates. Then EspeRare was approached by Edimer Pharmaceuticals to revive DMX-101'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 DMX-101 to 3 unborn XLHED fetuses.

The development of DMX-101 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, DMX-101 also benefits from Orphan Drug Designation in the EU and the US and "Fast-Track" Designation by the FDA in the US.

### 2018

Dermelix and EspeRare, who share the mission of advancing treatments for rare diseases through a patient-centered approach, entered into partnership at the end of 2018 for the co-development of DMX-101 in XLHED.

EspeRare and Dermelix prepare to start a pivotal clinical trial in 2019 with the goal of obtaining a market authorization worldwide. The trial will start recruiting patients in Europe, with Prof. Holm Schneider as principal investigator at Erlangen University Hospital in Germany.

### 2019 and beyond

In view of recent advice from EU and US regulatory agencies, EspeRare and Dermelix aim to start enrolling patients in Europe in the second half of 2019, followed by the US. ■

### DMX-101 CARD:

**Name:** DMX-101  
**Target:** EDAR (EDA protein receptor) and the activation of the NFκ-B pathway during development  
**Originator:** Edimer Pharmaceuticals Inc., an American biotech  
**Indications:** X-Linked Hypohidrotic Ectodermal Dysplasia  
**Drug development phase:** comprehensive non-clinical and phase I clinical data package; a phase II clinical trial in newborn babies failed to show benefits.  
**Opportunity:** In the second half of 2019, EspeRare and Dermelix aim to start patient enrollment into a pivotal study, first in Europe and then in the US.

"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."

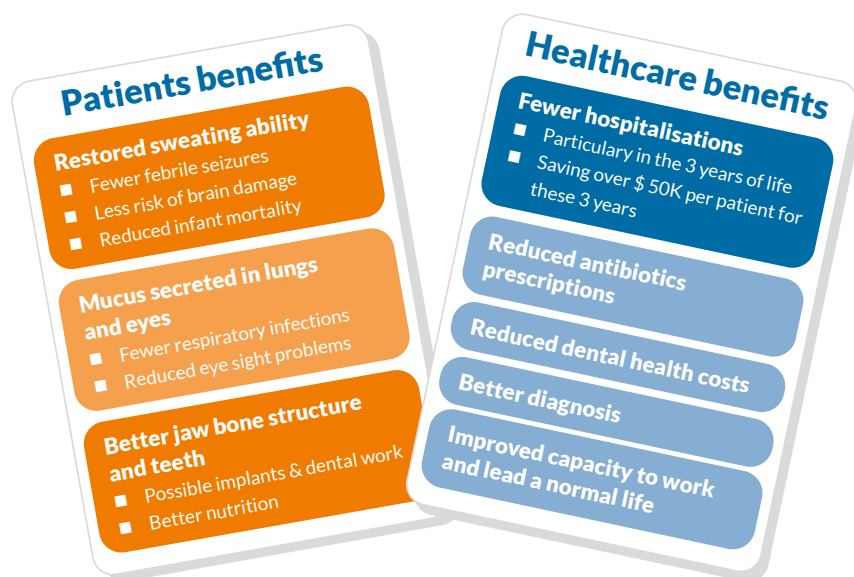
Caroline Kant, Founder & CEO



## DMX-101: A “SINGLE COURSE” THERAPY TO INDUCE NORMAL ECTODERMAL DEVELOPMENT

DMX-101 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.***



We are delivering in a major way on our model with the DMX-101 programme (more on [the next page](#)) where we have concluded a co-development deal with Dermelix, a US biotech. Under the terms of the agreement, EspeRare remains the sponsor of DMX-101 clinical development in Europe, while Dermelix will lead

clinical activities outside of Europe. Our partner is financing the development of the product and will be responsible for its commercialization worldwide. In exchange for DMX-101 commercial rights, EspeRare is receiving upfront and milestone payments as well as royalties on future sales. Delivering on EspeRare not-

for-profit model, these financial returns are being shared, on one hand with initial contributors of DMX-101 development and on the other hand reinvested to scale EspeRare's organization and portfolio of therapeutic programmes with a new strategic focus in prenatal therapies. ■



## OUR COMMITMENTS, PRINCIPLES AND VALUES

### COMMITMENTS TO THE XLHED PATIENT COMMUNITY

Both Partners regard 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 and Dermelix 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 apply not only to the collaboration between Dermelix and EspeRare but also guide all other 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.

#### **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.

**TRANSPARENCY** about roles, responsibilities, constraints, potential conflicts of interest as well as the outcomes of the DMX-101 programme.

**INTEGRITY** of behaviors, processes, use of funds, as well as being driven by moral soundness and accountability.

EspeRare and Dermelix also agreed within its **Ethics and Social Responsibility Charter** on convening 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 Dermelix/EspeRare in order to streamline information sharing and collect input of the patient community into the development of DMX-101.

## THE PATIENT ADVISORY COUNCIL (PAC)

The PAC serves as a patient advisory resource to EspeRare and Dermelix team members, senior management, and shared governance in the development and commercialization of DMX-101 for XLHED. It offers a safe venue for patient groups representatives to:

- Share views of the XLHED patient community concerning the DMX-101 programme;
- Receive regular programme updates and information to foster patients' and families' access to key programme insights;
- Provide input into DMX-101 development activities to co-development Partners;
- Make recommendations to help plan, implement, and refine efforts towards meaningful patient involvement. ■





# Duchenne Muscular Dystrophy (DMD)

## ABOUT DUCHENNE MUSCULAR DYSTROPHY (DMD)

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

Patients affected by DMD have **progressive weakness and loss of muscle function in their early childhood.** The degeneration of muscle cells is accompanied by an immune reaction (inflammation) and scarring of the muscle (fibrosis). This progressive muscle wasting typically leads to loss of ambulation 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 has 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.

No specific treatment exists or is in development for DMD cardiomyopathy. **Currently, there is unfortunately no cure for this disease.**

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**



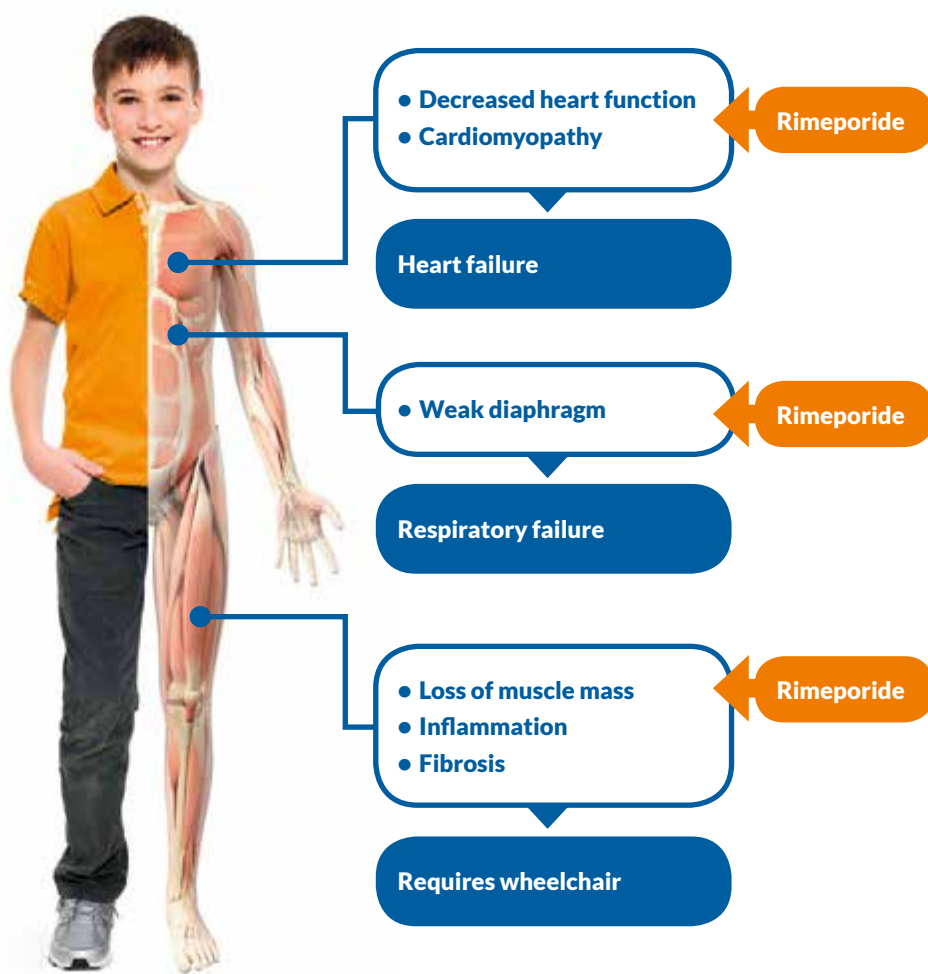
Affects the  
longest gene  
in the body:  
**the dystrophin**  
**gene**



Symptoms  
appear  
between  
the ages of  
**2 and 5 years**



Described by  
**Dr. Duchenne**  
in 1861





## RIMEPORIDE PROGRAMME IN DUCHENNE MUSCULAR DYSTROPHY (DMD)

### BACKGROUND

#### 2013

EspeRare obtained the rights to develop Rimeporide in neuromuscular diseases.

#### 2014

Two non-clinical 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 conducted 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). Good tolerability was demonstrated in young DMD boys, confirming the safety and tolerability obtained previously in adult healthy subjects. In addition, there was **preliminary evidence for biological efficacy on several serum/plasma biomarkers** of inflammation and muscular function and injury, supporting the therapeutic potential of Rimeporide in patients.

- **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 and beyond

EspeRare is seeking for a partner to further develop Rimeporide as a major life changing treatment to prevent DMD boys from developing fatal cardiomyopathy.

In the past decades, there has been progress in the care and management of DMD patients but heart failure secondary to dystrophin deficiency is becoming the predominant cause of death in these patients and there is a high need and urgency to develop therapeutic strategies to protect the heart of these patients.

**Cinical and non-clinical studies are in favour of pursuing the development of Rimeporide in patients with DMD as a cardioprotective treatment.**

Discussion on the design of a phase II/ III pivotal study is been conducted with Clinicians, Patients groups and Health Authorities. ■

Rimeporide is a safe, potent and 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 pulmonary artery hypertension.

“ Non-clinical data suggest that 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 has the potential to treat the fatal cardiomyopathy symptom*

*in Duchenne, which is at present a progressive condition with very limited therapeutic options. To our knowledge, Rimeporide is the only clinical stage therapy intended to reduce inflammation and fibrosis both in skeletal muscles and in the heart.*

#### RIMEPORIDE IDENTITY CARD:

**Name:** Rimeporide  
**Target:** Sodium-Proton Exchanger protein (NHE-1)

**Originator:** Merck Serono

**Indications:** Duchenne Muscular Dystrophy (DMD, active development by EspeRare) and Chronic Heart Failure (CHF, inactive development)

#### **Drug development phase:**

Administered to more than 150 healthy and adults (7 phase I trials). Robust preclinical data package Phase Ib clinical trial in children with DMD completed. Nonclinical translational study underway.

#### **Opportunity:**

Clinically relevant beneficial anti-inflammatory, anti-fibrotic and cardioprotective effects in DMD.

## 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) support ongoing 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), AltroDomaniOnlus (Italy), Duchenne UK (United Kingdom).



**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 NEWBORN AND PULMONARY ARTERY BANDING



*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 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. ■*

## THE FLOWATCH DEVICE IS CLEARLY SUPERIOR TO CONVENTIONAL PAB

Conventional PAB is far from being optimal. The implantation of the band is conducted under general anaesthetic and artificial respiration which makes the adjustment of the device very difficult. Long stays in intensive care and further operations to re-adjust 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. ***FloWatch 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 physically access the device. It results in ***shorter stays in intensive***

***care and the need for re-operations to adjust the banding.*** In addition, the innovative adjustment capabilities of the system allow surgeons and cardiologists to develop new treatment possibilities tailored to their patients' needs. ***This device has proven medical benefits during its commercialisation and has been implanted successfully in children in Europe and Asia between 2002 and 2012.*** ■



## DEVELOPMENT OF THE NEOCARE FLOWATCH

*FloWatch is a unique pulmonary artery banding system that can be adjusted remotely through the chest avoiding repeated surgeries. It was commercialised until 2012 when the company went bankrupt.*

*EspeRare is working on an improved FloWatch device: the NeoCare and is looking to expand its use to a broader number of babies affected by severe cardiac defects. FloWatch already proved its ability to remotely reduce pulmonary*

*artery blood flow and thus protect the heart and lungs of newborns while waiting for a intracardiac surgery. The current FloWatch had technological limitations which prevented its use in a broad patient population affected by severe CHDs.*

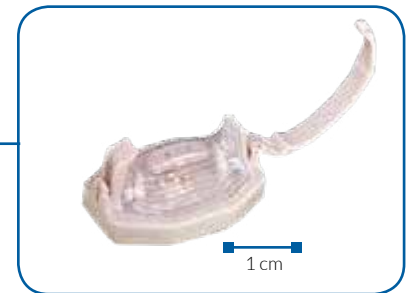
*While some features of FloWatch such as clamping geometry, the PEEK casing and membrane are still relevant, other features need to be redesigned to integrate current patients and user needs and meet the new medical directives.*

*EspeRare, in collaboration with Haute Ecole d'Ingenierie Vaudoise (HEIG-VD) is optimizing the technology, its quality, and also upgrade its regulatory documentations and manufacturing processes in order to enable European and US market authorisation within the next years.* Fulfilling EspeRare's Humanitarian Commitments, part of the FloWatch devices produced will be distributed in Africa and in Asia. In these regions, only a small number of newborns have access to the heart repair surgery so protecting these babies' heart with FloWatch is even more pressing and can prove to be of vital importance. ■

### FloWatch® -Control Unit



External Antenna



**FloWatch®**  
implant on the pulmonary artery

“The FloWatch device has proven, since 10 years, to provide an adaptable regulation of heart blood flow and protect the pulmonary circulation of patients not amenable to immediate complete surgical repair.”

Prof. Maurice Beghetti

### BENEFITS OF FLOWATCH

#### TECHNICAL INNOVATION

- Unique technology able to remotely and precisely adjust the pulmonary artery diameter
- Electro-mechanical implant with a biocompatible encapsulation
- Wireless control, no battery required

#### MEDICAL ENHANCEMENT

- Fast and precise banding procedure with no need for re-operation
- Remote blood pressure control
- Infant homecare
- Safer final cardiac repair surgery

#### PROVEN MEDICAL BENEFITS

- 30 % less mortality
- 70 % reduction in hospital stay
- Reduction in overall healthcare costs

From Corno et al., J thorac Cardiovasc Surg.  
2007, Dec; 134(6):1413-9

### FLOWATCH IDENTITY CARD:

**Name:** FloWatch  
**Target:** Heart  
**Originator:** EndoArt S.A – a Swiss start-up company acquired by Allergan in 2007  
**Indications:** Severe Congenital Heart Defect in newborns  
**Development phase:** Technological enhancements to produce NeoCare a second generation of FloWatch.  
**Opportunity:** Clinically-proven benefits for severe forms of CHD and potential other indications. In developing countries, wider range of use because of lack of intracardiac surgery.

# 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.

Over the next 1-2 years, pending funding, EspeRare aims to launch a pre-clinical development programme for several paediatric cancer indications in parallel in order to fast-track the development of this therapy into young patients and start clinical testing in 2021. ■

## 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 consistent data 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-toxic to normal healthy fibroblasts.

#### 2019 and beyond

The next steps are to evaluate ER-005 alone and in combination with other anti-cancer agents in rare paediatric liver cancers.

In addition, its collaborations with academic partners, EspeRare explores the scientific rationale to redevelop ER-005 in other rare cancers with high unmet medical need such as neuroblastoma, neuroendocrine tumors, sarcoma and lymphomas. ■

#### 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.

### 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.

### DENIS MORTIER

Denis Mortier is chairing EspeRare's Business Advisory Committee. During his extensive career he served, among others, as a Partner of Collier 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.

### 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.

### EWEN SEDMAN

Ewen Sedman is Chief Business Officer and Head of the US Research Institute at Merck Serono in Boston, Massachusetts. 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 widerange leadership expertise across the whole pharmaceutical R&D value chain.



Sharon F. Terry - President



Béatrice Greco



Denis Mortier



Peter Potter-Lesage



Ewen Sedman

## MANAGEMENT TEAM

### CAROLINE KANT

#### *Founder & Chief Executive Officer*

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.

### 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. Florence co-founded EspeRare and after a successful carrier of 20 years of experience in pharmaceutical R&D. 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.

### 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.

### 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.

### 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.

### NICOLAS MARSAULT

#### *Chief Financial Officer*

Nicolas Marsault provides more than 15 years of executive experience in healthcare and industrial finance, with earlier career tenure in engineering. Prior to EspeRare, he was CFO of Prexton Therapeutics, a Pharma start-up acquired by Lundbeck in 2017 and CFO of Endosense, a MedTech start-up company acquired by St Jude Medical in 2013. Previously, he held various positions within Merck Serono's commercial controlling, forecasting and internal audit departments, where he developed an expertise in business development within pharmaceutical industry.



Caroline Kant



Florence Porte



Sylvie Ryckebusch



Monique A. Caillat



Julian Gray



Nicolas Marsault

## TEAM

---

### CHRISTOPHE BARCELLA

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

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.

### SARAH DELACOSTE

Sarah is an accounting and controlling specialist, with Human Resources and IT expertise. She is active in not-for-profit organisations for various humanitarian causes to help creating a better world. At EspeRare, Sarah links ledger accounting to reporting and auditing activities, as well as support Human Resources Management.

### CAROLINE DURAND-AVALLONE

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 a clinical programme.

### CHRISTOPHER GREENWOOD

Christopher is an international fundraiser for NGOs and social businesses. At EspeRare, he supports interactions with impact investors, philanthropists and foundations. He is a graduate of Harvard, Cambridge and London Universities.

### AGNÈS JAULENT

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 DMX-101.

### DELPHINE LABOLLE

Delphine is a clinical research expert. She has many years experience in clinical operations, mainly in Eastern and Western Europe. At EspeRare, she provides her clinical operational expertise to DMX-101 as well as support the Quality System.

### CÉDRIC MERLOT

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.

### CAMILLE PREZIOSO

Camille had held previous positions at international NGO's and foundations that have led her to gain expertise in leveraging their strengths and managing their organizational constraints to maximize their impact. Camille is responsible for the development of EspeRare's "patient-centered" approach. She implements of its patient engagement strategy and establishes interface with patient organizations.

### CAROLE PUGH

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.

### TINA RIEDEL

Tina is the Translational Project Manager of ER-005. She obtained her PhD in bioorganic chemistry at the University of Zurich in 2011 on the design of synthetic vaccines and is an expert in all fields pertaining to peptide and protein chemistry. For her postdoctoral work she joined the EPFL, where she focused on the pre-clinical development of ruthenium based anticancer drugs and drug combinations therapies for various cancer types.

### ERIC TEILLAUD

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.

### DUÇ TRAN

Duc has 18 years of experience in drug discovery and drug development in large pharmaceutical companies and start-ups. Duc provides EspeRare with his expertise in non-clinical, early clinical and manufacturing, in support of the Foundation's R&D activities.

### JÉRÔME WOJCIK

Jérôme is a senior bioinformatics scientist specialized in exploratory biomarker analyses and precision medicine approaches, with 20 years of experience in the biotech and pharma industries. He founded Quartz Bio SA which was acquired by the US Precision for Medicine group in 2017.

## 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. He is chairing EspeRare's Scientific Advisory Committee.

### PROF. JEAN-YVES BLAY

Prof. Blay is a medical oncologist and researcher. He served as the President of the European Organisation for Research and Treatment of Cancer (EORTC) from 2001 to 2009. He holds the position of General Manager of the Centre Léon Bérard in Lyon, France, since 2014 and in 2016 he became Secretary of the Oncology Commission of the French Academy of Medicine.

### 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.

### DR. SERGE BRAUN

Dr. Braun is the Scientific Director of one of the biggest patient association in the world: the French Association against Myopathies (AFM-Telethon). In this role, he drives the development of research for new treatments in rare diseases. He was named "Inspirational Stakeholder of the Year" at the 5th Annual "World Orphan Drug Congress". He advises EspeRare on the strategic development of Rimeporide in Duchenne.

### 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.

### 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 surgical procedures in the womb.

### 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. JOEL DUDLEY

Prof. Dudley is 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. He is providing his expertise to support EspeRare's IT platform development for drug rescue.

### 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.

### DR. CHRISTIAN LAVEILLE

Dr. Laveille is Director of Cavagone 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.

### 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 advises EspeRare for the FloWatch 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 DMX-101 for Edimer, and pioneered the first intra-amniotic administrations of DMX-101 to 3 unborn XLHED children. Prof. Schneider is the Principal Investigator for the upcoming clinical intra-amniotic study of DMX-101 in XLHED.



---

**DR. TONY SCIALLI**

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

**PROF. UMBERTO SIMEONI**

Prof. Simeoni is Professor of Paediatrics at the Faculty of Biology and of Medicine at University of Lausanne and Director of the Division of Paediatrics and of the Developmental Origins of Health and Disease (DOHaD) Research Unit at CHUV University Hospital in Lausanne, Switzerland. His research is oriented towards the Developmental Origins of Health and Disease. He is also highly interested in perinatal bioethics.

**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 the Director of Genomics and Computational Biology at Boehringer Ingelheim. 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.

**SALOUT KUNZI**

Mr. Kunzi serves as Head of Quantitative solutions at EFG Asset Management SA. In the past, he has also held various financial engineering, asset liability and investment analysis roles both within private banks and investment companies. He supports EspeRare's financial quantitative and risk mitigation strategies.

**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 advises EspeRare in Intellectual Property 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, oncological 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, a CEO and two senior managers, with 12 employees, and 25 contractors. EspeRare as an organisation is exempt from cantonal and federal taxes and is the equivalent of an exempt organi-

sation 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 International 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 2018

The year was characterised by a number of factors. Considerable donations were received or confirmed for the future, staff were recruited, planning was activated and the portfolio was broadened and diversified to amount to 6 ongoing projects. Most important of all, Research & Development Project funding represented 85% of total expenses and amounted to CHF 1'955'737 (note 8 a-i), an increase of 32% as compared to CHF 1,485,351 in 2017.

This year, the foundation generated a surplus (more income than expenses) of CHF 887'973 (note 3).

### 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 2018 amounted to CHF 3'239'793, including an amount of CHF 1'296'339 deferred from 2017 for the clinical activities of DMX-101 (previously called ER-004) and FloWatch programmes. In relation with the DMX-101 (ER-004) project; a donation of CHF 100'000 from Fondation Pictet was received and fully recognised as well as a donation from a private donor, Mme Gertrude Hirzel, of CHF 200'000 out of which CHF 129'213 was recognized for 2018. A EUR 135'000

grant from Stichting Dioraphte was received and fully recognized in 2018 for this project. The principal donation related to the DMX-101 project for an amount of EUR 1'950'000 was received from EspoirXLHED Sàrl, the daughter company that holds the ER-004/DMX-101 intellectual properties following the co-development and licensing agreement signed between Orphan Star AG and EspoirXLHED Sàrl. For the project in paediatric cancer, a grant of CHF 34'600 from the Ella Fund via the Swiss Philanthropy Foundation has been received and fully recognized in 2018.

For the Rimeporide project; a CHF 14'490 grant from UK Duchenne was received in 2018 and fully recognized in 2018 (note 7).

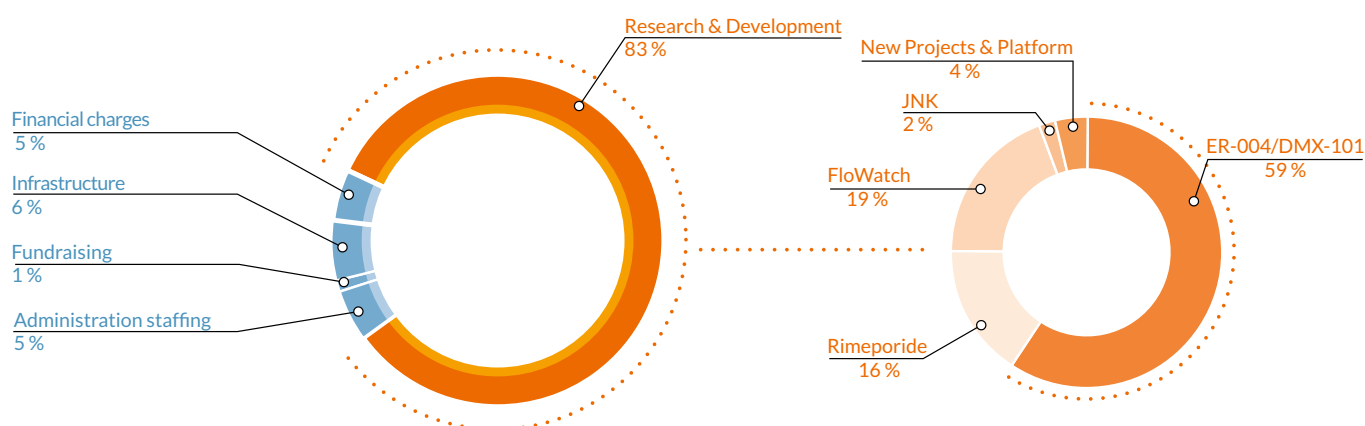
## Staff

At year-end the senior management team consisted of a Chief Executive Officer, a Chief Financial Officer and an R&D Director. Furthermore, EspeRare has a team of 7 Program Managers, a Senior Medical advisor, 25 contractors and counts as well as the support of many other people including Board members, Senior Scientific Advisors and Volunteers.

## General Administration

The total 2018 general and administration expenses amounted CHF 346'034. Expenses here reflect general foundation expenses in overall support of R&D activities (note 8h). ■

## SNAPSHOT OF ESPERARE EXPENDITURE 2018



## THE FINANCIAL YEAR AHEAD TO DECEMBER 2019

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 and GBP as per the various agreements signed with our collaborating organisations. Other general expenses will normally be in CHF. In addition, following the agreement signed between Orphan Star AG and EspoirXLHED Sàrl, clinical activities expenses for ER-004/DMX-101 will increase significantly. Those expenses will be recharged to Orphan Star AG in the currency of the original invoice received by EspeRare (EUR for EUR and USD for USD). This will result in a natural hedging of the exchange rate exposure for expenses. The resulting exposure or 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 and the expansion of our program portfolio, the analytical accounting has been implemented for 2019 in agreement with KPMG International 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. In the next two years additional

income will be mobilised in alignment with the foundation's fundraising strategy to enable EspeRare to 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, Cash Flow and Statement of Income & Expenditure – represent EspeRare in its sixth 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 ready for the scale-up of EspeRare activities for 2019-2021, thus allowing the foundation 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

	NOTES	2018 CHF	2017 CHF
<b>ASSETS</b>			
<b>Current Assets</b>			
Cash & Cash Equivalents	2i	2 679 186	2 586 872
<b>Prepaid &amp; Receivables</b>			
Trade Accounts Receivable - Third Parties		8 286	9 085
Other Current Receivables		50 367	2 542
VAT Receivable		254	10 347
Prepaid Expenses from 3rd Party		40 550	2 054
<b>TOTAL CURRENT ASSETS</b>		<b>2 778 643</b>	<b>2 610 901</b>
<b>Non-Current assets</b>			
Financial assets		13 957	8 464
Investments	4	20 000	-
Tangible Fixed Assets (Equipment)		44 467	21 787
Depreciation from Fixed Assets		(16 148)	(11 076)
<b>TOTAL NON-CURRENT ASSETS</b>		<b>62 276</b>	<b>19 175</b>
<b>TOTAL ASSETS</b>		<b>2 840 919</b>	<b>2 630 076</b>
<b>LIABILITIES</b>			
<b>Short Term Liabilities</b>			
Trade Accounts Payable - Third Parties		155 552	214 347
Other Short Term Liabilities		56 163	1 392
Accrued Expenses	2g	36 179	220 660
Deferred Income	7	807 713	1 296 339
<b>TOTAL SHORT TERM LIABILITIES</b>		<b>1 055 608</b>	<b>1 732 738</b>
<b>Capital &amp; Reserves</b>			
Foundation Capital	10	50 000	50 000
Operations Reserve	3	847 338	1 257 766
Net excess of (Expenditure)/Income		887 974	(410 429)
<b>TOTAL CAPITAL &amp; RESERVES</b>		<b>1 785 311</b>	<b>897 338</b>
<b>TOTAL LIABILITIES AND CAPITAL</b>		<b>2 840 919</b>	<b>2 630 076</b>

## CASH FLOW STATEMENT

	2018 CHF	2017 CHF
<b>OPERATING ACTIVITIES</b>		
Net excess of (Expenditure)/Income	887 974	(410 429)
Depreciation, amortization and impairment losses on non-current assets	6 663	2 987
(Gains)/losses arising from disposals of non-current assets	(1 591)	-
Decrease (increase) in Prepaid and Receivables	(80 921)	(3 887)
Changes in Short term Liabilities	(4 024)	197 203
Changes in Provisions	-	(38 967)
Changes in Accruals	(184 481)	5 399
Changes in Deferred income	(488 626)	727 002
<b>Cash from operating activities (operating cash flow)</b>	<b>134 994</b>	<b>479 308</b>
<b>INVESTING ACTIVITIES</b>		
Acquisition of company participation	(20 000)	-
Acquisition of tangible fixed assets	(31 352)	(9 845)
Proceeds from sale of tangible fixed assets	8 672	-
<b>Cash inflow/drain from investing activities</b>	<b>(42 680)</b>	<b>(9 845)</b>
<b>Cash inflow/drain from financing activities</b>	<b>-</b>	<b>-</b>
<b>NET CASH</b>	<b>92 314</b>	<b>469 463</b>
Cash and cash equivalents at beginning of period	2 586 872	2 117 410
Cash and cash equivalents at end of period	2 679 186	2 586 872
<b>NET CASH</b>	<b>92 314</b>	<b>469 463</b>



## ESPERARE STATEMENT OF INCOME & EXPENDITURE

	NOTES	2018 CHF	2017 CHF
<b>INCOME</b>			
Income from R&D donations	2b/7a	3 239 793	1 232 754
<i>of which income from allocated funds</i>		1 611 589	1 032 754
Other Operating Income		9 793	1 098
<b>TOTAL INCOME</b>		<b>3 249 586</b>	<b>1 233 851</b>
<b>EXPENDITURE</b>			
<b>Research &amp; Development Expenditure</b>			
ER004/DMX-101 Direct Costs	8a	508 801	-
ER004/DMX-101 Support Costs	8a	642 517	-
<b>TOTAL ER004/DMX-101</b>		<b>1 151 319</b>	<b>-</b>
Rimeporide Direct Costs	8b	189 358	527 781
Rimeporide Support Costs	8b	126 422	284 075
<b>TOTAL RIMEPORIDE</b>		<b>315 781</b>	<b>811 856</b>
Flowatch Direct Costs	8c	99 344	166 430
Flowatch Support Costs	8c	268 144	290 353
<b>TOTAL FLOWATCH</b>		<b>367 488</b>	<b>456 783</b>
JNK Direct Costs	8d	23 795	463
JNK Support Costs	8d	24 639	19 258
Cilengitide Direct Costs	8e	5 016	205
Cilengitide Support Costs	8e	-	13 495
New projects prospect Direct Costs	8f	11 005	19 683
New projects prospect Support Costs	8f	-	116 565
Repositioning Platform Direct Costs	8g	30 353	31 583
Repositioning Platform Support Costs	8g	26 341	15 459
<b>TOTAL OTHER R&amp;D PROJECTS</b>		<b>121 150</b>	<b>216 711</b>
<b>TOTAL R&amp;D EXPENDITURES</b>		<b>1 955 737</b>	<b>1 485 351</b>
<b>GENERAL FOUNDATION ADMINISTRATION</b>	8h		
Administration staffing	8i	148 952	94 362
Patient Association Consultancy		15 834	-
Office Rental		42 224	48 714
Office Costs		19 481	3 872
Audit Expenses and accounting		44 674	12 779
IT Expenses		4 659	3 830
Communications		8 295	6 084
General Legal Fees		9 051	1 529
Fundraising direct costs		35 433	41 498
Advertising Costs		4 803	2 126
Board meeting		2 016	836
Other Operating Expenses	8j	3 949	-
Depreciation	2d	6 663	2 987
<b>TOTAL GENERAL ADMINISTRATION EXPENDITURE</b>		<b>346 034</b>	<b>218 616</b>
<b>TOTAL EXPENDITURE</b>		<b>2 301 772</b>	<b>1 703 966</b>
<b>OPERATING RESULT</b>		<b>947 814</b>	<b>(470 115)</b>
<b>FINANCIAL INCOME AND EXPENSES</b>			
Financial Income	2k	-	-
Financial Charges		2 175	2 280
Exchange Differences loss (gain)	2c	57 665	(61 967)
<b>TOTAL FINANCIAL INCOME AND EXPENSES</b>		<b>59 840</b>	<b>(59 686)</b>
Dutes and Taxes		-	-
<b>NET EXCESS OF (EXPENDITURE) / INCOME</b>	3	<b>887 974</b>	<b>(410 429)</b>

# NOTES TO FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2018

## 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 and 3 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 1.126900

1 USD = CHF 0.985784

1 GBP = CHF 1.255280

### 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	2017 CHF	Acquisitions	Disposals	2018 CHF
IT Equipment	16 138	4 479	3 023	17 593
Furniture	5 649	26 874	5 649	26 874
<b>TOTAL</b>	<b>21 787</b>	<b>31 352</b>	<b>8 672</b>	<b>44 467</b>

Depreciation	2017 CHF	Depreciation	Disposals	2018 CHF
IT Equipment	9 590	2 071	105	11 556
Furniture	1 486	4 592	1 486	4 592
<b>TOTAL</b>	<b>11 076</b>	<b>6 663</b>	<b>1 591</b>	<b>16 148</b>

<b>TOTAL NET VALUE</b>	<b>10 711</b>	<b>24 689</b>	<b>7 081</b>	<b>28 319</b>
------------------------	---------------	---------------	--------------	---------------

### 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 2018, there were no significant capital expenditure commitments.

### 6. SUBSEQUENT EVENTS

No events occurred subsequent to 31 December 2018 and prior to the approval of the financial statements that would require modification of or disclosure in the financial statements.

### 7. INCOME

#### a) Donations received, recognised and deferred

During 2018 the following donations were granted:

Donors	Notes	Currency	Exch. rate	Total Grant	Deferred from 2017 CHF	Received during 2018 CHF	Recognised during 2018 CHF	Deferred to 2019 CHF	Notes
Private Geneva Foundation		CHF		700 000	381 179		381 179	0	Grant - FloWatch
Private Geneva Foundation		CHF		1 000 000	865 160		865 160	0	Grant - New Projet/Espoir-004
Prim'enfance		CHF		20 000	20 000		0	20 000	Grant - FloWatch
Loterie Suisse Romande		CHF		90 000	30 000		30 000	0	Grant - Platform
Fondation Pictet	1	CHF		100 000		100 000	100 000	0	Grant - Espoir-004 /DMX-101
Private Donor	2	CHF		200 000		200 000	28 532	171 468	Grant - Espoir-004 /DMX-101
Swiss Philantrophy Foundation	3	CHF		34 601		34 601	34 601	0	Grant - JNK
Stichting Dioraphte	4	EUR	1,168	135 000		157 626	157 626	0	Grant - Espoir-004 /DMX-101
UK Duchenne	5	CHF		14 490		14 490	14 490	0	Grant - JNK
EspoirXLHED Sàrl	6	EUR	1,151	1 950 000		2 244 450	1 628 204	616 246	Grant - R&D program & foundation
<b>TOTAL</b>					<b>1 296 339</b>	<b>2 751 167</b>	<b>3 239 793</b>	<b>807 713</b>	

1. A CHF 100'000 grant from Fondation Pictet was received in 2018 for Espoir-004 project. CHF 100'000 was recognized in 2018.

2. A CHF 200'000 grant from a private donor was received in 2018 for Espoir-004 project. CHF 129'213 was recognized in 2018 and CHF 70'786 deferred to 2019.

3. A CHF 34'600 grant from Swiss Philantrophy Foundation was received in 2018 for JNK project. CHF 34'600 was recognized in 2018.

4. A EUR 135'000 grant from Stichting Dioraphte was received in 2018 for Espoir-004 project. EUR 135'000 was recognized in 2018.

5. A CHF 14'490 grant from UK Duchenne was received in 2018. CHF 14'490 was recognized in 2018.

6. A EUR 1'950'000 grant from EspoirXLHED Sàrl was received in 2018. CHF 1'628'204 was recognized in 2018 and CHF 616'246 deferred to 2019.

As a comparison during 2017 the following donations were granted:

Donor	Notes	Currency	Total Grant	Deferred 2016 CHF	Received 2017 CHF	Recognised 2017 CHF	Deferred 2018 CHF	Notes
Private Geneva Foundation		CHF	300 000			128 000	-	Grant - FloWatch
ARES Trading SA (Merck Serono Affiliate)		EUR	500 000	273 800		273 800	-	I&E Statement - Rimeporide
AFM telethon		EUR	150 175	77 538		77 538	-	Grant - Rimeporide
Association Altrodomani		EUR	4 000		4 273	4 273	-	Grant - Rimeporide
Parent Project Onlus		EUR	4 000		4 273	4 273	-	Grant - Rimeporide
Duchenne Trust UK		GBP	5 000		6 210	6 210	-	Grant - EspoiR-003
Foundation Tell et Un Tel		CHF	10 000		10 000	10 000	-	Grant - FloWatch
Foundation Tell et Un Tel		CHF	15 000		15 000	15 000	-	Grant - New Projet/EspoiR-004
Private Geneva Foundation		CHF	200 000		200 000	200 000	-	Grant - Foundation Support
Private Geneva Foundation	1	CHF	700 000		700 000	318 821	381 179	Grant - FloWatch
Private Geneva Foundation	2	CHF	1 000 000		1 000 000	134 840	865 160	Grant - New Projet/EspoiR-004
Prim'enfance	3	CHF	20 000		20 000		20 000	Grant - FloWatch
Loterie Suisse Romande	4	CHF	90 000	90 000		60 000	30 000	Grant - Platform

<b>TOTAL</b>			<b>569 338</b>	<b>1 959 756</b>	<b>1 232 754</b>	<b>1 296 339</b>
--------------	--	--	----------------	------------------	------------------	------------------

#### Off Balance Sheet:

UK Duchenne	GBP	33462	33 462	Research & Development- ER-003
-------------	-----	-------	--------	--------------------------------

1. Out of a total of CHF 700 000 received from a Private Geneva foundation to co-finance the FloWatch programme, CHF 318 821 was recognised in 2017 to fund the program and CHF 381 179 was deferred to 2018 to further fund the programme
2. Out of a total of CHF 1 000 000 received from a Private Geneva foundation for a new projet called EspoiR-004, CHF 134 840 was recognised in 2016 for the set-up of the programme and CHF 865 160 deferred to 2018 to continue setting-up the clinical trial for the programme
3. A CHF 20 000 grant from Prim'enfance was received in 2017 and deferred to 2018 to fund the access to treatment activities for the FloWatch programme
4. A total of CHF 90 000 from Loterie Suisse Romande was deferred from 2016, as the projet runs until 2018, CHF 60 000 was recognised in 2017 and CHF 30 000 deferred to 2018 for the enhancement of the repositioning platform

#### b) Other operating income: Furnitures were sold for an amount of CHF 9'792.

### 8. EXPENSES

- a) Development of ER-004/DMX-101 in X-linked Ectodermal Dysplasia;
- b) Development of Rimeporide in Duchenne muscular dystrophy;
- c) Re-development of the FloWatch medical device for infants with Cardiac defects;
- d) Development of JNK-inh in Duchenne muscular dystrophy and in Paediatric Cancer;
- e) Development of Cilengitide in Focal Segmental Glomerulosclerosis in partnership with Merck KGaA;
- f) Prospection & generation of new drug development projects for rare diseases;
- g) Repositioning platform development to support the systematic discovery and evaluation of new projects;
- h) General Foundation expenses in overall support of R&D activities;
- i) Relates to staff and travel costs that are recorded and allocated to the specific activities. The staff headcount represented three senior managers and seven R&D program managers and one senior medical advisor. In addition, EspeRare benefits from a number of consultants and volunteers. Total staff benefits for 2018 amount to CHF 1'237'016 (Salaries & Social charges amount to CHF 1'154'559, Travel Expenses amount to CHF 64'427, Volunteers reimbursements amount to CHF 13'593 and Training and other costs totals CHF 4'434). The allocation of salaries & social charges to the five R&D projects, prospection & generation of new drug development projects, repositioning platform and to the Foundation General Administration according to the percentage of the time spent by employee on the eight activities.
- j) The change of the accounting software licence, from desktop to an rented SAAS version, generated an operational loss of CHF 2'918 and the sale of furniture, an impairment of CHF 1'031.

### 9. FOUNDATION CAPITAL

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

### 10. GOVERNANCE

The Foundation Board is the Foundation's supreme body. It takes all decisions necessary or effective for the achievement of the Foundation's aims. It has general responsibility for the affairs of the Foundation and supervises all activities carried out under its authority by the Foundation's other bodies to which power and authority have been delegated.

Members of the Board act on a voluntary basis and may not claim any financial compensation other than expenses incurred such as travel and accommodation. For activities over and above the normal requirements of the position, each Member may receive appropriate reimbursement and compensation. Payment of any such reimbursement or compensation is only permissible where it corresponds to a service carried out for the benefit of the Foundation.

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

### 11. 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 can not 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.

### 12. 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, a total of 491 hours were incurred, representing a total of CHF 147'300.- (2016: CHF 18'000, 2017: CHF 70'500, 2018: CHF 58'800) EspeRare has not accrued nor provisioned these probable costs (off balance sheet).

### 13. 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.





**KPMG SA**  
**Audit Western Switzerland**  
111 Rue de Lyon  
CH-1203 Geneva

P.O. Box 347  
CH-1211 Geneva 13

Telephone +41 58 249 25 15  
Fax +41 58 249 25 13  
[www.kpmg.ch](http://www.kpmg.ch)

## 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 Fondation EspeRare for the year ended 31 December 2018.

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, 12 April 2019

#### *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.

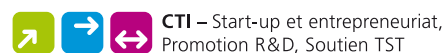
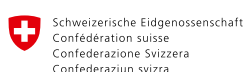
### I WANT TO ESTABLISH A CORPORATE PARTNERSHIP

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 :

[foundation@esperare.org](mailto:foundation@esperare.org)

## THEY SUPPORT US





Campus Biotech Innovation Park  
Avenue de Sécheron 15  
CH-1202 Geneva - Switzerland  
Phone +41 22 794 4004  
Fax +41 22 794 4005  
Email [foundation@esperare.org](mailto:foundation@esperare.org)  
Website [www.esperare.org](http://www.esperare.org)

