



ANNUAL REPORT 2017





Mission & vision

MISSION

At EspeRare, we address the translational gap in paediatric rare diseases by uncovering the potential of existing therapeutic interventions to tackle unmet life-threatening medical needs.

As a non-profit organisation, we achieve this through a collaborative approach centred on patient engagement with the aim of providing patients universal access to these therapies.

VISION

A world in which patient representatives, scientists, pharmaceutical experts and health authorities come together to address the medical needs of children affected by rare diseases, ultimately alleviating the healthcare burden of their conditions.

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

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Established in Switzerland in 2013, **EspeRare** is a new nonprofit foundation with global reach, focused on accelerating the development of treatments for underserved patients affected with rare diseases.



Message from the Co-founder and Chief Executive Officer

EspeRare was launched at the International Rare Diseases Research Consortium first Congress in Dublin in April 2013. Our goal is to pioneer a collaborative model that accelerates and de-risks the development of treatments for underserved patients affected by rare diseases. Our product development partnership model for rare diseases is a unique non-profit business model that brings together public, private, academic and philanthropic sectors to develop unexplored or shelved treatments for debilitating rare diseases.

“Success is not how high you have climbed, but how you make a positive difference to the world.”

Roy T. Bennet

Dear Friends,

As this 2017 Annual Report goes to print, EspeRare will have proudly blown its 5 candles and reached this 5th anniversary with a certain sense of accomplishment.

The story which started to be written 5 years ago has turned into a book with 5 chapters, each corresponding to a new therapeutic programme in a life-threatening rare disease affecting children. Some of these 2017 chapters include:

- The first programme in Duchenne muscular dystrophy is now ready to enter into late clinical development and licensing negotiations are taking place with several pharmaceutical partners (see page 20).
- The Flowatch lifesaving technology for infants born with severe heart defects is being redeveloped and enhanced to broaden the scope of the technology applications to other vascular diseases and cardiomyopathies (see page 26).
- EspeRare is also expanding the development of Rimeporide in the field of pulmonary hypertension with an ongoing study at the Johns Hopkins university (see page 6).

2017 has also been the year we have consolidated our non-profit business model aspiration. Bringing innovative therapies to patients while integrating social responsibility and solidarity commitments early in the clinical development phase is our driver. This entails to ensure that the hope generated by clinical research for patients is translated into accessible treatments for all. Indeed, our model addresses the current limitations traditional drug developers face due to the lack of funding available to reimburse these much-needed yet high priced life changing treatments.

Bringing together all actors from the rare disease ecosystem, developing commercial partnerships, having a committed and passionate team, a strong network of partners and donors is the cornerstone of EspeRare's growing success over these 5 years.

Looking ahead, thanks to the promising perspective of seeing its first treatment (Rimeporide) be transferred to a large drug development partner, and to the launch of a sixth ambitious programme for the treatment of XLHED, a debilitating ectodermal dysplasia (see page 24), EspeRare can look forward to a very exciting 2018.

What EspeRare aims to achieve by reducing risk, time frames and cost during early drug development goes beyond the satisfaction of developing a new venture philanthropic approach for patients with also and most important aims at rare diseases. It bringing hope, faith and confidence to the rare disease community.

It is therefore with profound gratitude that we wish to thank all our employees, consultants, donators and partners without whom this beautiful book could not continue to be written.

Sincerely,

Caroline Kant
Founder & CEO



2017 highlights

FEB.
2017

EspeRare receives financial support from AltroDomani Onlus and Parent Project Onlus

AltroDomani Onlus and Parent Project Onlus associations sponsored EspeRare's first clinical study, conducted with Rimeporide in patients with Duchenne Muscular Dystrophy in Europe (RIM4DMD).

This support will provide financial back up for the follow-up of patients who participate in this clinical trial in Italy. ■



JUNE
2017

Prim'enfance supports the FloWatch project

Prim'enfance is a Swiss non-profit foundation focused on understanding, preventing, detecting and treating diseases arising in early infancy. During an event celebrating the foundation's 10th anniversary, Prim'enfance awarded EspeRare a grant for its FloWatch project. EspeRare is delighted and honored to partner for the first time with Prim'Enfance, joining forces to bring health to children born with severe heart defects. ■



JULY
2017

EspeRare renews hope for children suffering from a disabling skin disease

An American biotech offered to EspeRare the possibility to give a second chance to its programme aiming to address X-Linked Hypohidrotic Ectodermal Dysplasia (XLHED). XLHED is a serious rare disease that is life-threatening, particularly in the first years of life. Administered at the right time during pregnancy, the therapeutic candidate ER-004 has the potential to correct the most severe symptoms of the disease throughout patients lives. ■

JULY
2017

A new therapeutic perspective for Rimeporide

EspeRare initiated a study to test Rimeporide's potential in Pulmonary Arterial Hypertension, in collaboration with Johns Hopkins University School of Medicine. This pre-clinical study will explore the therapeutic potential of Rimeporide, using *in vitro* and *in vivo* models. Positive results from this study will support the initiation of a Phase II clinical trial in patients with Pulmonary Arterial Hypertension. ■



SEPT.
2017

Rimeporide receives support from USA health authorities

The Food and Drug Administration (FDA), the US Department of Health and Human Services, has granted an Orphan Drug Designation (ODD) for Rimeporide for the treatment of Duchenne Muscular Dystrophy (DMD). ODD is designed to promote the development of drugs that may provide significant benefit to patients suffering from rare, life-threatening diseases. This ODD grants Rimeporide a 7-year market exclusivity in the US. ■



OCT.
2017

*European health
authorities recognise ER-004
as priority*

The ER-004 project developed for a debilitating ectodermal dysplasia has been accepted into the EMA's "PRIME – PRiority MEDicines scheme", a scheme aimed at accelerating the development of therapies with high unmet needs. It constitutes an encouraging recognition that this therapy represents a promising benefit for the patients. Under this scheme the Agency will support a plan to streamline the development of this life changing therapy. ■



**"Everyone has some inner power
that awaits discovery."**

Richard Paul Evans

OCT.
2017



*EspeRare, ambassador
of the Health Valley*

As ambassador of the Health Valley, EspeRare featured on the Swiss TV show "Toute Taxes Comprises", at the occasion of its 10th anniversary. The Health Valley Switzerland is a grouping of private and public actors in the biomedical sector of the French-speaking Switzerland. It includes more than 1'000 member companies and 25'000 employees. EspeRare illustrated, alongside Sophia Genetics and Mindmaze, the diversity, complementarity and dynamics of this ecosystem. ■

OCT.
2017

*EspeRare completed
recruitment for its first
clinical study*

20 patients were successfully recruited for its first clinical study, using Rimeporide for young boys affected by Duchenne Muscular Dystrophy (DMD). This study aims at assessing safety and tolerability of the Rimeporide at various doses. Patients were recruited in 4 centres in Europe: San Raffaele Hospital (Milano, Italy), Armand Trousseau Hospital/ I-motion (Paris, France), Great Ormond Street Hospital (London, UK) and Santa Creu i Sant Pau Hospital (Barcelona, Spain). ■

DEC.
2017

*The Fondation Pictet
supports EspeRare*

The Fondation Pictet has financially supports EspeRare's new programme in XLHED, a disabling rare skin disease. EspeRare is honoured that such a prestigious foundation acknowledges this new project, designed to cure the most threatening symptoms of this disease during pregnancy. ■

DEC.
2017

*Launch of an EspeRare
"Friends of" within the King
Baudoin's Foundation.*

The American Friends of EspeRare fund is hosted by the King Baudoin Foundation USA and is a 501 (c) (3) organisation allowing US donors to reclaim taxes on donations made to the fund, consistent with US tax law. This is an important step for EspeRare as we have strong links with US-based foundations and research organisations. ■





Addressing rare diseases

WHAT IS A RARE DISEASE?

In Europe, any disease affecting less than **1 person in 2000** is considered rare. In the US, 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

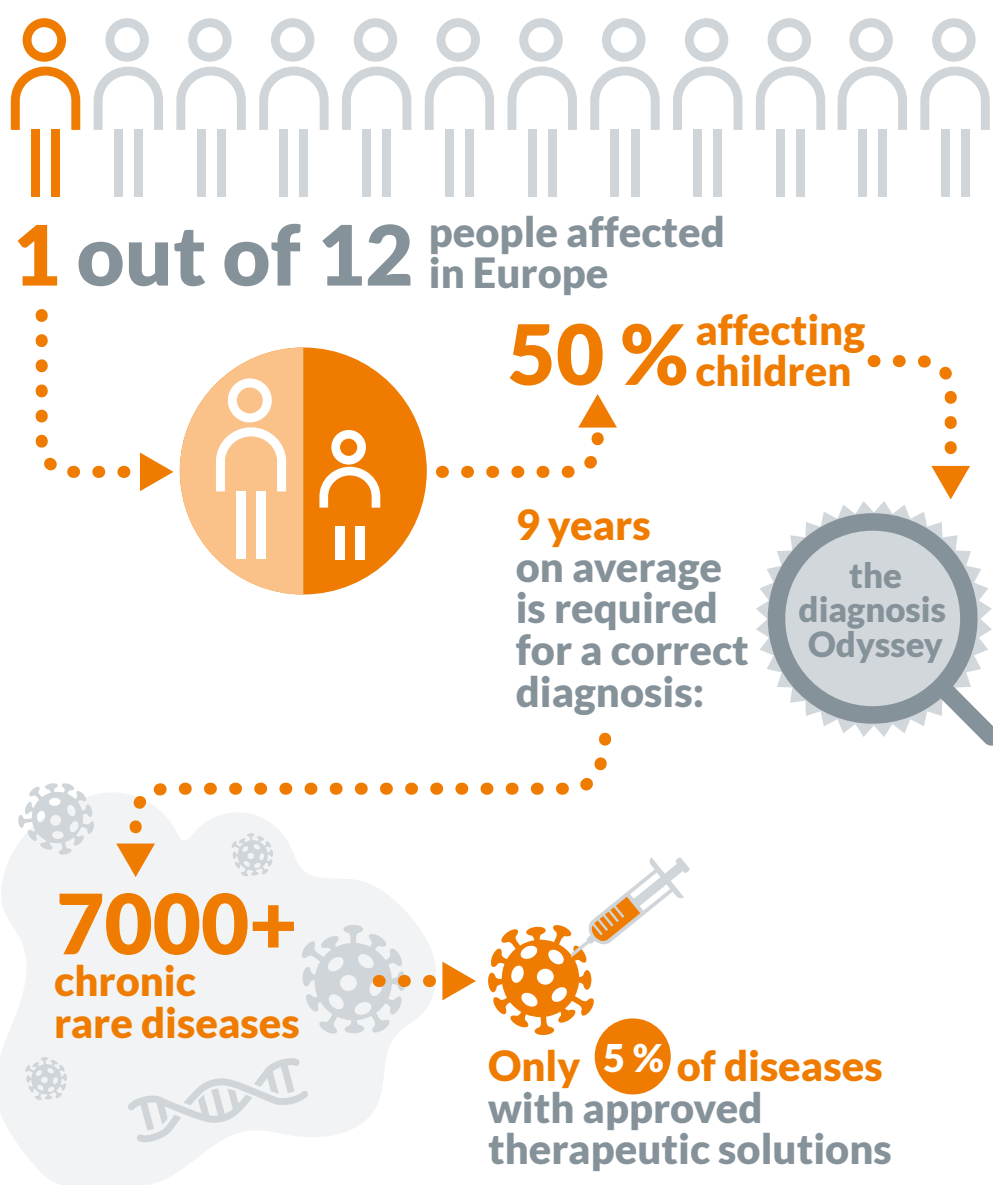
PATIENTS ARE AT THE CORE OF CURRENT PROGRESS IN RARE DISEASES:

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 gain from the great leverage of 'patient centrality', in particular 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-centred drug development.

Advancing rare disease treatments

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

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.

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.** On one hand, 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. On the other hand, pharmaceutical companies are reluctant to invest in these diseases for which commercial profit is limited due to the small market size, and for which risks are very high.

ESPERARE DISEASE FOCUS

EspeRare opted to **concentrate most of its activities on rare paediatric diseases that represent nearly 50 % of rare diseases.** Considering that EspeRare cannot develop the knowledge and network of experts required in thousands of diseases, the foundation 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.). ■



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

Further developing existing or abandoned drugs for novel diseases offers an **accelerated and “de-risked” way of developing new treatments**.

There are some inherent incentives to this approach:

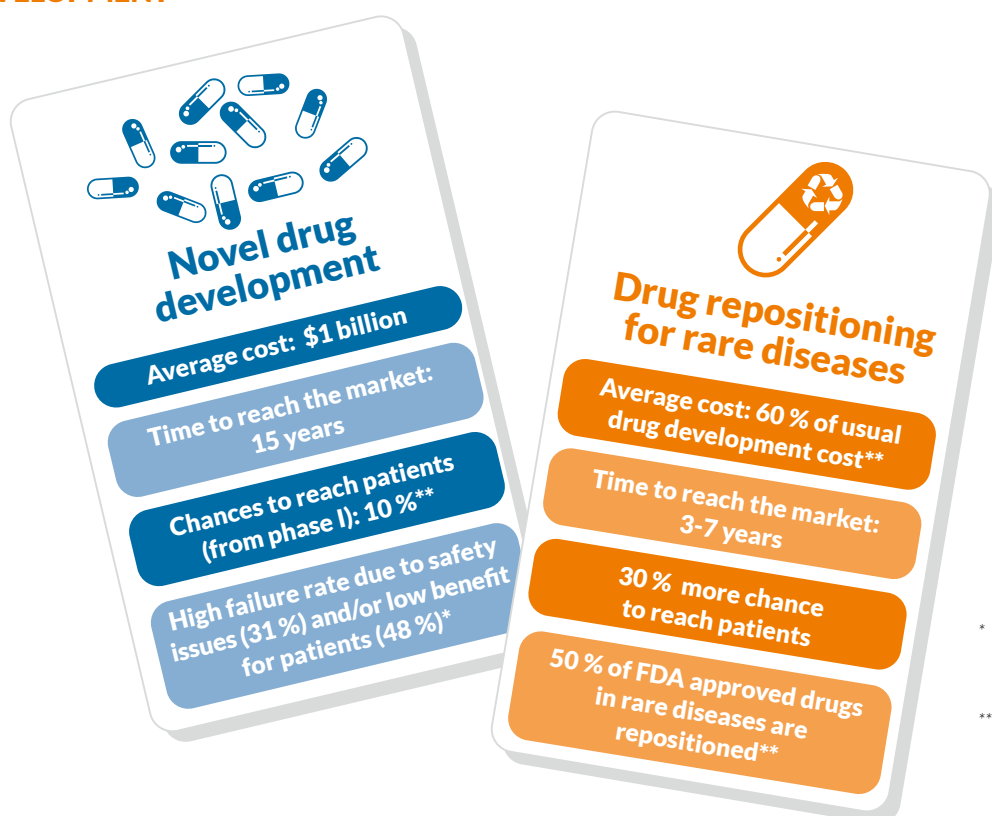
- Existing drugs are already known to exert a biological response in humans and this response may become beneficial for other health conditions.
- Many steps in the drug development process such as drug activity and good safety profile in humans have already been demonstrated during the initial development of the drug.

However, repositioned drugs cannot be commercialised at high prices as compared to *de novo* therapeutics. Thus, so far, despite its clear therapeutic appeal for patients, the approach has never become a strategic focus for biopharmaceutical companies, leaving many of these opportunities to treat rare diseases unexplored.

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.

By repositioning or rescuing drugs, EspeRare accelerates the development, reduces costs, and increases chances of success for patients to access new treatments. **The foundation's model allows the development of drug repositioning opportunities that remain economically attractive for commercial partners and beneficial for patients and the health-care system at large.** ■

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



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

** Ref: Anne Pariser,
Director at CDER

EspeRare's strategy drug development in rare diseases:

- **Faster, de-risked and cost contained approach to drug development***
- **More affordable treatments & quicker access to medicine for rare disease patients**



The translational gap, a major roadblock for new treatments

ESPERARE FOCUSES ON ADDRESSING THE “VALLEY OF DEATH” IN TRANSLATIONAL RESEARCH

The translational gap is the major roadblock for new treatments to reach rare diseases patients. This transition requires translating research efforts – often conducted in academia – into robust drug development activities – traditionally conducted by biopharmaceutical companies.

Using a collaborative approach and its solid industrial drug development expertise, the foundation coordinates all necessary R&D activities to address this gap.

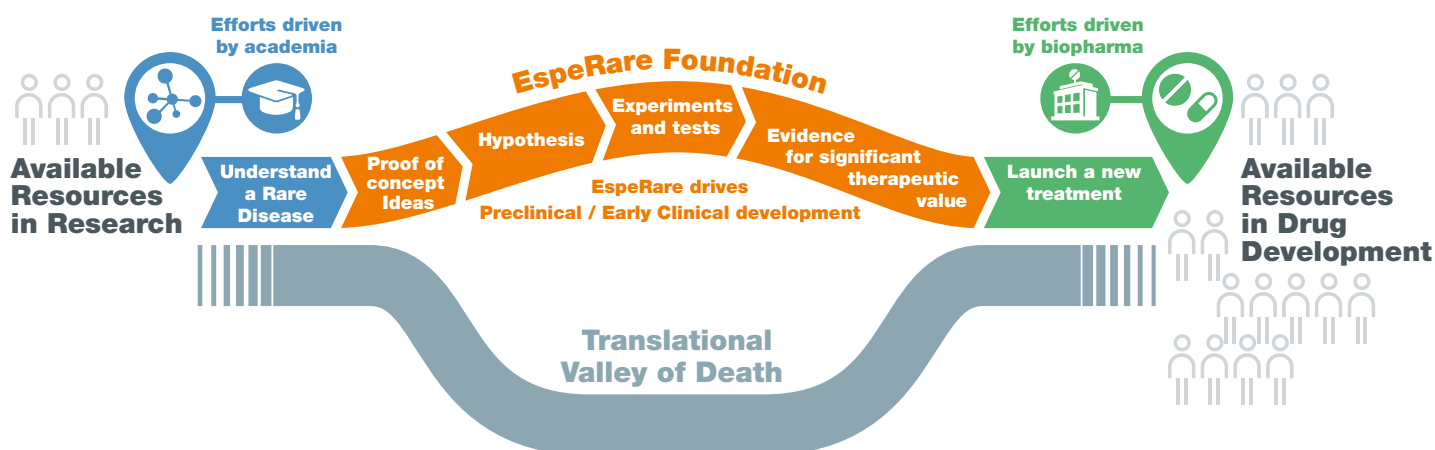
More specifically, EspeRare focuses on driving preclinical and early clinical development activities that are required to demonstrate the efficacy of the drugs under investigation. For each of its drug development programmes, the foundation develops **Product Development Partnerships** that:

- integrate “**Patients' voice**” through alliances with patients advocacy groups;
- mobilise **research and clinical experts**, and **biomedical centres of excellence** to conduct preclinical and clinical development activities;
- interact directly with **regulatory agencies** and health authorities to best pave the way to drug approval and patient s' access to treatment;
- ethically partner with **industry** to manage late clinical development and commercialisation at an accessible price.

Once proof of concept in humans is reached and a conclusive data package generated, programmes can either go back to the originator or be transferred to industry partners who will have the necessary capacities to drive later stage clinical trials, registration and commercialisation.

To secure the integrity of programmes, EspeRare agrees with commercial partners on ‘guiding principles’ for drug development, marketing and access to treatment, thus safeguarding the ethical principles of a drug initially developed within a philanthropic structure. ■

ESPERARE FOUNDATION BRIDGES THE TRANSLATIONAL “VALLEY OF DEATH”



ESPERARE'S ACTION: BRIDGING PATIENT AND COMMERCIAL INTERESTS TO ACCELERATE AND "DE-RISK" DRUG DEVELOPMENT



Many therapeutic opportunities to treat rare disease patients exist. However they remain forgotten on the shelves of Universities or pharmaceutical companies. These opportunities are never tested nor developed because on one hand, academia often lacks the know-how to conduct robust drug development, especially in late phases of clinical development; and on the other hand, biopharmaceutical companies are skeptical to risk investing R&D budget in small markets with low potential of financial return.

EspeRare's non-profit drug development model has been developed to scientifically and financially enable the early exploration of therapeutic opportunities to treat rare diseases.

Increasing financial pressure on the healthcare system and on treatment pricing is calling for a new R&D model that can develop affordable drugs.

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

The advantage of the Foundation lies in its unique and viable model allowing unexplored treatments to be developed. Our model comprises all the ingredients of a comprehensive solution: pharmaceutical R&D and project management expertise, patient centrality and hybrid financing mechanisms. EspeRare bridges patient and commercial interests into a system that accelerates and "de-risks" drug development with the goal of bringing affordable new treatments to rare disease underserved patients. ■

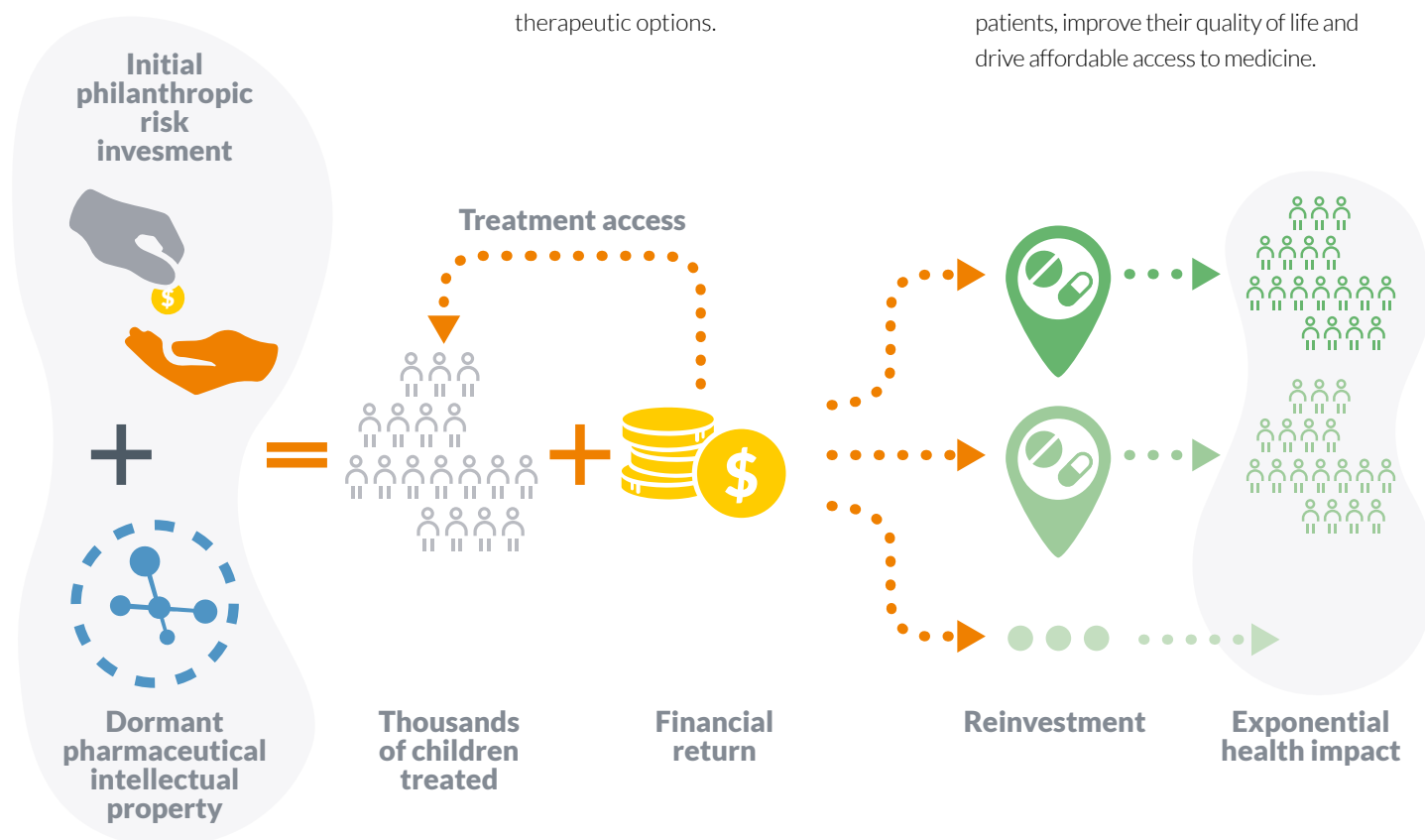
Our alternative business model

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

OUR NON-PROFIT MODEL MULTIPLIES THE IMPACT OF PHILANTHROPIC INVESTMENTS AND PHARMACEUTICAL KNOW-HOW, TO ADDRESS THE BURDEN OF MILLIONS OF CHILDREN WITH RARE DISEASES AND THEIR FAMILIES

→ EspeRare combines pharmaceutical know-how and philanthropic investments to **revive existing yet shelved 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 non-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.



“It is time to renovate and accelerate the discovery and development of drugs for rare diseases. EspeRare is pushing the boundaries of drug development, by creating a new dynamic within an innovative and collaborative ecosystem, to ensure a real impact on patients with rare diseases and their families.”

Sharon Terry
President of EspeRare and CEO of Genetic Alliance

ESPERARE'S PROOF OF CONCEPT

ESPERARE'S VENTURE PHILANTHROPY MODEL IMPROVES THE LIVES OF RARE DISEASE PATIENTS IN A SUSTAINABLE WAY

Five years after its creation, EspeRare has reached an important turning point in its history and is currently demonstrating the power and viability of its innovative model.

A clinical study for its first therapeutic candidate in Duchenne muscular dystrophy, Rimeporide, is now completed. EspeRare is engaging discussions with commercial

partners who have the infrastructure and manpower to conduct late clinical validation and commercialisation for this treatment. Once this partnership is established, **EspeRare will reinvest its returns to develop additional treatments against rare diseases.** Moreover, these returns will help fund access to medicine and health efforts in Duchenne, as illustrated above.

Over time, EspeRare is striving to multiply the impact of philanthropic support, allowing the development of many more treatments for these underserved patients, while focusing on fostering equitable and affordable access to rare disease therapeutic innovation. ■



Building our portfolio

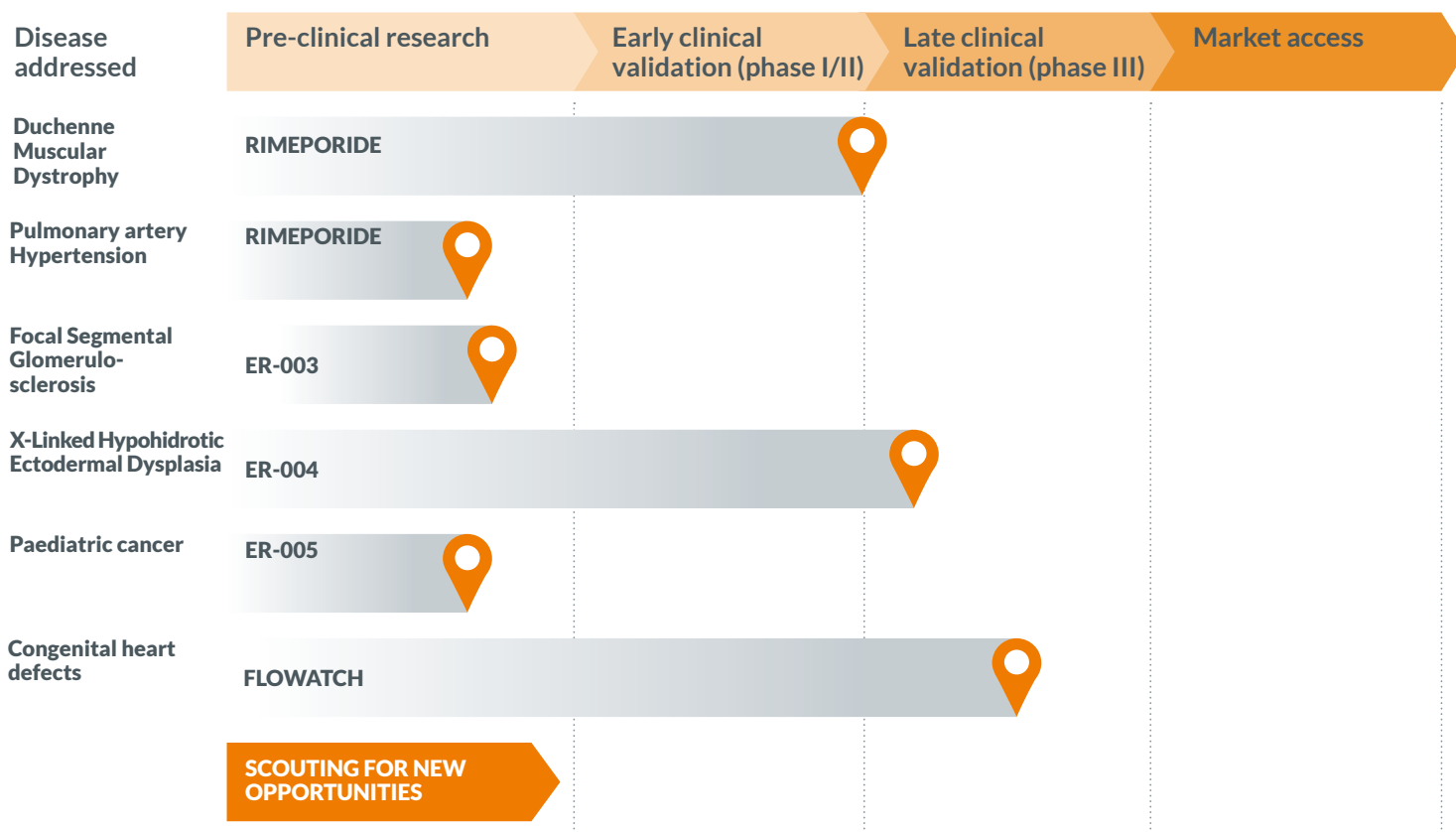
With its first programme in Duchenne muscular dystrophy, EspeRare has proven its ability to give a chance to dormant therapeutic opportunities. **After four and a half years, the foundation has now demonstrated the therapeutic potential of Rimeporide, a shelved drug that EspeRare has tested in children affected by this debilitating disease** (see pages 20-22). This first programme is also a validation of the strength of EspeRare's philanthropic model to drive and fund drug development in rare diseases.

Beyond this first programme, the foundation is building a robust and diversified portfolio of programmes that has the potential to address critical unmet medical needs of children affected by rare diseases. Towards this goal EspeRare is developing an existing treatment in a rare renal disease (see pages 22-23), is giving a second chance to a stalled therapy that has the potential to cure a debilitating skin disease (see pages 24-25), and is re-launching an existing therapeutic device for infants affected by severe cardiac defects (see pages 26-27).

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 identify opportunities that fit EspeRare's development model and address high unmet medical needs;
- evaluating proposals from academia and biopharmaceutical companies to further develop their existing therapeutic assets;
- developing the Drug Repositioning Platform, a biomedical informatics engine that systematically identifies and evaluates drug rescue and repositioning opportunities. ■

A PROGRAMME PORTFOLIO UNDER DEVELOPMENT WITH MULTIPLE PARTNERS



ESPERARE'S PROPRIETARY PLATFORM FOR THE IDENTIFICATION OF DRUGS TO BE RESCUED OR REPOSITIONED IN RARE DISEASES

An *in silico* approach enables EspeRare to discover novel therapeutic opportunities for existing drugs. EspeRare is developing a proprietary computational **Drug Repositioning Platform** to systematise the discovery of such opportunities. The Platform consists of two entities.

- 1. The Treatment database** compiles data on 2,000 existing drugs with the potential to be "re-developed" in rare diseases. This database structures information about these drugs such as their initial area of development, their safety and toxicity profile and their biological mechanism of action. Thanks to a collaboration with the National Institute of Health (NIH, USA), EspeRare has access to data on drugs developed worldwide.
- 2. The Rare disease analytics system** integrates biomedical data on the molecular pathophysiology of 30 rare diseases targeted in priority by EspeRare. The information is extracted from scientific literature and specialised databases. This understanding of the biological mechanisms involved in these diseases is validated and enhanced by biomedical experts in EspeRare's network.

By combining a wise selection of existing de-risked drugs within its *treatment database*, and identification of new disease applications using the *rare disease analytics system*, the Drug Repositioning platform enables EspeRare uncover repositioning opportunities with strong therapeutic potential for rare diseases.

A first version of the Drug Repositioning platform was launched in March 2014. The performance of the platform is being developed as other data sources are constantly being integrated.

EspeRare is grateful to the Loterie Suisse Romande that has awarded the foundation a grant to finance the IT infrastructure of the Drug Repositioning platform. EspeRare is now looking for additional endowments to finance the platform development. ■



GAUGERX, A COLLABORATIVE PROJECT WITH GENETIC ALLIANCE

GaugeRx is an open access, interactive, web-based tool under development, integrating and translating available scientific knowledge on rare diseases to support drug development. It also aims to assist advocacy organisations in strengthening the drug development

ecosystem in their disease. GaugeRx enriches EspeRare's Drug Repositioning platform by integrating multidisciplinary information for drug development to better assess potential in different rare diseases.



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 degenerescence 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. 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 such as increased risks for diabetes, fractures, oedema and respiratory infections upon chronic use. While additional therapies and treatments exist to alleviate symptoms, they do not alter the ultimate outcome of the disease.

There is therefore a critical 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
EspeRare's founder and R&D Director

300 000
boys 
affected
worldwide



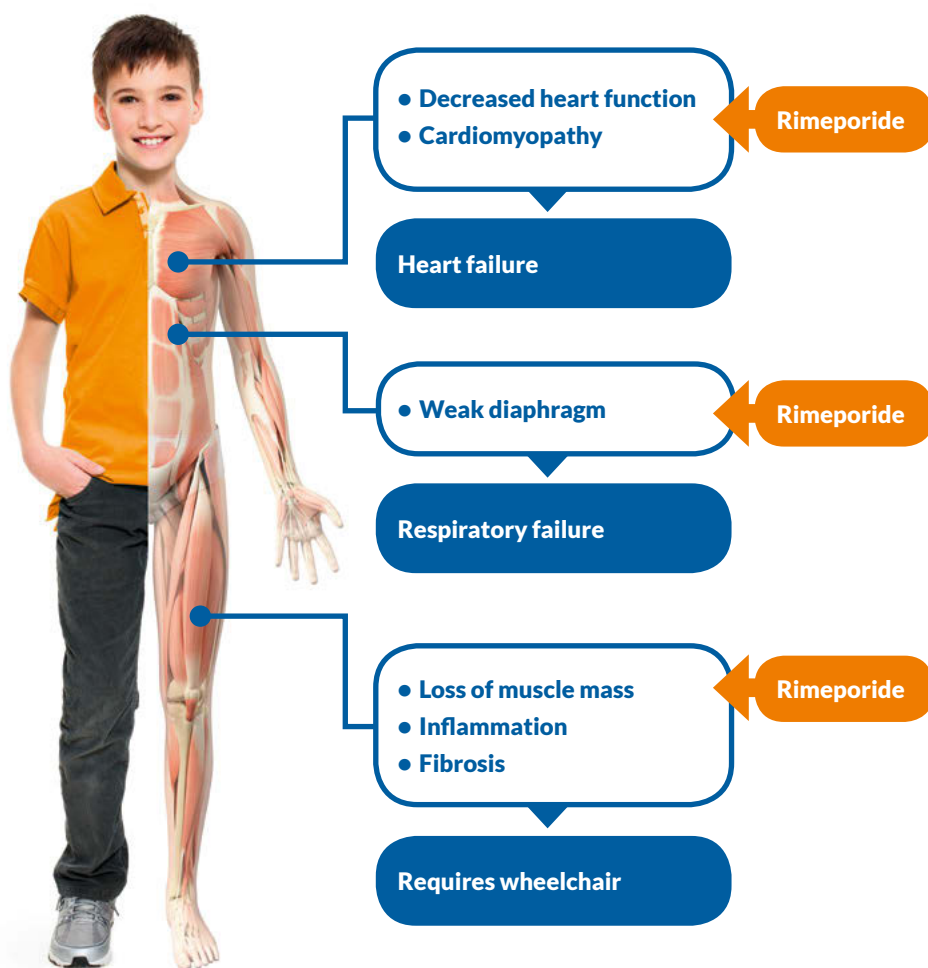
Affects the
longest gene
in the body:
the dystrophin
gene



Symptoms
appear
between
the ages of
2 and 5 years



Described by
Dr. Duchenne
in 1861





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 preclinical study.

2015

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

2016

Phase Ib clinical trial is launched, to examine the safety, tolerability and pharmacokinetic of Rimeporide, in children affected by DMD. This study was enabled thanks to several years of research and collaboration with researchers at leading institutions including the Children National Medical Center (Washington DC, USA) and the Sherbrooke University (Canada).

2017

• **Phase Ib clinical trial enrolment completed, reaching 20 young patients with DMD.** The study, coordinated by Pr. 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 results obtained previously in adult healthy subjects.

• **Large nonclinical 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.

• **US FDA grants Orphan Drug Designation for Rimeporide in DMD.**

2018 and beyond

Once the results of the safety phase Ib study and the nonclinical translational study are available, **discussion on the design of a phase II/III pivotal study will be engaged with Clinicians**, patients groups and Health Authorities. The clinical trial should start in 2019.

As the required funding of this clinical trial is above what EspeRare can raise, the subsequent clinical development of Rimeporide will be conducted by a pharmaceutical partner who has the adequate infrastructure to manage worldwide clinical trials, and to lead manufacturing and commercialisation activities. Along the development path, EspeRare will strive to ensure that patients who should benefit from the therapy will have access to it. ■

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



Rimeporide represents a novel treatment that has the potential to delay the long term accumulation of skeletal muscle degeneration and dilated cardiomyopathy in patients with DMD. It could be used by all DMD patients, alone or in combination with other therapies.

“ 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 centres 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).

Focal Segmental Glomerulosclerosis (FSGS)

ABOUT FOCAL SEGMENTAL GLOMERULOSCLEROSIS

Focal Segmental Glomerulosclerosis (FSGS) is a **rare kidney disease with an incidence of 7 per million people**. It affects both children and adults with peaks at 6-8 and 20-30 years of age, respectively.

Kidneys are the filters of the body: when blood passes through filtering units called glomeruli, some of its components are filtered out to make urine. To act as efficient filters, glomeruli need an intact physical filtration barrier, which is made up of tightly associated cells called podocytes. The disease is due to podocyte injury, resulting in the loss of the physical integrity of the filtration barrier.

A protein produced by the podocytes, called $\alpha\beta3$ integrin, is crucial for 'gluing' the podocytes to the glomeruli structure. Disregulation in $\alpha\beta3$ integrin pathway could lead to the dysfunction of the glomeruli filtration and apparition of scars in the glomeruli, called sclerosis or fibrosis. The damaged glomeruli allow large molecules, in particular proteins, to pass into the urine. This so-called proteinuria and symptoms secondary to it, such as swelling (oedema) of the tissues (often the legs and feet) can be the first signs of FSGS. Diagnosis is confirmed by kidney biopsy. **Management of FSGS can require dialysis and 50% of all cases progress rapidly to end-stage renal disease (ESRD), necessitating a kidney transplant.**

Current treatments essentially aim at controlling the symptoms of the disease and are often inadequate and toxic. FSGS is a lifelong chronic disease and the disease burden on patients is tremendous. The life expectancy of a 10 year-old child on haemodialysis due to end stage kidney disease is dramatically reduced. For FSGS patients, the need for novel and targeted medicines is a matter of urgency. ■



- Proteinuria
- Renal fibrosis

EspoiR-003

Renal failure leading to kidney transplant

ESPOIR-003 PROGRAMME IN FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSGS)

Espoir-003 is a safe, potent and selective $\alpha\beta3$ integrin antagonist. It was developed by Merck Serono in a cancer application but was discontinued in Phase III when it failed to meet its primary endpoints.



Espoir-003 has been validated *in vitro* as a potentially beneficial therapy and represents an innovative and promising approach targeting podocyte loss in FSGS patients. This therapy has the potential to translate into slowing down the decline of FSGS patients' renal function.

BACKGROUND

2013

EspeRare obtained the rights to study Espoir-003 in Focal Segmental Glomerulosclerosis (FSGS).

2014

EspeRare started working on the repositioning opportunity for Espoir-003 in FSGS. A non-clinical study was initiated with Prof. Moin Saleem's team, a nephrology and FSGS-specialised team from the School of Clinical Sciences, Bristol University (UK).

2015

Prof. Saleem's team completed the *in vitro* study to assess the potential of Espoir-003 in FSGS. Espoir-003 was found to be non-toxic to podocytes and to reduce the FSGS-induced $\alpha\beta3$ integrin activation. This effect has the potential to improve the renal functions of FSGS patients.

2016

Beginning of a **partnership is with Dr Rachel Lennon**, a Wellcome Senior Research Fellow in Clinical Science at the University of Manchester and an Honorary Consultant in Pediatric Nephrology at the Royal Manchester Children's Hospital.

“What we learn from rare disorders often has profound consequences for our understanding of more common conditions.”

Dr Francis Collins,
Director of the National
Institutes of Health

2017

Study by Dr Lennon's team aiming to determine whether $\alpha\beta3$ integrin activation can be used to establish a stratification strategy, to select patients for whom the $\alpha\beta3$ integrin pathway is activated.

2018 and beyond

Once a patient stratification method is established, it will need confirmation on a bigger patient cohort. **EspeRare will then seek to engage FSGS clinical experts worldwide to design a Proof of Concept clinical trial.** It will use Espoir-003 in FSGS patients that present over-activated $\alpha\beta3$ integrins. ■

ESPOIR-003 IDENTITY CARD:



Name: Espoir-003
Target: $\alpha\beta3$ integrin inhibitor
Originator: Merck Serono
Indications: Focal segmental glomerulosclerosis (FSGS, active development by EspeRare) and oncology (inactive development)

Drug development phase:

Administered to over 1,600 patients (adults and children, Phases I to III) for cancer; now under pre-clinical evaluation for FSGS

Opportunity: Good safety profile in humans.
Proven activity on $\alpha\beta3$ integrins, a protein that inappropriate activation is thought to play a major part in the progression of FSGS

A WORLDWIDE NETWORK OF DISEASE EXPERTS TO ADVISE AND STRENGTHEN ER-003 CLINICAL DEVELOPMENT STRATEGY



Strategic partnership with clinical centres of excellence: Key Opinions Leaders Profs. Gipson and Kretzler (University of Michigan and NEPTUNE study, USA).



Key collaborations with Dr Lennon (Manchester, UK) and with Prof. Saleem (University of Bristol, FSGS patient registry, UK).



R&D funding: £ 650k MRC grant (UK) awarded to Prof Saleem, EspeRare and an industrial partner.

X-Linked Hypohidrotic Ectodermal Dysplasia (XLHED)

ABOUT X-LINKED HYPOHIDROTIC ECTODERMAL DYSPLASIA

XLHED is a **rare genetic disorder** caused by a defect in the EDA-A1 gene located on the X-chromosome. Individuals with XLHED lack a functional EDA-A1 (EDA) protein, essential to the normal development of a dermal layer during foetal development. Consequently, **the development of 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, who can be affected variably.

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. Other disease burdens include psychosocial challenges that persist into adulthood. Unfortunately, today, there are no treatments for XLHED.

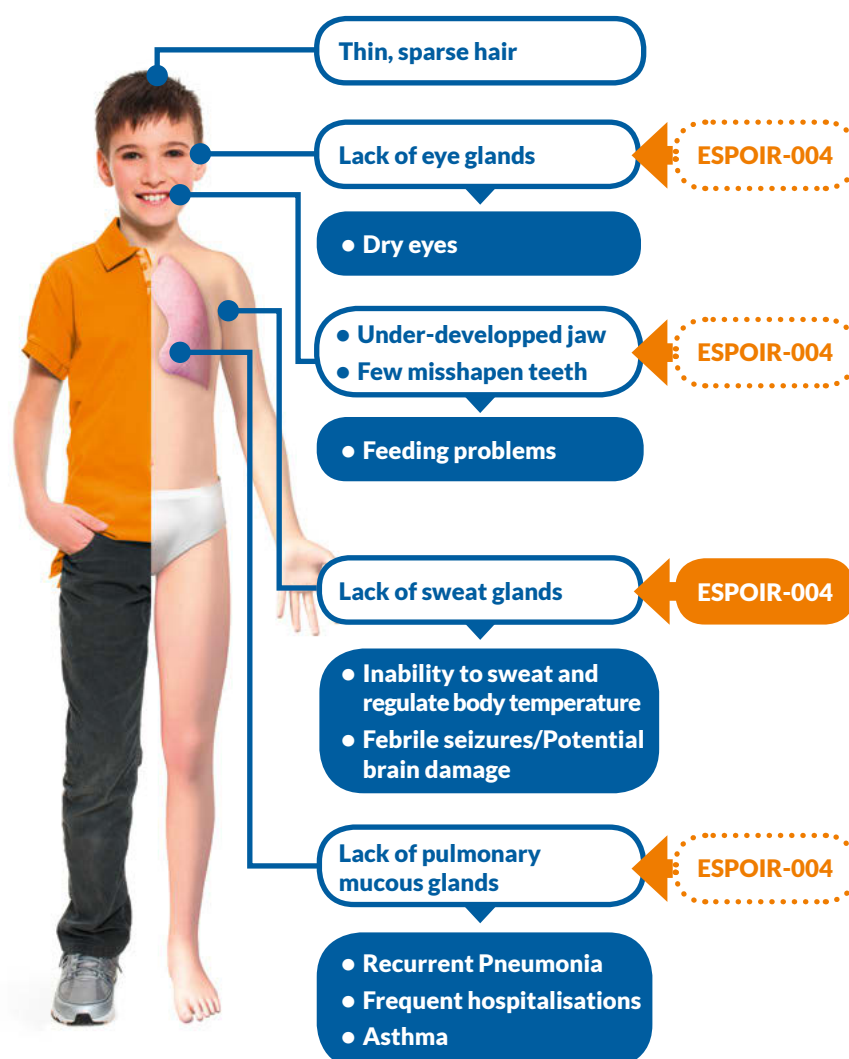
The first and only therapy ever developed for the disease was stopped in 2015 following a clinical setback. Indeed, when administered to newborn babies, the treatment did not seem to provide therapeutic benefits.

In 2016 however, Prof. Holm Schneider, a German medical expert, renewed hope for XLHED patients when he administered this same treatment (EspeIR-004) *in-utero* to 3 fetuses. The promising results obtained with this new mode of administration during pregnancy have un-

covered the strong potential of the therapy, which addresses the most debilitating aspects of XLHED.*

Building on Prof. Holm Schneider's promising *in-utero* approach, EspeRare is now restarting the development of this unique therapy.

EspeRare is about to initiate the first pivotal intra-amniotic clinical study ever conducted in patients. More broadly, these efforts will also open the way to establishing *in-utero* administration as a new therapeutic approach to correct other genetic diseases during pregnancy. ■



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

ESPOIR-004 PROGRAMME IN X-LINKED HYPOHIDROTIC ECTODERMAL DYSPLASIA

Espoir-004 is a well-tolerated, potent therapy developed by Edimer to treat XLHED. It was discontinued in 2015 due to lack of clinical efficacy when administered to newborn babies.



Administered during pregnancy into the amniotic fluid surrounding the foetus, Espoir-004 has the potential to correct the most severe symptoms of XLHED.

BACKGROUND

2017

Edimer Pharmaceutical Inc. approached EspeRare to revive Espoir-004's clinical development (previously named EDI200), previously stalled because of the lack of positive results when administered to newborn babies

- EspeRare established a collaboration with Prof. Holm Schneider, a German paediatrician who worked on the development of ER-004 and pioneered the first intra-amniotic administrations of ER-004 to 3 unborn XLHED fetuses.
- The development of Espoir-004 in XLHED using an *in-utero* administration was accepted in the European Medicines Agency's PRiority MEDicines scheme, "PRIME scheme", as a programme aimed at accelerating the development of therapies for unmet needs.

"This breakthrough could change forever treatment options for XLHED"

Prof. Holm Schneider

2018 and beyond

- EspeRare plans to start a pivotal clinical trial aiming at obtaining market authorisation worldwide. The trial will start recruiting patients in Europe, with Prof Schneider as principal investigator at Erlangen University Hospital in Germany.

ESPOIR-004 IDENTITY CARD:



Name: Espoir-004
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 nonclinical and phase I clinical data package; a phase II clinical trial in newborn babies failed to show benefits.
Opportunity: based on promising results in 3 fetuses treated *in-utero*, initiation of a pivotal clinical trial using an intra-amniotic administration approach.

A PROMISING NEW PROJECT, BUILDING ON A STRONG NETWORK OF COLLABORATIONS IN ECTODERMAL DYSPLASIAS



R&D funding: More than CHF 1,5 million raised from foundations and private donors



Key collaborations established with patient associations: National Foundation for Ectodermal Dysplasias (NFED) in the US and the Ectodermal Dysplasias International Network (EDIN)



Strategic partnership with key medical stakeholder: Prof. Holm Schneider

Congenital Heart Defects (CHD)

ABOUT NEWBORNS WITH CARDIAC HEART DEFECTS AND PULMONARY ARTERY BANDING



Present at birth, Cardiac Heart Defects (CHD) are structural malformations of the heart that trigger a wide range of crippling cardiac dysfunctions. Nearly 1 in 100 infants are born with CHD that range from mild to severe. In 5 % of cases, CHD is life-threatening. When available, early corrective heart surgery to repair the defects is the preferred intervention, but it requires an open-heart operation on a very small heart. In some cases, this surgical operation can not be conducted in neonates and a palliative and provisional procedure is elected instead.

One of these palliative procedures is known as Pulmonary Artery Banding (PAB) and is currently used in the USA and Europe for approximately 1000 cases each year. PAB involves suturing an implantable 'tape' around the pulmonary artery to narrow the latter. This device allows to tamper down the abnormal blood pressure and thereby to protect the babies' heart and lungs functions. This buys newborns and doctors alike precious time before the babies can undergo the final corrective open-heart surgical procedure. ■

ESPERARE WANTS TO GIVE FLOWATCH A SECOND CHANCE

EspeRare is reviving and re-introducing the FloWatch device for newborns affected by severe cardiac defects. This previously marketed therapeutic device has proven its medical ability to remotely reduce pulmonary blood flow and thus protect the heart and lungs of these newborn babies while they wait to undergo a surgical operation to repair their hearts.

The FloWatch technology was developed at EPFL (Switzerland) and combines a micro-motor inspired by Swiss watchmakers with a remote control system. **EspeRare is relaunching the quality, regulatory and manufacturing processes in order to seek the European and US market access authorisation.**

Over the next 3-4 years, EspeRare wishes to produce and distribute the first units. Fulfilling EspeRare's not-for-profit goals, 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 PROGRAMME FOR NEWBORNS WITH SEVERE CONGENITAL HEART DEFECTS (CHD)

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 mor-

bidity. 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 pressure without having to physically access the device. It results in **shorter**

stays in intensive care and by-passing the need for re-operations. 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 and has been implanted successfully in children in Europe and Asia between 2002 and 2012. ■

FloWatch® -Control Unit



FloWatch®
implant on the pulmonary artery

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

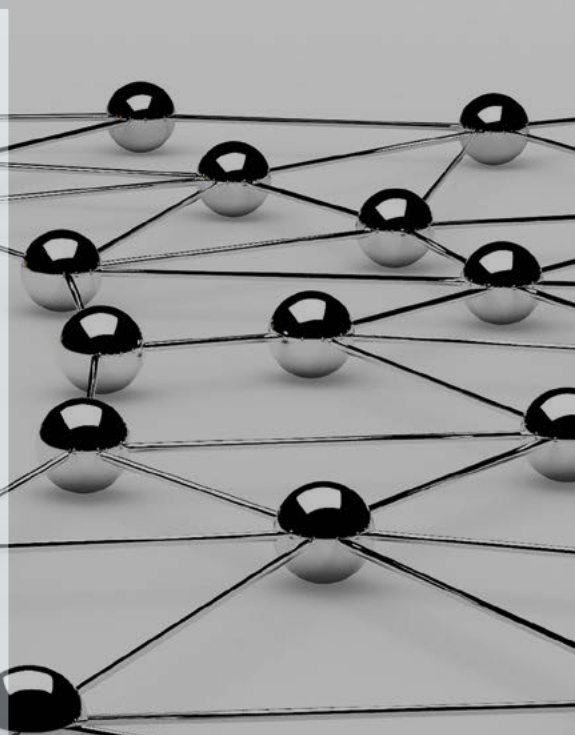
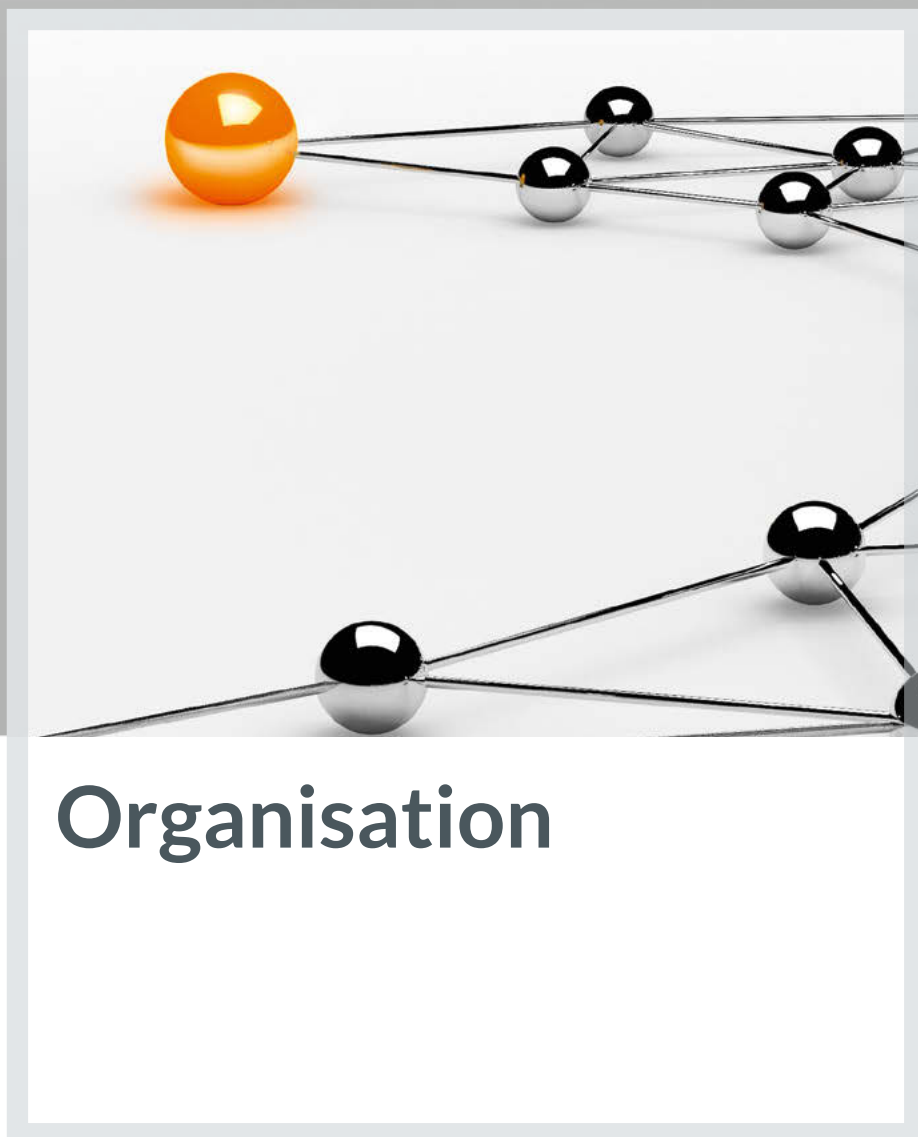
“The FloWatch device has proven, since 10 years, to provide an adaptable regulation of heart blood flow and protect the pulmonary circulation of patients not amenable to immediate complete surgical repair.”

Prof. Maurice Beghetti

FLOWATCH IDENTITY CARD:

- Name:** FloWatch
- Target:** Heart
- Originator:** EndoArt S.A – a Swiss start-up company acquired by Allergan in 2007
- Indications:** Congenital Heart Defect applications in newborn babies
- Drug development phase:** Previously marketed, market re-launch by EspeRare. Bespoke distribution model under development by EspeRare to enable poorer countries to access FloWatch.
- Opportunity:** Clinically-proven benefits for some severe forms of CHD. In developing countries, wider range of use because of lack of reparative surgery. Possible expansion in cardiomyopathy.

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



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 nonprofit 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 programs. ■

"As a nonprofit 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

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.

Beatrice'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 wide-range leadership expertise across the whole pharmaceutical R&D value chain.

SHARON F. TERRY

Sharon 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



Denis Mortier



Peter Potter-Lesage



Ewen Sedman



Sharon F. Terry - President

MANAGEMENT TEAM

CAROLINE KANT-MAREDA

Founder and 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

Founder & R&D Director

Florence Porte is in charge of developing the Foundation's R&D portfolio, driving the programmes from preclinical validation to proof of concept in human. As a founder, she also sits on EspeRare's board. Florence brings 15 years of experience in drug development. She joined the pharmaceutical industry in 1997 in the field of clinical pharmacology, leading translational research and managing early clinical studies. Within Merck, she became a program leader and successfully led several R&D programs in various therapeutic areas. Growing up with a cousin affected with Duchenne Muscular Dystrophy and seeing him gradually decline, Florence has an unconditional motivation to drive this foundation 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 worked with 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 NGOs. While specialised in the counsel to pharmaceutical companies, start-ups and nonprofit 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

Medical and Regulatory advisor

Julian Gray supports EspeRare in all medical aspects. In addition, he advises on clinical development strategies and assists in the interactions with regulatory agencies. As a medical expert in the Central Nervous System (CNS) clinical research for the pharmaceutical industry, he led clinical studies on Parkinson's and Alzheimer's diseases. Since 2004 he has worked as an independent consultant in drug development. He has a strong track record in the in-licensing of new medicine, orphan drug development, and 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. Dr. Gray holds the title of Specialist in Pharmaceutical Medicine (Switzerland).



Caroline Kant



Florence Porte



Sylvie Ryckebusch



Monique A. Caillat



Julian Gray

TEAM

STÉPHANIE CARNESECCHI

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

SARAH DELACOSTE

Sarah Delacoste is an accounting and controlling specialist, with additional IT expertise. In parallel to her work in various big companies (computer, telecoms, real estate...) she is active in non-profit organisations for various humanitarian causes to help creating a better world. At EspeRare, Sarah links ledger accounting to reporting and auditing activities.

MARIE DENIZET

Marie is a scientific communication specialist. After a PhD in neurobiology in Paris, she is now focusing on communicating and disseminating scientific facts to the general public. She elaborates and implements EspeRare's communication strategy.

LAETITIA GALEA

Laetitia is a material science engineer, specialised in materials for biomedical applications. She has 9 years of experience in the medical device industry. She brings her technical and regulatory expertise to the FloWatch device project.

HANANE GHEIT

Hanane is specialised in orphan and pediatric drug development in different areas such as metabolic diseases and neuro-oncology. She provides her clinical operational expertise to EspeRare's programmes.

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 programme leader.

DELPHINE LABOLLE

Delphine is a clinical research expert. She has 5 years of experience in clinical operations, mainly in Eastern and Western Europe. At EspeRare, she manages the on-going clinical trial of Rimeporide in Duchenne Muscular Dystrophy.

CÉDRIC MERLOT

Cédric is the CEO of Drugdesigntech which he founded in 2007. He has vast experience in molecular modeling and computer-assisted drug design. He applies his bioinformatics and data management expertise to support the development of the foundation's proprietary Repositioning Platform.

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.

PAN SALVARIDIS

Pan has over 45 years of experience in R&D and Production of medical equipment and devices, he served in senior management positions in multinational corporations, distribution, outsourcing and organisational performance. He supports EspeRare's Medical Device program.

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.

DUC 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.

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 pediatric 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 and in particular the golden retriever muscular dystrophy model.

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.

DR. PIERRE CARLIER

Dr. Carlier, MD, PhD, is head of the NMR laboratory of the Myology Institute in Paris. He is a leading specialist in magnetic resonance imaging and spectroscopy (MRI&S) of muscle. He focuses on developing truly quantitative imaging, which may enable the detection of very early and pre-clinical signs of a positive response to treatment. He provides EspeRare with his expertise in the imaging of muscles using MRI&S.

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. CONRAD HAUSER

Prof. Hauser was, during 15 years, chief of the Department of Dermatology of Western Switzerland (Bern) and chief of the Allergy Unit, division of Immunology and Allergology, within the University Hospital of Geneva. In 2008, he joined the Merck Serono pharma company as head of early development & head of biomarker strategy, global clinical development in the Unit of Rheumatology. He provides to the foundation his expert biomedical understanding in immunology.

PROF. BEHROUZ KASSAI-KOUPAI

Prof. Kassai-Koupai is a medical doctor at the University Hospital of Lyon (France) where he is in charge of the Pediatrics clinical trial unit. He is an expert in clinical pharmacology and in drug development for pediatrics studies. He is part of EspeRare's scientific advisory board and member of the Safety Committee Board for the on-going clinical Duchenne project.

PROF. RUDOLF KORINTHERBERG

Prof. Korintherberg, MD, is Professor of Pediatrics and Child Neurology at the Department of Pediatrics 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. He is part of EspeRare's scientific advisory board and member of the Safety Committee Board for the on-going clinical Duchenne project.

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 dossiers 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. KANNEBOYINA NAGARAJU

Prof. Nagaraju is an immunologist with an expertise in molecular mechanisms of tissue injury in muscle diseases. He is Founding Chair and Professor at the School of Pharmacy and Pharmaceutical Sciences at Binghamton University (USA). One of the main focuses of Dr. Nagaraju's laboratory is to develop and validate animal models for neuromuscular diseases. He is a preclinical advisor for EspeRare Duchenne programme.

PROF. RENÉ PRÊTRE

Prof. Prêtre is the Head of the Pediatric Cardio-Vascular surgery unit at Lausanne University. He is recognised as one of the world's leading pediatric 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. MOIN A. SALEEM

Prof. Saleem is Professor of Pediatric Renal Medicine at the Academic Renal Unit, Southmead Hospital, Bristol and Children's Renal Unit, Bristol Children's Hospital. As part of his research on renal function, he developed a technique for growing human renal cells in the laboratory. This new methodology allows EspeRare to test molecules that are potential treatments for Focal Segmental Glomerulosclerosis, such as ER-003.

PROF. HOLM SCHNEIDER

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

Prof. Schneider is the Principal Investigator for the upcoming clinical study of intra-amniotic ER-004 in XLHED.

DR. WOLFGANG SCHOLZ

Dr. Scholz completed his medical education at the Universities of Mainz and Frankfurt. After 16 years of experience in cardiovascular research at former Hoechst AG, heading a Research Team, he became the head of cardiovascular research at Merck KGaA Darmstadt. He is now heading the drug repositioning activities at Merck Serono. He provides his know-how and expertise to EspeRare's project in Duchenne Muscular Dystrophy.

DR. LAURENT SERVAIS

Dr. Servais is a pediatrician and the director of the clinical research department at the Institute of Myology in Paris after 15 years of clinical research in rare diseases. In addition to his medical practice, he develops clinical trials and clinical outcome measures in muscular dystrophies. He brings medical expertise to the clinical strategy of EspeRare's programme in Duchenne Muscular Dystrophy.

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. Bragulia 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 counseling to EspeRare.

MR. SALOUT KUNZI

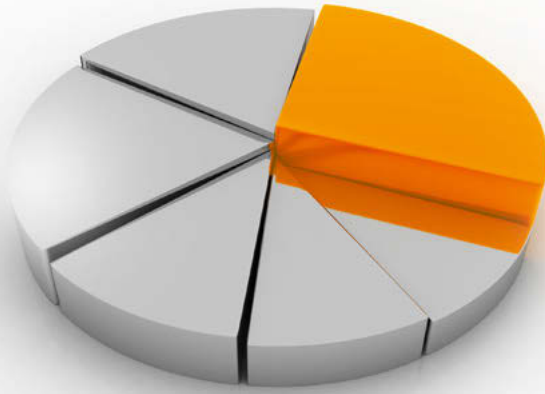
Mr. Kunzi serves as Head of Quantitative solutions at EFG Asset Management SA. In the past, he has also held various financial engineering, asset liability and investment analysis roles both within private banks and investment companies. He supports EspeRare's financial quantitative and risk strategy.

DR. ALEXANDRA RICHARDSON

Dr. Richardson heads marketing and business development for Clayton Biotechnologies, Inc. She has over fifteen 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.

"Optimism is a strategy for making a better future. Because unless you believe that the future can be better, you are unlikely to step up and take responsibility for making it so."

Noam Chomsky



Financial view

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 centres and regulatory agencies to drive effective development and foster affordable access to new treatments for rare disease patients. Established as a not for profit Swiss foundation under statutes dated 28 March 2013, EspeRare is managed by a foundation board, a CEO and two senior managers, with 6 employees, and 15 contractors. EspeRare as an organisation is exempt from cantonal and federal taxes and is the equivalent of an exempt organisation within the meaning of Section 501(c)(3) of

the United States Internal Revenue Code.

Accounting is entrusted to 'Eclosion', the Geneva Life Science incubator facility within which EspeRare was initially located, 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 2017

The year was characterised by a number of factors. Considerable donations were received and/or confirmed for the future, staff were recruited, planning was activated, the portfolio was broadened and diversified to amount to 6 ongoing projects. Most important of all, **Research & Development Project funding represented 87% of total expenses and amounted to CHF 1,485,351** (note 8 a-i), stable as compared to CHF 1,568,381 in 2016.

Importantly, EUR-CHF fluctuation have benefited EspeRare in 2017 causing a CHF 84,219.96 gain while GBP-CHF exchange rate has caused a loss of CHF 17,444.23. Additionally, USD-CHF exchange rates have occasioned minor exchange gains amounting to CHF 48.22. Altogether these

fluctuations have resulted in an unrealised exchange gain of CHF 66,823.95. Exchange rates between the reception of invoices and payments fluctuated as well, causing a loss of CHF 4,857.40. The total financial income gain (note 2k) thus amounts to CHF 61,966.55 as opposed to an exchange loss of CHF 12,564 in 2016 (note 2c).

This year, the foundation suffered an excess of expenditure over income of CHF 410,423.77 (note 3) which is mainly due to expenses incurred for higher-cost activities due to a 6 months delay experienced with the clinical development of Rimeporide in Duchenne muscular dystrophy that was induced by a drug manufacturing issue.

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 2017 amounted to CHF 1,232,753.74, including an amount of CHF 569,338 deferred from 2016 for the clinical activities of Rimeporide and FloWatch programs. A total of CHF 273,800 was recognised from Merck Serono in 2017 to finance the completion of the clinical trial activities of Rimeporide in Duchenne muscular dystrophy. A CHF 4,273 contribution from Association Altrodomani and EUR 4,273 from Parent Project Onlus, both patient organisations based in Italy, were received to finance the enrolment of patients into the Rimeporide clinical trial at

the Milano clinical site. From the contribution from AFM Telethon of CHF 155,075 received in 2016, CHF 77,538 has been recognised in 2017 to finance the completion of the ongoing translational study with Rimeporide. From the donation amounting to CHF 300,000 granted in 2016 to finance the FloWatch project by a Private foundation based in Geneva, an amount of CHF 128,000 was recognised in 2017. A donation of CHF 10,000 from Tell et Un Tel was recognised for the FloWatch project in 2017, another CHF 20,000 donation from Prim'Enfance was differed to 2108 for this project. In addition, from another CHF 700,000 received in 2017 from a Geneva Foundation, CHF 318,821 was recognised this year to fund this same project. In 2016

another endowment of CHF 66,924 was also granted from UK Duchenne, a patient organisation based in London, to initiate the development of ER-002, a new program in Duchenne Muscular dystrophy. From this donation, EspeRare has recognised in 2017 CHF 6,210 and an off-balance sheet amount of CHF 33,462 was recognised as a direct payment to our research partner in the United Kingdom. In 2017 another donation of CHF 1,000,000 from a Geneva Private foundation was also received for a new project, ER-004 in a rare skin disease, out of which CHF 134,840 was recognised in 2017. The Foundation Tell et Un Tel granted another CHF 15,000 for the project that was fully recognised in 2017. Finally, a Foundation Support donation from a Geneva

Foundation of CHF 200,000 was recognised in 2017 (note 7).

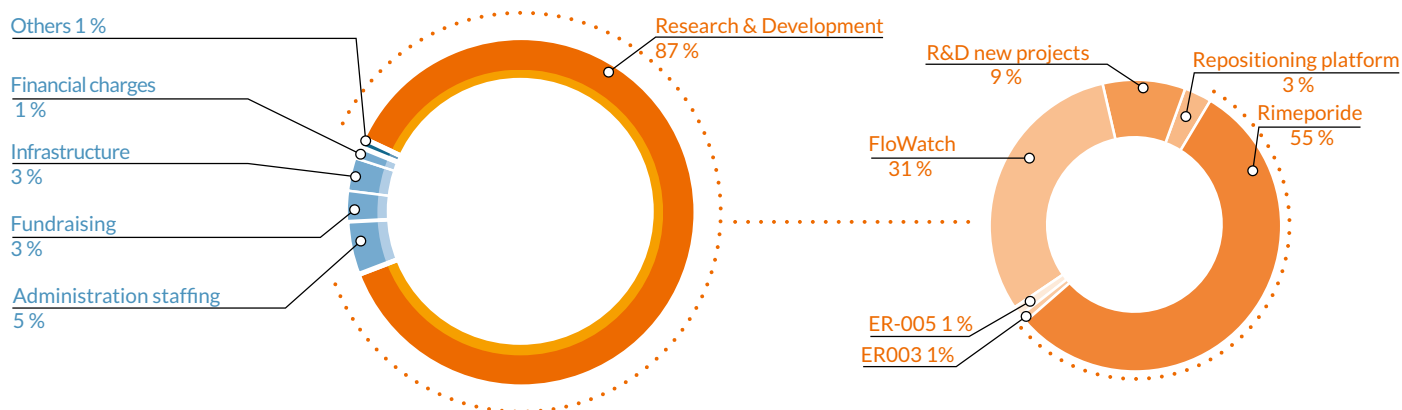
Staff

At year-end the senior management team consisted of a Chief Executive Officer, and an R&D director. Furthermore, EspeRare has a team of 6 Program Managers, 15 contractors and counts as well on the support of many other people including board members, senior scientific advisors and volunteers.

General Administration

Expenses here reflect general foundation expenses in overall support of R&D activities (note 8h) ■

SNAPSHOT OF ESPERARE EXPENDITURE 2017



THE FINANCIAL YEAR AHEAD TO DECEMBER 2018

EspeRare operates in a complex multi-currency environment in Geneva, Switzerland. The bulk of donations are currently received in Swiss Francs, although other currencies such as Euro or US dollars 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 Swiss Francs. 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.

This implies a well-developed treasury management and accounting approach, matching inflows to outflows by currency and taking timely multi-currency investment and foreign exchange decisions. Moreover, to better reflect increasing scientific activity and the expansion of our program portfolio, a new internal accounting structure was consolidated 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. Current forecasts, given certain fundraising assumptions, amount to about CHF 3 million for 2018 for future EspeRare rare disease Research and Development project funding. By the beginning of 2019 it is expected that EspeRare's first programme in Duchenne muscular dystrophy will be out-licensed to a commercial partner. This transaction is expected to generate a significant inflow of capital that will be used to fund the expansion of the foundation programme portfolio in rare diseases, as well as to finance the "expensive" clinical development of its current portfolio and the scale-up of its infrastructure, including its Repositioning platform and its organisation. As the EspeRare portfolio of therapeutic programmes is maturing and moving into these later stages of develop-

ment, 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 its impact, thus diminishing the burden on those patients suffering from rare diseases.

Conclusion

The detailed financial tables that follow – Balance Sheet, Statement of Income & Expenditure – represent EspeRare in its fifth 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 in preparation of the scale-up of EspeRare activities for 2018-2019, 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 TO 31 DECEMBER 2017

	NOTES	2017 CHF	2016 CHF
ASSETS			
Current Assets			
Cash & Cash Equivalents	2i	-	-
BCGE Current Accounts	2i	2 586 872	2 117 410
Prepaid & Receivables			
Accounts Receivable		9 085	-
Prepaid (transitory)		2 054	1 188
Other receivables		2 542	22 642
Withholding Tax & VAT Receivable		10 347	4 004
TOTAL CURRENT ASSETS		2 610 901	2 145 244
Non-Current assets			
Mid Term Financial assets (Deposits)		8 464	771
Computers & Equipment (less depreciation)	2d	21 787 (11 076)	11 941 (8 089)
TOTAL NON-CURRENT ASSETS		19 175	4 624
TOTAL ASSETS		2 630 076	2 149 868
LIABILITIES			
Current Liabilities			
Suppliers		214 347	12 563
Employees Accounts		1 392	-
Social Charges		-	5 973
Due VAT		-	-
Provisions	2f/9	-	38 967
Accruals	2g	220 660	215 261
Deferred Income	7	1 296 339	569 338
TOTAL CURRENT LIABILITIES		1 732 738	842 102
Capital & Reserves			
Foundation Capital	10	50 000	50 000
Operations Reserve	3	1 257 766	1 304 627
Net excess of (Expenditure)/ Income		(410 429)	(46 861)
TOTAL CAPITAL & RESERVES		897 338	1 307 766
TOTAL LIABILITIES AND CAPITAL		2 630 076	2 149 868

CASH FLOW AS OF 31 DECEMBER 2017

	2017 CHF	2016 CHF
OPERATING ACTIVITIES		
Net excess of (Expenditure) / Income	(410 429)	(46 861)
+Depreciation	2 987	1 133
+decrease (increase) in Prepaid and Receivables	(3 887)	(20 284)
+increase (decrease) in Short term Liabilities	197 203	(120 514)
+increase (decrease) in Provisions	(38 967)	12 567
+increase (decrease) in Accruals	5 399	172 946
+increase (decrease) in Deferred income	727 002	(87 525)
Cash from operating activities (operating cash flow)	479 308	(88 539)
INVESTING ACTIVITIES		
Outflows for purchase of tangible fixed assets	(9 845)	(4 173)
Cash inflow/drain from investing activities	(9 845)	(4 173)
Cash inflow/drain from financing activities	-	-
NET CASH	469 463	(92 712)
Cash and cash equivalents at beginning of period	2 117 410	2 210 121
Cash and cash equivalents at end of period	2 586 872	2 117 410
NET CASH	469 463	(92 712)

ESPERARE STATEMENT OF INCOME & EXPENDITURE FOR THE PERIOD FROM JANUARY 1ST TO DECEMBER 31, 2017

	NOTES	2017 CHF	2016 CHF
INCOME			
Donations Received for R&D	2b/7a	972 754	1 225 343
Financial Income	2k	61 967	0
Other Income		261 098	502 175
TOTAL INCOME		1 295 818	1 727 518
EXPENDITURE			
Research & Development Expenditure	2e		
R & D Projects	8a		
Rimeporide			
Research & Development	8b	527 781	878 291
Support Costs	8i	284 075	369 752
Legal Fees		-	-
TOTAL R&D PROJECTS, RIMEPORIDE		811 856	1 248 043
NEW PROJECTS	8c		
Repositioning Platform	8d	31 583	3 624
Support Costs	8i	15 459	58 144
ER-003	8e	205	(2 675)
Support Costs	8i	13 495	17 896
New prospects- pre project		19 683	28 771
Support Costs	8i	116 565	12 433
JNK Project	8g	463	-
Support Costs	8i	19 258	17 120
Flowatch	8f	166 430	96 182
Support Costs	8i	290 353	88 843
TOTAL NEW PROJECTS		673 494	320 338
TOTAL RESEARCH & DEVELOPMENT EXPENDITURE		1 485 351	1 568 381
GENERAL FOUNDATION ADMINISTRATION	8h		
Administration staffing & volunteers	8i	94 362	94 806
Patient Association Consultancy		-	975
Office Rental & Costs		52 586	23 612
Office Rental		48 714	17 500
Office Costs		3 872	6 111
Accounting & Audit Expenses		12 779	36 176
Audit Expenses		12 779	36 176
Accounting Expenses		-	-
Other Expenses		9 913	5 028
General Insurance		-	0
IT Expenses		3 830	173
Communications		6 084	4 855
General Legal Fees		1 529	0
Fundraising		43 624	12 047
Fundraising direct costs		41 498	9 304
Travel & Conference Costs		-	-
Advertising Costs		2 126	2 335
Other Operating Expenses		-	408
Financial Charges		2 280	3 228
Exchange Differences	2c	0	12 564
Board meeting		836	8 750
Depreciation		2 987	1 133
Duties and Taxes		-	7 679
TOTAL GENERAL ADMINISTRATION EXPENDITURE		220 896	205 998
TOTAL EXPENDITURE		1 706 247	1 774 379
NET EXCESS OF (EXPENDITURE) / INCOME	3	(410 429)	(46 861)

NOTES TO FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2017

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 2 senior managers.

With its head-office in Plan-les-Ouates, 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 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.

As with all Swiss foundations recognised 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, articles 957 to 960e.

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.

1 EUR = CHF 1.170150

1 USD = CHF 0.974475

1 GBP = CHF 1.318256

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	2016 CHF	Acquisitions	Disposals	2017 CHF
IT Equipment	11 941	4 196	-	16 138
Furniture	-	5 649	-	5 649
TOTAL	11 941	9 845	-	21 787

Depreciation	Cum. 2016 CHF	Yearly Depreciation	2017 CHF
IT Equipment	8 089	1 501	9 590
Furniture	-	1 486	1 486
TOTAL	8 089	2 987	11 076

TOTAL NET VALUE	3 853	6 858	10 711
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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 recognised 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

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. FINANCIAL INSTRUMENTS

a) Foreign currency risk

EspeRare incurs foreign currency risk on pledged or effective contributions that are denominated in a currency other than Swiss Francs, and on cash and deposits that are denominated in other currencies.

EUR currency fluctuation have benefit to EspeRare by CHF 84'219.96 (unrealised gain) while GBP has caused a loss of CHF 17'444.23 (unrealised loss), USD has created a minor gain of CHF 48.22. Exchange rates between the reception of invoices and payments fluctuate as well, causing a loss of CHF 4'857.40. Total exchange gain is CHF 61'966.55

b) Interest rate risk

EspeRare does not have any significant exposure to interest rate risks.

c) Credit risk

In accordance with credit policy, exposure to credit risk, principally as regards contributions, is monitored on an ongoing basis.

EspeRare's liquid assets are kept in cash or low-risk short-term deposits.

At the balance sheet date there were no significant concentrations of credit risk. The maximum exposure to credit risk is represented by the carrying amount of each financial asset in the balance sheet, principally accounts receivable, short-term deposits and cash.

d) Fair value

The fair value of financial instruments held at 31 December 2017 does not differ from their carrying amounts shown in the balance sheet.

5. COMMITMENTS

As at 31 December 2017, there were no significant capital expenditure commitments.

6. SUBSEQUENT EVENTS

No events occurred subsequent to 31 December 2017 and prior to the approval of the financial statements that would require modification of or disclosure in the financial statements.

7. INCOME

Donations received

a) 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
TOTAL				569 338	1 959 756	1 232 754	1 296 339	

Off Balance Sheet:

UK Duchenne	GBP	33 462	33 462	Research & Development- ER-003
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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) As a comparison during 2016 the following donations were granted:

Donor	Currency	Total Grant	Received 2016 CHF	Recognised 2016 CHF	Deferred 2017 CHF	Notes
R&D Income						
ARES Trading SA (Merck Serono Affiliate) *	EUR	1 200 000		656 863		I&E Statement- Rimeporide - Deferred from 2015
ARES Trading SA (Merck Serono Affiliate)**	EUR	500 000	547 600	273 800	273 800	I&E Statement - Rimeporide
AFM telethon**	EUR	150 175	155 075	77 538	77 538	Grant Rimeporide
DPP ESPANA	EUR	25 000	27 143	27 143		Grant Rimeporide
Geneva Foundation	CHF	300 000	300 000	172 000	128 000	Grant FloWatch
HES	CHF	10 000	10 000	10 000		Grant Rimeporide
SEFRI	CHF	8 000	8 000	8 000		Grant Rimeporide
Sub-total			1 047 818	1 225 344	479 338	R&D Income
Awards & Foundation Support						
Geneva Foundation	CHF	500 000	500 000	500 000		For foundation Scale-up
Loterie Suisse Romande ***	CHF	90 000	90 000		90 000	Deferred Income for platform enhancement
Miscellaneous Income	CHF		2 175	2 175		
Sub-total			592 175	502 175	90 000	Awards & Support
TOTAL				1 727 518	569 338	
Off Balance Sheet:						
UK Duchenne	GBP	53 290			33 462	Research & Development- ER-003

* Out of a total of CHF 536,000 received from ARES Trading SA to co-finance the rimeporide clinical trial in Duchenne, CHF 268,000 was recognised in 2016 to fund the clinical trial activities of Rimeporide, CHF 268,000 are deferred to 2017 and will fund the completion of the clinical trial activities for Rimeporide.

** Out of a total of CHF 160,988 received from AFM Telethon to co-finance translational studies for rimeporide R&D, CHF 80,494 was recognised in 2016 and CHF 80,494 deferred to 2017 and will fund the completion of these studies.

*** A total of CHF 90,000 received from Loterie Suisse Romande in 2016 was deferred to 2017 as the enhancement of the repositioning platform starts in January 2017

8. EXPENSES

- Principal current R&D projects in rare diseases.
- Development of Rimeporide in Duchenne muscular dystrophy.
- Prospection & generation of new drug development projects for rare diseases. Including the evaluation of restarting the development of EspoIR-04 in X-linked Ectodermal Dysplasia
- Repositioning platform development to support the systematic discovery and evaluation of new projects.
- Development of ER-003 in Focal Segmental Glomerulosclerosis in partnership with Merck KGaA.
- Re-development of the FloWatch medical device for infants with cardiac defects.
- Development of JNK-inh in Duchenne muscular dystrophy
- General Foundation expenses in overall support of R&D activities.
- Relates to staff and travel costs that are recorded and allocated to the specific activities. The staff headcount represented three senior managers and five R&D program managers and one senior medical advisor. In addition, EspeRare benefits from a number of consultants and volunteers. Total staff benefits for 2017 amount to CHF 833'567.41 (*Salaries & Social charges* amount to CHF 787'999.20 *Travel Expenses* amount to CHF 39'061.09, *Volunteers reimbursements* amount to CHF 960.47 and *Training and other costs* totals CHF 5'546.65). The allocation of salaries & social charges to the four 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 seven activities

9. PROVISIONS

As of the 31st of December 2017 EspeRare has exited the Incubation support provided by Eclosion a Geneva State foundation that subsidises Start-ups in the life science sector. As per the Incubation Contract, Eclosion has subsidised EspeRare's office rate and infrastructure charges for its main office since April 2013, now that EspeRare is out of the incubation scheme, it has 5 years, until 31st of December 2022 to reimburse the foundation Eclosion for this mid-term invoice that amounts to CHF 77'292. (VAT included). It is recognised into accounts payable. Instalments are to be defined by EspeRare, this debt bears no interest. Provisions raised in previous year were reverted for CHF 38'967.

10. FOUNDATION CAPITAL

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

11. 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.

12. 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.

13. CONTINGENT LIABILITIES

EspeRare has potential liability that may occur, depending on the outcome of an uncertain future event. The first 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 295 hours were incurred, representing a total of CHF 88'500.- (2016: CHF 18'000, 2017: CHF 70'500) EspeRare has not accrued nor provisioned these probable costs (off balance sheet).

14. FULL-TIME EQUIVALENTS

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



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Report of the Statutory Auditor on the Limited Statutory Examination to the Board of Trustees of

Fondation EspeRare, Plan-les-Ouates

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 2017.

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

Pierre-Henri Pingeon
Licensed Audit Expert
Auditor in Charge

Cédric Rigoli
Licensed Audit Expert

Geneva, 7 May 2018

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.

I WANT TO TAKE ACTION TO SUPPORT ESPERARE

If you think you have useful skills to help fight rare diseases, we would be happy to integrate you in our team of volunteers.

I WANT TO HELP ESPERARE TO GET RENOWNED

You can very easily help us with our mission by circulating the link to our website (www.esperare.org) on your facebook or tweeter account.

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

Individuals:

donate@esperare.org

Corporate organisations:

partnership@esperare.org

THEY SUPPORT US





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