ANNUAL REPORT
2016

esperare foundation

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, we achieve this through a collaborative approach centred on patient engagement with the aim of giving people universal access to these therapies.

VISION

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

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

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 President

The EspeRare foundation 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.

In our age of great medical and technological advances, it is hard to comprehend that 30% of children's mortality is due to untreated rare diseases. Despite the lack of financial incentives to develop treatments for these underserved diseases, **it is EspeRare's mission to recognize that these children matter.**

Fired up by this goal and the inspiring courage of these children, **2016 has been an extremely important year in the growth and continuing evolution of EspeRare. During this forth year we have expended our portfolio to five therapeutic programs in four life-threatening diseases, thus having the potential to transform the lives of over 2 million children.** To accelerate these programs, EspeRare's team has more than doubled in 2016 and moved into new facilities at the Campus Biotech, a hub in the heart of Geneva grouping together research institutes, biotechnology companies and NGOs rooted in the Switzerland's "Health Valley".

We share our deepest appreciation with all of our loyal and dedicated advisors, volunteers, partners, and sponsors. You helped to make this year a success as we developed new paths for treatments for rare diseases. We share with you some of our achievements.

- In February, EspeRare was invited to present its innovative business model at the expert meeting of the United Nations Conference on Trade and Development (UNCTAD). It was a privilege to be able to share our business model with policy makers, investment experts, academia and private sector development institutions that shape international development policies.

- In March, EspeRare started the clinical development of Rimeporide in Duchenne Muscular Dystrophy. After encouraging preclinical results and an Orphan Drug Designation granted by the European Medicines Agency, the recruitment of patients with Duchenne Muscular Dystrophy started in a Europe-wide first trial of Rimeporide in children affected by this life-limiting disease. This trial is EspeRare's first project to reach the clinic and represents an important progress for patients living with Duchenne. Completion of this trial is anticipated for mid-2017 and discussions are underway with international experts for planning the next clinical stage.

- In June, EspeRare obtained the rights to re-introduce to the market a medical device, FloWatch. FloWatch is a device that protects the heart and lungs of newborn babies suffering from severe congenital heart defects. The device has clinically proven benefits, but is not commercially available any more. EspeRare's medical device team is working hard to re-instate the device's regulatory authorizations and manufacture new units. Fulfilling EspeRare's not-for-profit goal, part of the FloWatch devices produced will be distributed in Africa and in Asia through a philanthropic distribution scheme. The first devices should be available for implantation before the end of 2017.

- In August, thanks to funding from the Duchenne UK patient organization, EspeRare launched a new program in Duchenne. In collaboration with the Royal Veterinary College (UK), EspeRare started to test the therapeutic potential of ER002, a repositioned drug, in a Duchenne mouse model. These first studies are expected to be completed by mid-2017. If these are positive, both Duchenne UK and EspeRare have committed to ER002's development and the compound will be able to go straight to a Phase II Proof of Concept study in DMD patients. To find out more about ER03 in Duchenne.

- This year, EspeRare has been selected to be one of the 12 social enterprises to take part in the Ashoka Globalizer Program on Health sponsored by Philips. This 6-month accelerator program focused on matching social enterprises with leading advisors to develop its scaling strategy. During a closing summit at the Philips main campus in Eindhoven, EspeRare presented its strategy focused on handing over its model to other like-minded teams to maximize its impact while remaining agile and focused.

> **"Discovery consists of seeing what everybody has seen, and thinking what nobody has thought."**
>
> **Albert Szent-Gyorgyi, prix Nobel de Physiologie-Médecine 193**

Strikingly, this year we experience an important turning point. In the past, we actively scouted for new therapeutic gold nuggets to reposition. This year, several clinical researchers, like-minded organizations, and investors approached us with therapeutic opportunities to hand over to the foundation. This dynamic shift has further revealed the extent of opportunities that have little to no chance of being developed within the traditional commercial setting, and the impact that our nonprofit drug development model offers. Building on the strategy developed during the Ashoka Globalizer Program to maximize its impact and to stay agile, the foundation is starting to build the capacity to scale through the development of systems to hand over to like-minded teams. We see here a path to fast-forwarding treatments in rare diseases in a collaborative fashion.

In conclusion, the support and contributions we have received from all of our collaborators and sponsors have been instrumental in our achievements and have given us the courage to strive in a new direction. We thank you warmly for your contributions in taking EspeRare this far down the road. We feel energized to carry on the task ahead in 2017 and look forward to your extended support throughout the years,

Sincerely,

Sharon F. Terry,
President EspeRare

2016 highlights

FEB. 2016

ICRC Global Partnerships for Humanitarian Impact and Innovation event

EspeRare was invited to present its business model at the GPHI2 conference. Over 200 leaders from the business, humanitarian, health and academic sectors were gathered at the IMD Business School in Lausanne to address priority issues in the field of health in fragile environments. ■

FEB. 2016

EspeRare's model presented at the United Nations

EspeRare presented its innovative business model at the expert meeting of the United Nations Conference on Trade and Development (UNCTAD). It was a privilege to be able to share EspeRare's unique approach with policy makers, investment experts, academia and private sector development institutions whose mission is to shape international development policies. ■

MARCH 2016

An important progress for patients living with Duchenne: Rimeporide started its clinical development

After encouraging preclinical results and an Orphan Drug Designation granted by the European Medicines Agency, the recruitment of patients with Duchenne Muscular Dystrophy started in a Europe-wide first trial to test Rimeporide in children affected by this life-limiting disease. Rimeporide is EspeRare's first project to reach the clinic and represents an important progress for patients living with Duchenne. Completion of this trial is anticipated for mid-2017. ■

JUNE 2016

EspeRare launched a new program for newborn babies with congenital heart defects

EspeRare obtained the rights to re-introduce to the market a medical device, FloWatch. This device protects the heart and lungs of newborn babies suffering from severe congenital heart defects. The device has clinically proven benefits, but is no longer commercially available. EspeRare's new Medical Device team is working on legal and technical issues to successfully complete this new program. ■

JUNE 2016

EspeRare at the G21 Swisstainability Forum

The foundation's co-founders participated to the 6th edition of the Swisstainability Forum in Lausanne. This annual event is meant to be the platform for the economic transition in Switzerland. Along with other actors from the scientific, economic, political and non-governmental spheres, EspeRare's founders debated new business models to foster economic and social sustainability in Switzerland. ■

> “ Discovery consists of seeing what everybody has seen, and thinking what nobody has thought.”
>
> **Albert Szent-Gyorgyi**
> Nobel Prize in Physiology or Medicine

JULY 2016

EspeRare receives key support from Duchenne Parent Project Spain

Duchenne Parent Project (DPP) Spain have been instrumental in setting up the clinical activities to test Rimeporide in patients affected by Duchenne Muscular Dystrophy in Spain. DPP Spain is also providing administrative help and funding for the travel and accommodation of patients and families who participate in this first clinical trial in Duchenne patients. ■

AUG. 2016

EspeRare initiates the development of a new therapeutic approach for Duchenne

Thanks to funding from the Duchenne UK patient organization, EspeRare launched a new program in Duchenne. In collaboration with the Royal Veterinary College (UK), EspeRare started testing the therapeutic potential of ER002, a repositioned drug, in a Duchenne mouse model. This study is expected to be completed by mid-2017. If results are positive, Duchenne UK and EspeRare have committed to ER002’s development and the compound will go straight to a Phase II Proof of Concept study in DMD patients. ■

OCT. 2016

Update on the development of Rimeporide in Duchenne presented at the 21th World Muscle Society Congress

EspeRare actively participated in the 21th International World Muscle Society Congress in Madrid (Spain). This meeting brings together specialists of muscle biology, physiology and clinics. EspeRare presented a poster showing the latest results from the translational development of Rimeporide in Duchenne Muscular Dystrophy. The data presented included preclinical results and future plans for further pre-clinical and clinical studies. ■

OCT. 2016

EspeRare has taken part in the ASHOKA Globalizer program on Health sponsored by Philips.

This 6-month accelerator program focused on matching twelve social enterprises with leading advisors to develop its scaling strategy. During a closing Summit at the Philips main campus in Eindhoven, EspeRare presented its strategy focused on handing over its model to other like-minded team to maximize its impact while remaining agile and focused. ■

OCT. 2016

EspeRare’s CEO becomes an ambassador for UBS’ social innovators program

Caroline Kant was named an ambassador for “UBS Social Innovators Program”. In this role, and in partnership with ASHOKA, Caroline helped select UBS Swiss social enterprises that bring innovative solutions to society’s most pressing challenges. As part of her mentoring role, Caroline is delighted to be able to share her experience in pioneering social impact for orphan diseases. ■

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 ADVOCACY ORGANISATIONS IN RARE DISEASES

Particularly in rare conditions, disease advocacy organisations are key partners at each stage of drug development:

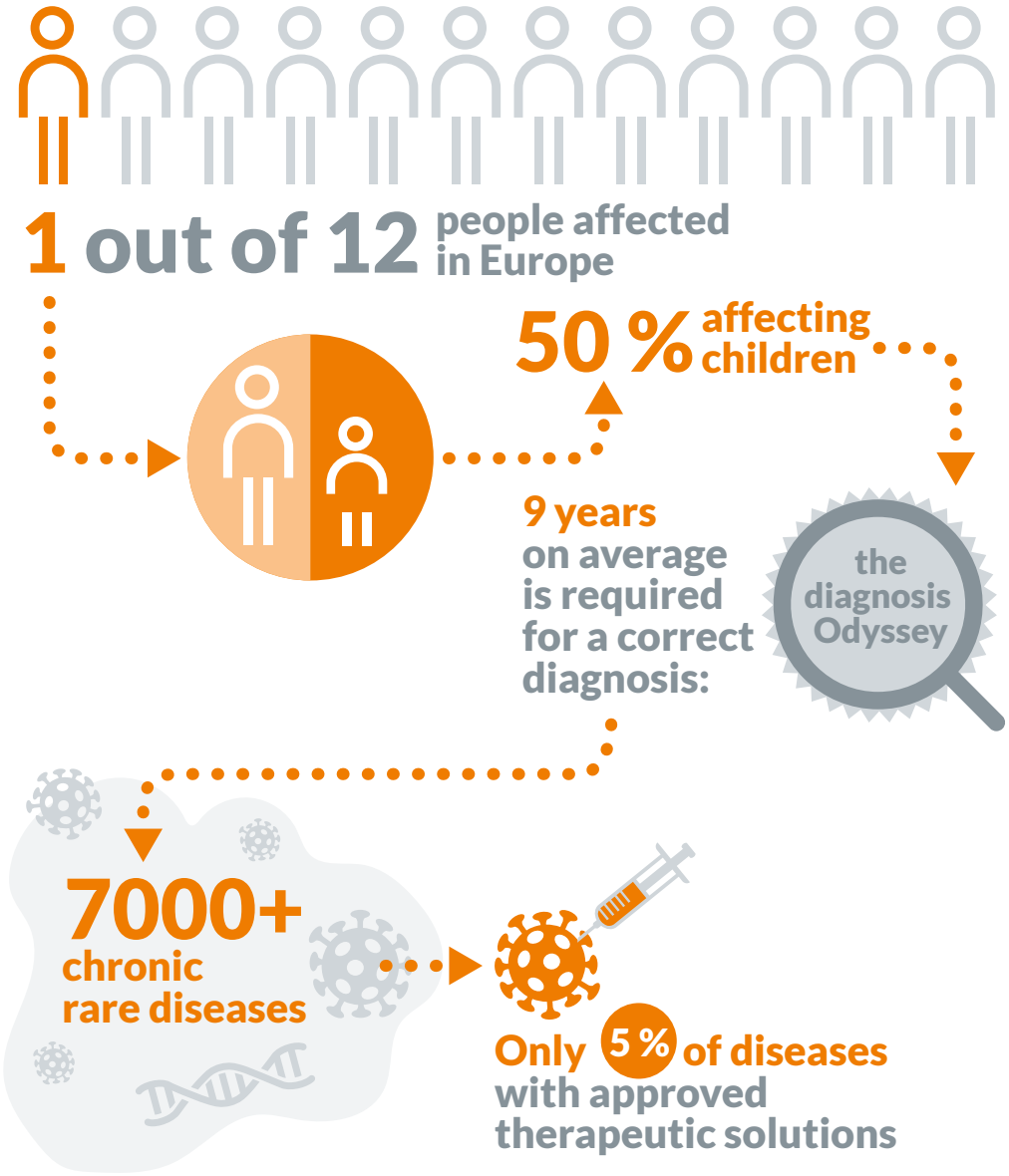
- Given the scarcity and fragmentation of medical expertise, patients are highly knowledgeable and have a strong influence on drug development
- Through support, research, fundraising and lobbying, they actively develop expert networks, manage disease related knowledge, engage in and support biomedical 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 centricity', 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 AFFECTING CHILDREN



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

Advancing rare disease treaments

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

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

DRUG DEVELOPMENT: A LONG, COMPLEX AND COSTLY PROCESS.

Developing new treatments is expensive, time-consuming and requires strong 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 $ and a time frame of ten to fifteen years to bring a drug to the market. Unfortunately, increased spending on drug R&D did not lead to an increase in the number of drug approvals.

INSUFFICIENT COORDINATED EFFORTS IN DRUG DEVELOPMENT FOR RARE DISEASES

Despite significant progress in scientific research and technologies, drug development remains inadequate to address critical medical needs in rare diseases. On one hand, therapeutic development is suffering from the heterogeneity and 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 somewhat reluctant to invest in these diseases for which commercial profit will be limited due to the small market size.

ESPERARE DISEASE FOCUS

EspeRare opted to concentrate most of its activities in rare paediatric diseases that represent nearly 50 % of rare diseases. Furthermore, given that EspeRare cannot develop the knowledge and network of experts required in thousands of diseases, the foundation has selected around thirty diseases on which first focusing its efforts. These diseases have been selected based on 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 text, etc.). ■

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

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:

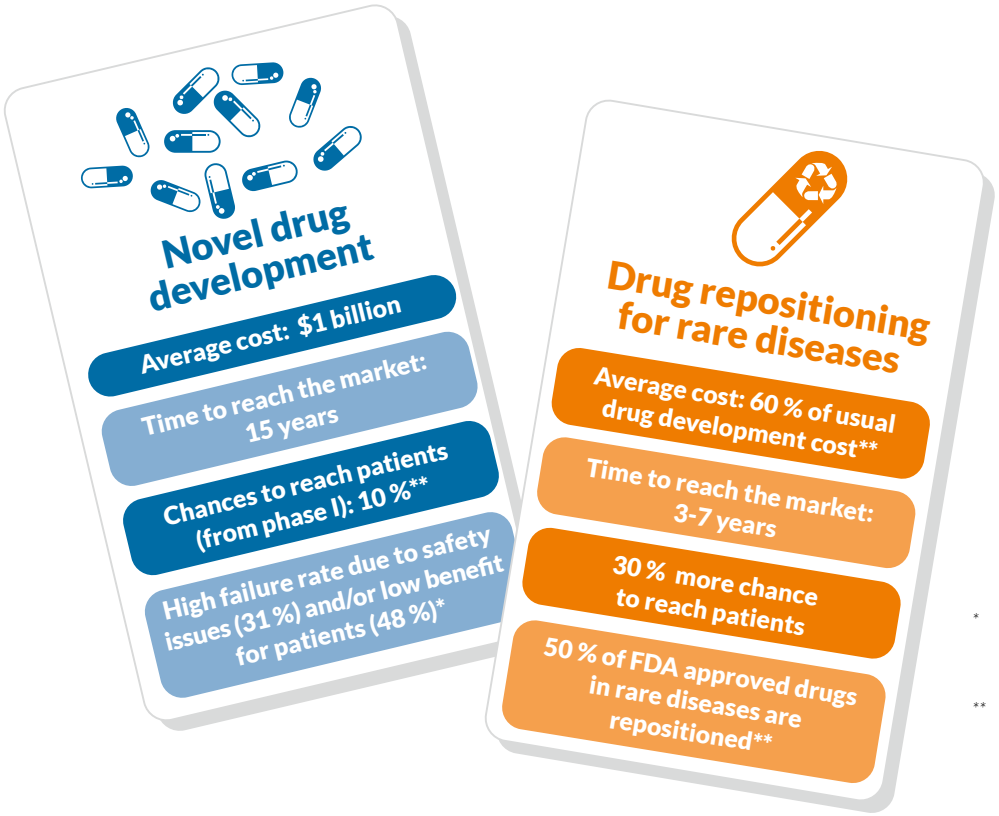
- Existing drugs are already known to exert a biological response in humans and this response may become beneficial for other health conditions.
- Many steps in the drug development process such as drug bioactivity and good safety profile in humans have already been demonstrated during the initial development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

Focused 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 medicines. **The foundation model allows the development of drug repositioning opportunities that remain economically attractive for commercial partners and beneficial for patients and the healthcare system at large.** ■

THE REPOSITIONING OF EXISTING 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 for rare disease drug development:

- **Faster, de-risked and cost contained approach to drug development***
- **Brings more affordable treatments & access to medicine to 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 the ability to translate research efforts often conducted in academia into robust drug development activities, traditionally managed by the biopharmaceutical companies.

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

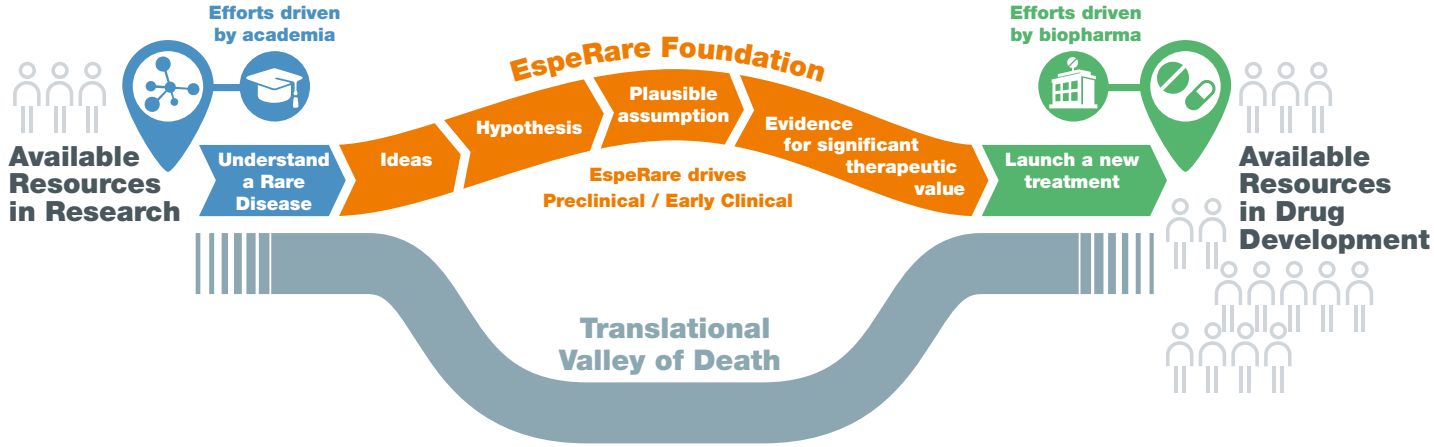
More specifically, EspeRare focuses on driving preclinical and early clinical development activities that are required to demonstrate the efficacy of the drugs under investigation. For each of its drug development programme, the foundation develops **Product Development Partnerships** that:

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

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 capacity to drive later stage clinical trials, registration and commercialisation.

At this point, 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 IMPACT: BRINGING TOGETHER PATIENTS AND COMMERCIAL INTEREST TO ADDRESS RARE DISEASES

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

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 ability to build a viable model allowing unexplored treatment to be developed. It applies all the ingredients of a comprehensive solution: pharmaceutical R&D and project management expertise, patient centricity and hybrid financing mechanisms to reduce R&D costs and timelines. 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. ■

Building our portfolio

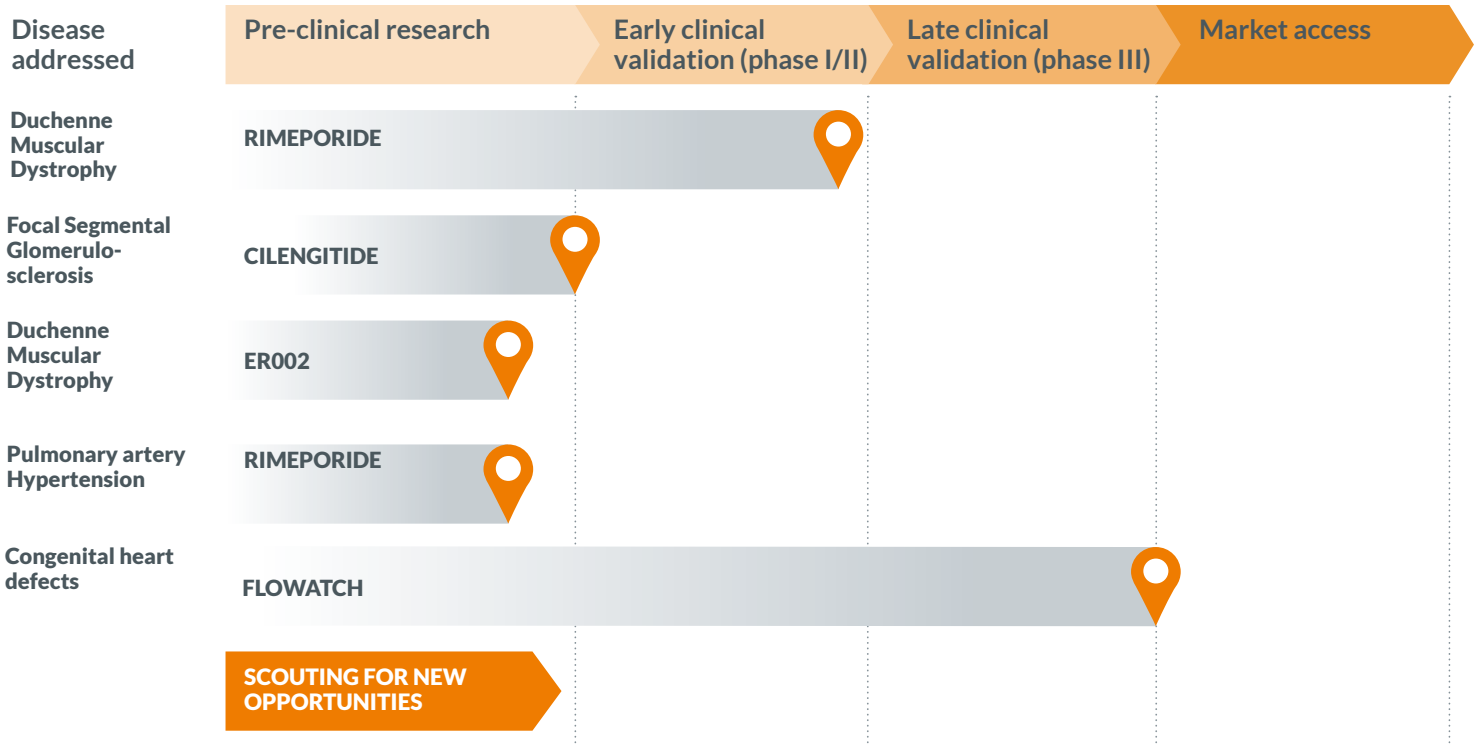
With its first programme in Duchenne muscular dystrophy, EspeRare has proven its ability to give a chance to **dormant therapeutic opportunities. After three and a half years, the foundation has now demonstrated the therapeutic potential of Rimeporide, a shelved drug that EspeRare is now testing in children affected by this debilitating disease** *(see pages 18-19)*. 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 conducting pre-clinical tests on another drug for Duchenne dystrophy *(see page 17)*, is developing another existing treatment in a rare renal disease *(see pages 20-21)*, and is re-launching an existing therapeutic device for infants affected by severe cardiac defects *(pages 22-23)*.

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 academic and biopharmaceutical companies to 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 PROPRIETY PLATFORM FOR THE IDENTIFICATION OF DRUGS TO BE RESCUED OR REPOSITIONNED IN RARE DISEASES

An *in silico* approach enables EspeRare to discover novel therapeutic opportunities for existing drugs. EspeRare is currently 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 disease(s) 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 wise selection of existing de-risked drugs within its *Treatment database* and identification of new disease applications using the *Rare disease analytics system*, our Drug Repositioning platform enables EspeRare to rescue drugs or to uncover repositioning opportunities with strong therapeutic potential for rare diseases.

A first version of the Drug Repositioning platform was launched in March 2014. The capability of the platform is being enhanced and 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 enhancement. ■

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 the 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.

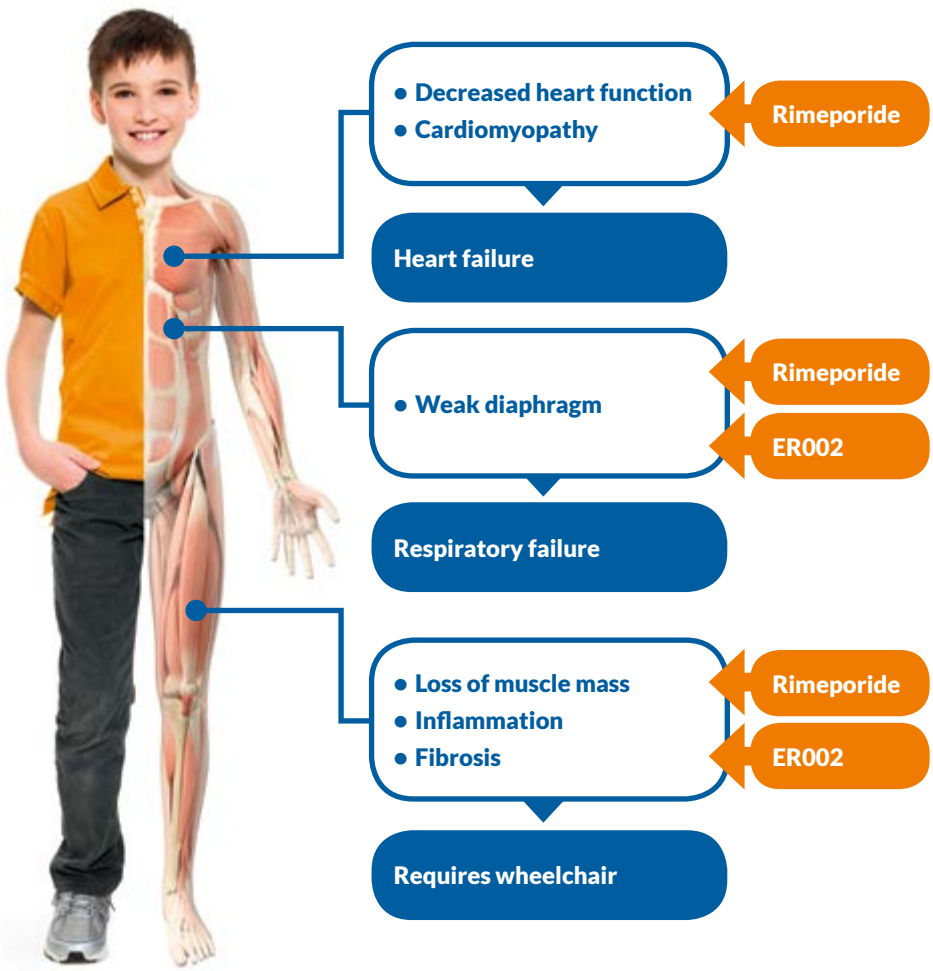
Patients affected by DMD have progressive loss of muscle function and weakness in their early childhood. This progressive muscle wasting typically leads to loss of ambulation around 10 years of age. It eventually spreads to the arms, neck and other areas. Later in the twenties, this progresses to complete paralysis and increasing difficulty in breathing due to respiratory muscle dysfunction requiring ventilator support as well as cardiac muscle dysfunction leading to heart failure.

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 still a critical need for new therapies to halt the progression of the disease and in particular the life-threatening cardiomyopathy for all Duchenne boys.

This year, EspeRare entered the clinic with its first DMD programme, Rimeporide in DMD.

Building on its experience, network and support in the DMD field, EspeRare also initiated a new development programme that aims to validate the re-positioning of a new molecule, ER002, into DMD.

It is EspeRare's hope that these 2 distinct approaches can play some role in the therapeutic solution to this debilitating disease. ■



ER002 PROGRAMME IN DUCHENNE MUSCULAR DYTROPHY (DMD)

ER002 is a clinically tested safe and selective oral molecule that has previously been tested in fibrotic diseases such idiopathic pulmonary fibrosis.

ER002 represents a novel therapeutic opportunity that may act on the fibrotic and inflammatory processes in Duchenne, thus delaying muscle damage in complement to treatments targeting the lack of dystrophin.

BACKGROUND

2015

Development of ER002 in all indications discontinued.

2016

EspeRare initiated the development of ER002 in DMD. Thanks to funding from Duchenne UK and through a collaboration established with Prof. Dominic Wells (Royal Veterinary College, London, UK), proof of concept studies in mdx mice were started. This preclinical work is looking at the scientific rationale to "re-position" the compound as a treatment for DMD. Using the well-established mdx mouse model, Prof. Wells and his team are investigating whether ER002's established anti-inflammatory and anti-fibrotic properties translate into a protective muscular effect on a panel of muscles in mdx mice.

2017 and beyond

If the proof of concept in mdx mice shows promise, both EspeRare and Duchenne UK have committed to taking ER002 straight to a Phase II Proof of Concept study in DMD patients.

EspeRare hopes that this new project will provide a new treatment avenue to this debilitating disease, to be used in combination with molecules that are targeting the lack of dystrophin. ■

ER002 IDENTITY CARD:

Name:
ER002
Target:
Fibrosis and inflammation pathways
Originator:
Merck Serono
Indications:
DMD (active development by EspeRare), idiopathic pulmonary fibrosis and endometriosis (inactive development)
Drug development phase:
Several animal studies in models of fibrosis and inflammation. Administered in several phase I and II clinical trials.Pre-clinical proof of concept studies alone and in combination with Rimeporide ongoing in mdx mice.
Opportunity: Clinically relevant anti-inflammatory and anti-fibrotic properties established in several animal models. Demonstrated safety and tolerability in human. Could be used in combination with other therapies in all patients with DMD, regardless of the causative genetic mutation.

A NEW DMD PROJECT BUILDING ON ESPERARE'S GROWING NETWORK AND EXPERIENCE IN THE NEUROMUSCULAR DISEASE FIELD

R&D funding: Duchenne UK funds the nonclinical studies in mdx mice.

Continuing support from patients associations: Duchenne UK

Strategic partnership with academic centres of excellence: Prof. Wells, Royal Veterinary College, London (UK)

RIMEPORIDE PROGRAMME IN DUCHENNE MUSCULAR DYTROPHY (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 Duchenne mice model (mdx mice).

2015

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

2016

- **Initiation of a phase Ib clinical trial of Rimeporide in young boys with DMD.** Leading European neuro-pediatricians have enrolled 11 patients with DMD in several clinical sites in France (Armand Trousseau Hospital/ I-motion, Paris), in the UK (Great Ormond Street Hospital, London), in Spain (Santa Creu i Sant Pau Hospital, Barcelona) and in Italy (the San Raffaele Hospital, Milan).

The aim of this clinical study is to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of multiple ascending oral doses of rimeporide in DMD patients. Four cohorts of five patients, aged 6-14 years, will be studied sequentially. In each cohort patients receive a fixed dose of Rimeporide given orally for 28 days according to their weight. Cohorts are studied in ascending order, dosing in the next cohort being started only after safety has been deemed satisfactory at the preceding dose level by an independent Safety Monitoring Committee
So far, no pattern of adverse events querying the safety of Rimeporide has occurred. This clinical study will be completed by mid-2017 and discussions are underway with experts in the field to design the next phase II clinical trial.

- **Initiation of a pre-clinical study in a dog model lacking dystrophin,** Golden Retriever Muscular Dystrophic (GRMD) dogs, by Prof. Stephane Blot's team at the Ecole Nationale Vétérinaire in Maisons-Alfort (France). This study is in part financed by the AFM Téléthon (France). It aims to further substantiate Rimeporide's mode of action and support the design the phase II clinical trial.

- **Translational biomarker study.** EspeRare filed a funding application to conduct a biomarker study on samples from both patients enrolled in the clinical trial and from the GRMD dogs.

Partnering discussions with several pharmaceutical companies have been initiated with the aim to provide drug development continuity at the end of the phase Ib study. EspeRare is seeking a partner to be responsible for the late stage clinical development, registration and commercialisation of Rimeporide.

Beyond 2017

Late stage clinical development of Rimeporide will be conducted by a partner who has the adequate infrastructure to conduct worldwide trials, manufacturing and commercialisation. Along the development path, EspeRare will strive to ensure that patients who are expected to benefit from the medication will retain access to it. According to our current development plans, Rimeporide aims to be marketed by 2020-2021. ■

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 of DMD, alone or in combination with other available treatments. In particular, Rimeporide has the potential to address the fatal cardiomyopathy in Duchenne, which is at present a progressive condition with very limited therapeutic options. To our knowledge, Rimeporide is one of the few clinical stage therapies intended to reduce inflammation and fibrosis both in skeletal muscles and in the heart.

RIMEPORIDE IDENTITY CARD:

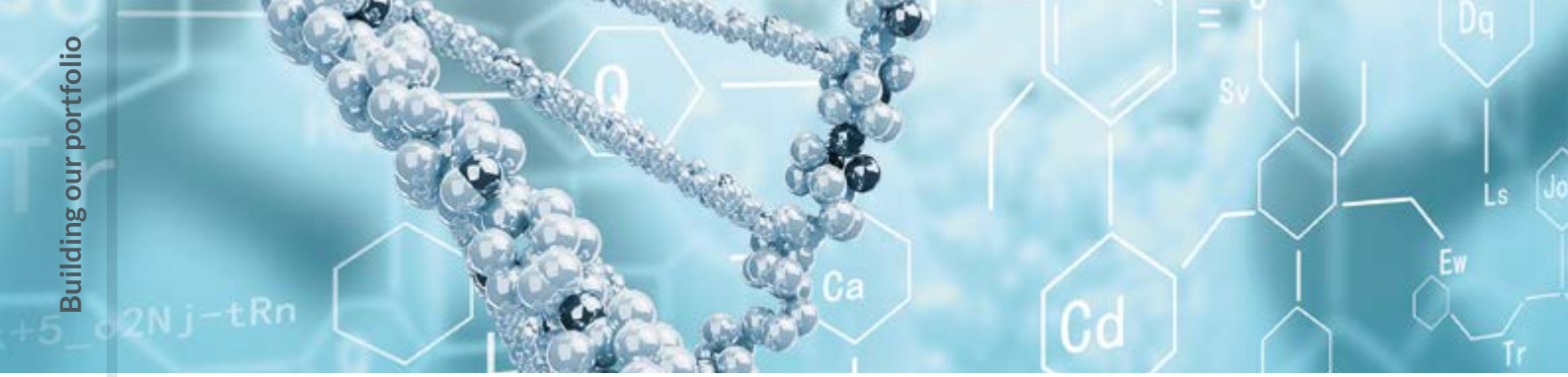
Name: Rimeporide
Target: Sodium-Proton Exchanger protein (NHE-1)
Originator: Merck Serono
Indications: Duchenne Muscular Dystrophy (DMD, active development by EspeRare) and Chronic Heart Failure (CHF, inactive development)
Drug development phase:
Administered to more than 150 healthy and CHF adults (7 phase I trials).
Robust data package in DMD animal model (mdx mice)
Phase Ib clinical trial in children with DMD underway
Study in dystrophic dogs initiated.
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: TREAT DMD ADVISORY COMMITTEE

R&D funding: French Telethon (AFM) & Swiss Technology & Innovation (CTI) supports ongoing research in non clinical studies and Merck Serono is supporting 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), the Santa Creu i Sant Pau Hospital (Barcelona, Spain) and the San Raffaele Hospital (Milan, Italy).

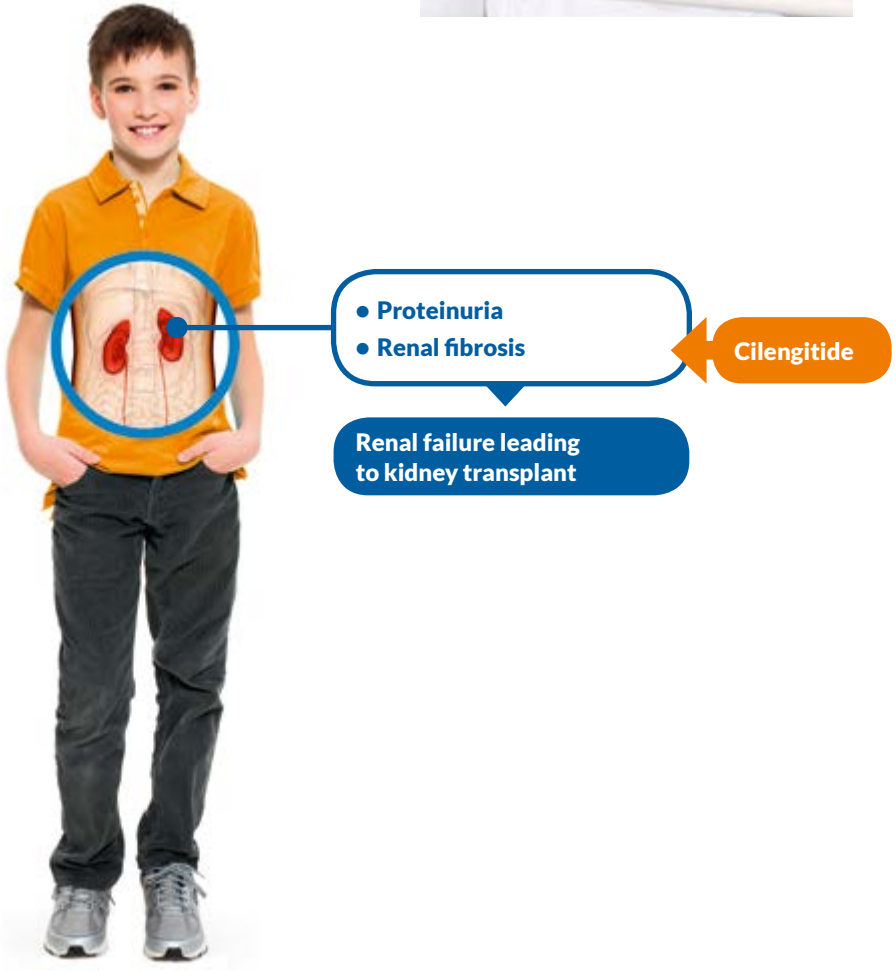


Focal Segmental Glomerulosclerosis (FSGS)

ABOUT FOCAL SEGMENTAL GLOMERULOSCLEROSIS

Focal Segmental Glomerulosclerosis (FSGS) is a rare kidney disease with an incidence of 7 per million. 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 throw filtering units called glomeruli, some of its components are filtered out to make urine. Focal segmental glomerulosclerosis is a disease that results in impaired renal function due to injury and scarring of the glomeruli. To act as efficient filters, glomeruli need an intact physical filtration barrier, which is made up of tightly associated specialized 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 αvβ3 integrin, is crucial for 'gluing' the podocytes to the glomeruli structure. Disregulation in αvβ3 integrin pathway could lead to the dysfunction of the glumeruli filtration. 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 are essentially aimed at controlling the symptoms of the disease and are often inadequate and toxic. FSGS is a lifelong chronic disease and the disease burden to 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. ■



CILENGITIDE PROGRAMME IN FOCAL SEGMENTAL GLOMERULOSCEROSIS (FSGS)

Cilengitide is a safe, potent and selectiveαvβ3 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.

Cilengitide 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 cilengitide in FSGS.

2014

EspeRare started working on the repositioning opportunity for cilengitide in FSGS. A non-clinical study was initiated with Prof. Moin Saleem's team, a nephrology and FSGS-specialized 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 cilengitide in FSGS. Cilengitide was found to be non-toxic to podocytes and to reduce the FSGS-induced αvβ3 integrin activation. This effect has the potential to translate into the clinic as an improvement of renal function for FSGS patients.

2016

As the potential therapeutic benefit in FSGS of Cilengitide was now established, EspeRare has sought to build up its network of international advisors with the objective of identifying a clear and consensual clinical path for Cilengitide in FSGS. One such newly established 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. Dr Lennon is currently leading a study to establish whether αvβ3 integrin activation can be identified in biopsies from patients diagnosed with FSGS. This is the first step towards establishing a stratification strategy, to select patients for whom the αvβ3 integrin pathway is activated.

> " 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 and beyond

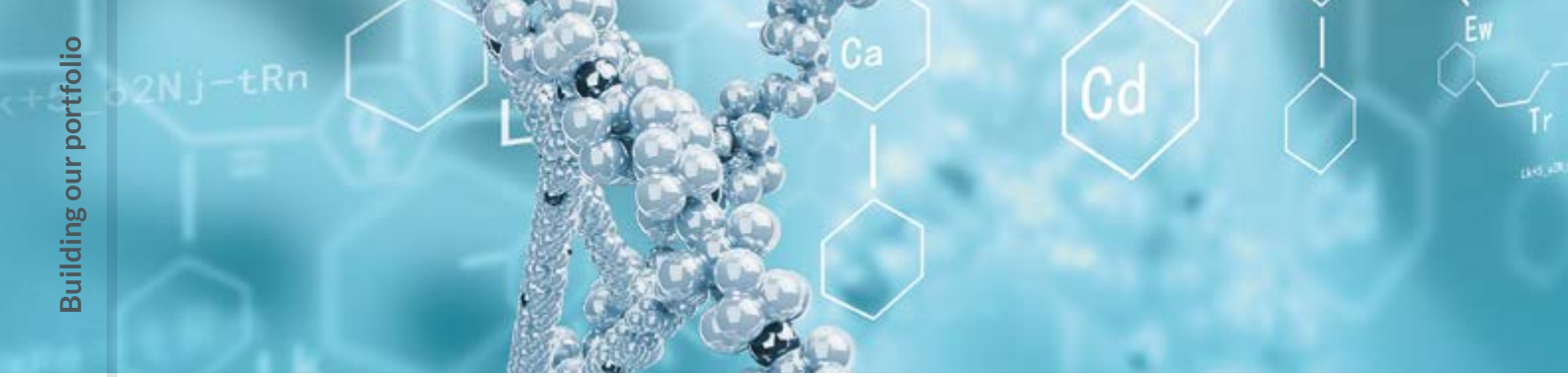
Once a patient stratification method is established, it will need confirmation on a bigger patient cohort. EspeRare will then seek to engage FSGS clinical experts worldwide to design a Proof of Concept clinical trial to use Cilengitide in FSGS patients that present over-activated αvβ3 integrins. ■

CILENGITIDE IDENTITY CARD:

Name:	Cilengitide
Target:	αvβ3 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 αvβ3 integrins, a protein whose inappropriate activation is thought to play a major part in the progression of FSGS

A WORLDWIDE NETWORK OF DISEASE EXPERTS TO ADVISE AND STRENGTHEN CILENGITIDE'S CLINICAL DEVELOPMENT STRATEGY

Strategic partnership with clinical centres of excellence: Key Opinions Leaders Profs. Gipson and Kretzler (University of Michigan and NEPTUNE study, USA), and Dr Lennon (Manchester, UK); on-going collaboration with Prof. Saleem (University of Bristol, FSGS patient registry, UK), European Nephrotic Syndrome Consortium, CoNeCon.



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 light to severe. In 5 % of all cases, the severity of 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 is not an option and a palliative and temporary procedure is elected instead.

One such common palliative procedure is known as Pulmonary Artery Banding (PAB) and is currently used in the USA and Europe in about 1000 cases per 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 protects the heart and lungs' functions of the babies. 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-PAB device for newborns affected by severe cardiac defects. This previously marketed therapeutic device has proven its medical abilitiy to 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-engine inspired by Swiss watchmakers with a remote control system developed at ETH Zurich (Switzerland). EspeRare is relaunching the quality, regulatory and manufacturing processes in order to seek the European market authorization by 2018.

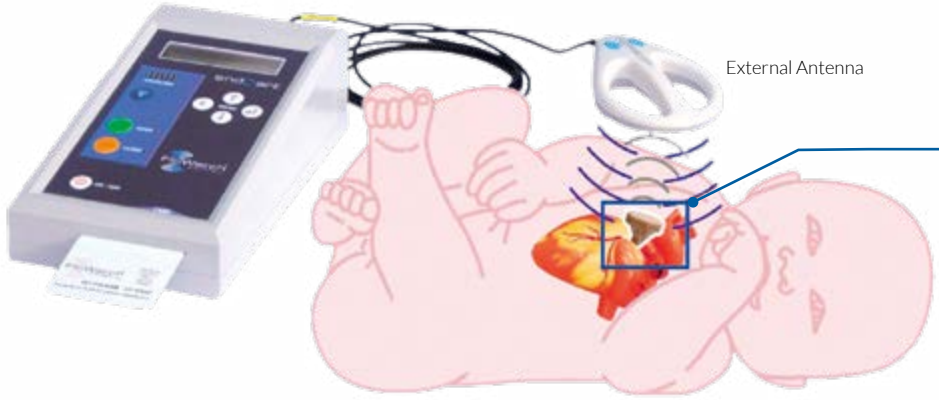
Over the next 3-4 years, EspeRare wishes to produce and distribute the first 150-200 units. Fulfilling EspeRare's not-for-profit goals, part of the FloWatch devices produced will be distributed in Africa and in Asia. In these regions, only a small number of newborns have access to the heart repair surgery 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, so that long stays in intensive care and further operations to re-adjust the band tightness are sometimes required. This situation is traumatic to newborn babies and their parents and results in increased mortality and morbidity. This problem is even more acute in developing countries where surgery and post-operative care are often basic at best. FloWatch is a remotely adjustable PAB medical device. The technology comprises an implant coupled to an external control unit; the latter allows the remote control and regulation of the blood pressure post-implantation without having to physically access the device, resulting 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 2015. ■

FloWatch® -Control Unit



FloWatch® -PAB implant on the pulmnary artery

BENEFITS OF THE FLOWATCH

TECHNICAL INNOVATION

- Electro-mechanical implant with a biocompatible encapsulation
- Wireless control, no batteries required
- Unique technology able to perform a precise mechanical adjustment inside the body

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

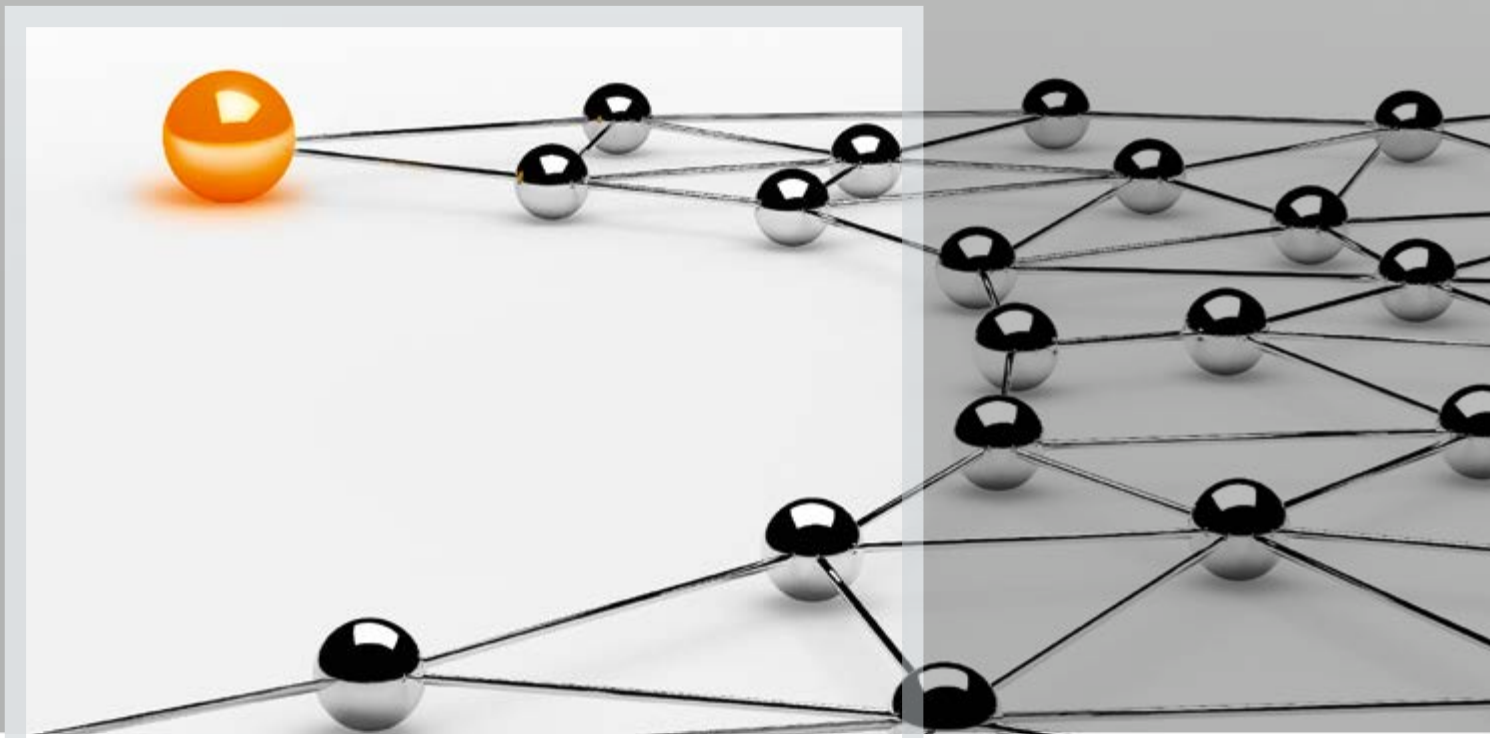
- 30 % less mortality
- 70 % reduction in hospital stay
- Reduction in overall medical costs

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

> "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-PAB
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. A 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.



Organisation

The Board and the Executive Committee 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 Head office, 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. In the start-up phase, the Executive Director and the R&D Director manage a number of employees, part-time consultants and volunteers to deliver on EspeRare's objectives.

During 2016, 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

MONIQUE A. CAILLAT

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 interest 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. As Board Member, Monique is the General Counsel of the foundation.

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.

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 personalized medicine initiative, a member of the board of Telethon-Italy and an Ashoka Fellow. Sharon links EspeRare with patients organisations and orphan disease advocacy.

Monique A. Caillat

Béatrice Greco

Peter Potter-Lesage

Ewen Sedman

Sharon F. Terry - President

HEAD OFFICE

Caroline Kant

Florence Porte-Thomé

CAROLINE KANT

Founder & Executive Director

Caroline leads the operations as well as develops and implements the foundation's strategic plans in concert with the Board and the R&D Director. She has co-founded EspeRare and represents the executive committee on EspeRare's board.

Before establishing EspeRare in 2013, Caroline has built an IT start-up in Silicon Valley and had a career within the pharmaceutical industry, including building the knowledge management capability within the R&D department at Merck Serono. She is also advising the Red Cross and the United Nations to find ways to apply venture philanthropy to health challenges. Caroline was educated in Geneva and the US and holds degrees in neurobiology and product development, she is an ASHOKA fellow and was appointed Swiss women entrepreneur of the year in 2015.

By establishing the EspeRare foundation, Caroline realised her dream of dedicating herself to address rare diseases in honour of her daughter, and for all children suffering from orphan diseases.

FLORENCE PORTE-THOMÉ

Founder & R&D Director

Florence 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 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. Recently returning to academia, she led pediatric studies in a Cancer Research Centre in Lyon. Florence holds degrees in clinical pharmacology and immunology.

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.

"Fostering access to health for patients that are the most in need is what this foundation is about, and is what I am about."

Beatrice Greco
Founder and member of the Board

TEAM

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 organizations for various humanitarian causes to help creating a better world. At EspeRare, Sarah links ledger accounting to reporting and auditing activities.

PIERRE FRIDEZ

Pierre graduated from EPFL with a physics doctorate and has vast experience in Medical Devices. In particular he was project leader on the FloWatch device during its initial development in the startup EndoArt. Pierre is Medical Device Director at EspeRare for the FloWatch project.

JULIAN GRAY

Julian has 25 years of experience in clinical development in the CNS area within the pharmaceutical industry, including drug development in Duchenne muscular dystrophy. Julian is the Medical Responsible for the Duchenne programme and subsequent programmes in neuromuscular diseases.

HANANE GHEIT

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

AGNÈS JAULENT

Agnès studied for her PhD in chemistry at Imperial College London. She is an expert in all fields pertaining to peptide chemistry. Agnès brings this experience to EspeRare as a project manager.

DENIS KLOPFENSTEIN

Denis started off his career as an electronics and embedded software engineer. He moved on to the Medical Devices industry, where he held key positions in R&D for over 20 years. Denis brings to EspeRare's Medical Devices team his expertise in the industrialization of medical devices, regulatory affairs and product certification.

GWENAËLLE LAPORTE

Gwenaëlle has several years of experience in commercial support and marketing in various industries and as a project management officer. With her broad experience, she brings a diversified support to EspeRare's executive team.

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. Cédric applies bioinformatics and data management expertise to support the development of the foundation's Translational Platform.

SYLVIE RYCKEBUSCH

Sylvie 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. For EspeRare, Sylvie is acting as the Chief Business Officer, providing business development and licensing support to EspeRare.

ACHIM SCHAEFFLER

Achim has more than 20 years experience in the field of Chemistry, Manufacturing and Controls with the Pharmaceutical Industry. Achim brings this solid expertise of drug manufacturing processes to support EspeRare's drug development programmes.

DUC TRAN

Duc brings 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. GHASSAN BKAILY

Prof. Bkaily, Ph.D., is a Professor at the Faculty of Medicine of Sherbrooke University, conducting research on biochemical processes in the cardiovascular system. He has held several important positions, including Chairman of the Department of Anatomy and Cell Biology and Director of the CIHR Group in Cardiovascular Interactions. He provides EspeRare expertise on the mechanism of action of Rimeporide in cardiomyopathy.

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. DENIS DUBOC

Prof. Duboc is a cardiologist at Cochin Hospital (Paris) with expertise in managing Duchenne patients. He is a scientific advisory member for the Comité d'Energie Atomique (CEA, France), and for ORPHANET. He was previously vice-president of the Universté Descartes in Paris and board member of the French Society of Cardiology. He is part of EspeRare's scientific advisory board and member of the Safety Committee Board for the on-going clinical Duchenne project.

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. ANTOINE HADENGUE

Prof. Hadengue is a Professor of Gastroenterology and Hepatology, at the University Hospitals of Geneva, Switzerland. Since 1994, he manages clinical activities, research and medical practice. In 2001, he was nominated Head of the Division of Gastroenterology and Hepatology, Department of Internal Medicine, at the University Hospitals of Geneva. He provides his clinical expertise to support EspeRare drug development in metabolic diseases.

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 KASSAÏ-KOUPAÏ

Prof. Kassaï-Koupaï 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.

PROF. JIRI MAREDA

Prof. Mareda obtained a PhD in physical organic chemistry at the University of Geneva. He then worked as research associate at the university of Pittsburgh, where he fully specialized 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 a 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.

DR. 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. 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 Cilengitide.

DR. PAN SALVARIDIS

Mr. Salvaridis holds an electrical/electronics engineering degree and post-graduate degrees in biomedical electronics and nuclear engineering. He has over 45 years of experience in R&D and Production of medical equipment, senior management in multinational corporations, distribution, outsourcing and organizational performance. He supports EspeRare's Medical Device program.

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.

PROF. NICOLAS J.C. SIMON

Prof. Simon, MD, PhD, is Professor and Chairman of the Department of Pharmacology at Aix-Marseille University, Director of the Clinical Pharmaco-Toxicology Unit and Addiction medicine specialist at Saint Marguerite Hospital, Marseille, France. He brings his expertise in pharmacokinetics and in the modeling of translational data to better optimise EspeRare's drug development strategy.

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 Centre 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.

DR. ERIC TEILLAUD

Dr. Teillaud is a doctor in Pharmacy with 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 his experience in Quality and Chemistry, Manufacturing and Control to support and advice EspeRare on the development of clinical projects.

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.

MR. DENIS MORTIER

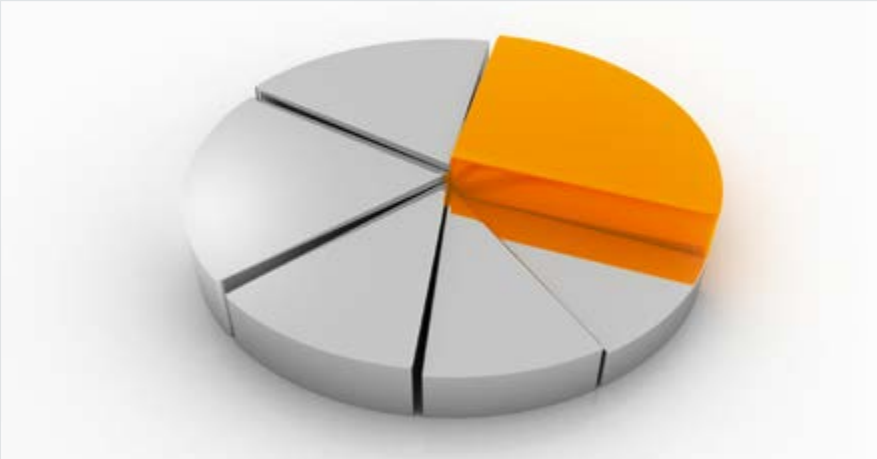
Mr. Mortier has served, among others, as partner of Coller Capital Ltd and on the Executive Committees of the Atomic Energy Commission (CEA) of France and of Credit National. He was the Founding CEO of CEA Industry and of Financière Saint Dominique. He also served on Advisory Boards and Investment Committees for multiple Venture Capital funds. He is chairing EspeRare's Business advisory committee.

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 advices EspeRare in Intellectual Propriety and Business Development topics.

"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 Duchenne."

Florence Porte-Thomé
Founder and R&D Director



Financial view

EspeRare receives funding from project partners, patient associations, private foundations and international governmental and public bodies. These funds are used to finance the EspeRare diverse activity portfolio geared to accelerating the cost-effective development of unexplored therapeutic opportunities for rare neurological, cardiovascular 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 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 3 employees, and 13 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 act as external auditors.

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 2016

The year was characterised by a number of factors. Further considerable donations were received or confirmed for the future, staff were recruited, planning was activated and the portfolio was broadened and diversified. Most important of all, **Research & Development Project funding represented 88 % of total expenses and amounted to CHF 1,568,381** (note 8 a-f), a sizeable increase as compared to CHF 1,221,561 in 2015.

Significantly, due to Brexit in June 2015, the GBP-CHF exchange rate dropped from 1.475340 to 1.255857, which caused a partially realised exchange loss of CHF 19,000.64. On the other hand, EUR-CHF and USD-CHF exchange rates have occasioned minor exchange gains amounting to CHF 5,923.58. Exchange rates between the reception of invoices and payments fluctuate as well, causing a gain of CHF 512.72. The total foreign currency loss thus amounts to CHF 12,564 as opposed to 2015, where a EUR-CHF exchange loss of CHF 188,589 was mainly due to the Swiss National Bank's withdrawal of the minimum floor exchange rate between Swiss Francs and Euros.

Additionally the foundation incurred this year a minor excess of expenditure over income of CHF 46,861 which is mainly due to expenses incurred for higher-cost activities related to the clinical development of Rimeporide in Duchenne muscular dystrophy as well as the initiation of activities to re-introduce the FloWatch device to the market.

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 2016 amounted to CHF 1,727,518. R&D income came to CHF 1,225,344 including an amount of CHF 656,863 deferred from 2015 for the clinical activities of Rimeporide. A total of CHF 547,600 was received from Merck Serono in 2016 with CHF 273,800 recognised this year and a further CHF 273,800 being deferred to 2017 to finance the completion of the current clinical trial activities of Rimeporide in Duchenne muscular dystrophy. Also received in 2016, was a

contribution from AFM Telethon of CHF 155,075, CHF 77,538 being recognised in 2016 and CHF 77,538 deferred to finance the completion of the ongoing translational study with Rimeporide. A CHF 27,143 contribution from DPP Espana, a patient organisation based in Spain, was received to finance the enrolment of patients into the Rimeporide clinical trial at the Barcelona clinical site. Additionally, to support the Rimeporide program, two Swiss public grants, respectively of CHF 10,000 and CHF 8,000 were received. In 2016 a donation amounting to CHF 300,000 was also granted to finance the initiation of the FloWatch project by a private foundation based in Geneva. Another grant of CHF 66,924 from UK Duchenne, a patient organisation based in London, was also granted to initiate the development of ER-002, a new program in Duchenne Muscular dystrophy. From this donation, an off-balance sheet amount of CHF 33,462 was recognised as a direct payment to our research partner in the United Kingdom. Finally, Foundation Support income of CHF 500,000 was recognised from a Geneva Foundation (Note 7).

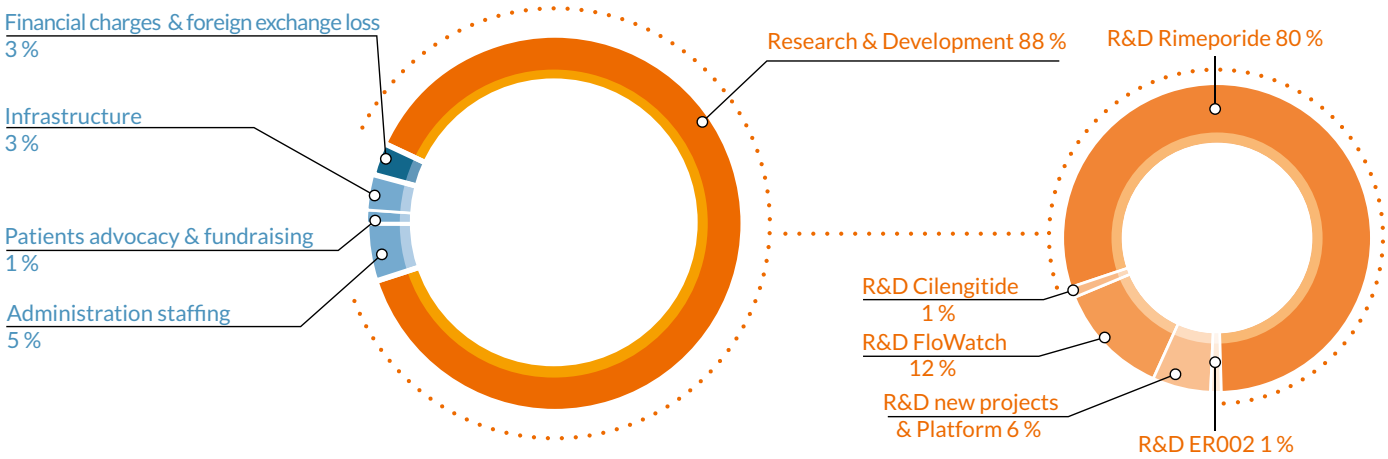
Staff

At year-end the senior management team consisted of a Chief Executive Officer, Chief Scientific Officer and a Senior Medical Device Director. Furthermore, EspeRare has a team of 3 Program Managers, 13 contractors and counts as well on the support of many other people including board members, senior scientific advisors and volunteers.

General Administration

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

SNAPSHOT OF ESPERARE EXPENDITURE 2016



THE FINANCIAL YEAR AHEAD TO DECEMBER 2017

EspeRare operates in a complex multi-currency environment in Geneva, Switzerland. The bulk of donations are currently received in Euros, although other currencies such as Swiss Francs 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 has been implemented and KPMG appointed as our auditors.

The philosophy underlining EspeRare 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, for future EspeRare rare disease Research and Development project funding are around CHF 2 million for 2017. By the beginning of 2018 it is expected that EspeRare's first programme 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 financing the "expensive" clinical development of its current portfolio and another new project that is under review and likely to start phase II clinical development in 2017. As the EspeRare portfolio of therapeutic programmes is maturing and moving into these later stages of development, the foundation's need for financial support is increasing. In the next two years additional income will be mobilised in alignment with the foundation's fundraising strategy and 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 fourth 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 2017-2018, 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 2016

	NOTES	2016	2015
ASSETS		**CHF**	CHF
Current Assets			
Petty Cash	2i	-	420
Bank accounts	2i	2 117 410	2 209 701
Receivables and Prepaid expenses			
Other receivables		22 642	-
Withholding Tax & VAT Receivable		4 004	8 322
Prepaid Expenses		1 189	-
TOTAL CURRENT ASSETS		**2 145 245**	**2 218 443**
Non-current assets			
Financial assets/Deposits		771	-
Computers & Equipment	2d	11 941	7 769
(less depreciation)		(8 089)	(6 956)
TOTAL NON-CURRENT ASSETS		**4 623**	**813**
TOTAL ASSETS		**2 149 868**	**2 219 256**
LIABILITIES			
Current Liabilities			
Trade Payables		12 563	125 097
Social Charges		5 973	2 353
Due VAT		-	11 600
Provisions	2f/9	38 967	26 400
Accruals	2g	215 261	42 315
Deferred Income	7	569 338	656 863
TOTAL CURRENT LIABILITIES		**842 102**	**864 628**
CAPITAL & RESERVES			
Foundation Capital	10	50 000	50 000
Operations Reserve	3	1 304 627	1 766 385
Net excess of Expenditure of the year		(46 861)	(461 758)
TOTAL CAPITAL & RESERVES		**1 307 766**	**1 354 627**
TOTAL LIABILITIES AND CAPITAL		**2 149 868**	**2 219 255**

CASH FLOW AS AT 31 DECEMBER 2016

	2016	2015
OPERATING ACTIVITIES	**CHF**	CHF
Net excess of (Expenditure) / Income	(46 861)	(461 758)
+Depreciation	1 133	2 590
+decrease (-increase) in Prepaid and Receivables	(20 285)	6 219
+increase (-decrease) in Short term Liabilities	(120 514)	80 878
+increase (-decrease) in Provisions	12 567	(164 500)
+increase (-decrease) in Accruals	172 946	42 315
+increase (-decrease) in Deferred income	(87 525)	631 454
Cash from operating activities (operating cash flow)	**(88 539)**	**137 198**
INVESTING ACTIVITIES		
Outflows for purchase of tangible fixed assets	(4 172)	-
Cash inflow/drain from investing activities	**(4 172)**	**-**
Cash inflow/drain from financing activities	**-**	**-**
NET CASH	**(92 711)**	**137 197**
Cash and cash equivalents at begining of period	2 210 121	2 072 924
Cash and cash equivalents at end of period	2 117 410	2 210 121
NET CASH	**(92 711)**	**137 197**

ESPERARE STATEMENT OF INCOME & EXPENDITURE FOR THE PERIOD FROM JANUARY 1ST TO DECEMBER 31, 2016

	NOTES	2016	2015
INCOME		**CHF**	**CHF**
Donations Received for R&D	2b/7a	1 225 343	804 698
Financial Income	2k	-	2 134
Other Income		502 175	329 991
TOTAL INCOME		**1 727 518**	**1 136 823**
EXPENDITURE			
Research & Development Expenditure	2e		
R &D Projects			
Rimeporide	8a		
Research & Development			
Support Costs	8b	878 291	695 136
Rimeporide Support Costs	8g	369 752	398 334
TOTAL R&D PROJECTS, RIMEPORIDE		**1 248 043**	**1 093 470**
NEW PROJECTS	8c		
Repositioning Platform	8d	3 624	-
Repositioning Support Costs	8h	58 144	80 381
Cilengitide	8e	-2 675	32 255
Cilengitide Support Costs	8h	17 896	15 455
New prospects- pre project		28 771	-
New prospects Support Costs	8h	12 433	-
JNK Support Costs	8h	17 120	-
Flowatch	8f	96 182	-
Flowatch Support Costs	8h	88 843	-
TOTAL NEW PROJECTS		**320 338**	**128 091**
TOTAL RESEARCH & DEVELOPMENT EXPENDITURE		**1 568 381**	**1 221 561**
GENERAL FOUNDATION ADMINISTRATION	8d		
Administration staffing & volunteers	8g	94 806	97 623
Patient Association Consultancy		975	335
Office Rental & Costs		23 612	14 053
Accounting & Audit Expenses		36 176	26 755
Other Expenses		5 028	5 071
General Legal Fees		-	2 322
Fundraising		12 047	31 707
Financial Charges		3 228	2 733
Exchange Differences	2c	12 564	188 589
Board meeting		8 750	5 242
Depreciation		1 133	2 590
Duties and Taxes		7 679	-
TOTAL GENERAL ADMINISTRATION EXPENDITURE		**205 998**	**377 020**
TOTAL EXPENDITURE		**1 774 379**	**1 598 581**
NET EXCESS OF EXPENDITURE OF THE YEAR	3	**-46 861**	**-461 758**

NOTES TO FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2016

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 organizations, 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.

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

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

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

a) Accounting principles

The accounting principles followed are those of the Swiss Code of Obligations, articles 957 to 960e.

b) Recognition of donations

Contributions from donors (both public, private and philanthropic sources) are recognised in the financial statements on accruals basis 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 1.072000

1 USD = CHF 1.016354

1 GBP = CHF 1.255857

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 5 years
- fixtures and installations 3 years
- computers and equipment 3 years

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 for 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

Accruals are recognised in the balance sheet when EspeRare has a fair certitude of the outflow of economic benefits that will be required to settle the expense.

h) Employee Benefits - Pension Plan

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

i) Cash and Cash Equivalents

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

j) Impairment

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

k) Financial Income

Interest income is recognized in the income statement as earned.

l) Income Tax

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

3. RESERVES

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.

Due to Brexit GBP-CHF exchange rate dropped from 1.475340 to 1.255857, this drop caused a loss of CHF 19,000.64. While EUR-CHF and USD-CHF exchange rates have caused a minor gain of CHF 5,923.58. Exchange rates between the reception of invoices and payments fluctuate as well, causing a gain of CHF 512.72. Total exchange rate loss is CHF 12,564.34

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 2016 does not differ from their carrying amounts shown in the balance sheet.

5. COMMITMENTS

As at 31 December 2016, there were no significant capital expenditure commitments.

6. SUBSEQUENT EVENTS

No events occurred subsequent to 31 December 2016 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 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 recognized 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 recognized 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 platfrom starts in January 2017

b) As a comparison during 2015 the following donations were granted:

Donor	Currency	Total Grant	Received 2015 CHF	Recognised 2015 CHF	Deferred 2016 CHF	Notes
R&D Income						
ARES Trading SA (Merck Serono Affiliate) *	EUR	1 200 000	1 285 560	628 697	656 863	I&E Statement - Rimeporide
ARES Trading SA (Merck Serono Affiliate)**	EUR	20 889	25 409	25 409		I&E Statement - Cilengitide
AFM telethon	EUR	143 231	150 592	150 592		Grant Rimeporide fully committed in 2015
Sub-total		**1 364 120**	**1 461 561**	**804 698**	**656 863**	**R&D Income**
Awards & Foundation Support						
Fondation Tell & Un tel	CHF	10 000	10 000	10 000		
Geneva Foundation	CHF	300 000	300 000	300 000		For foundation Scale-up
Miscellaneous	CHF		22 125	22 125		
Sub-total		**310 000**	**332 125**	**332 125**	**0**	**Awards & Support**
TOTAL			**1 793 686**	**1 136 823**	**656 863**	**Awards & Support**

* Out of a total of CHF 1,285,560 received from AERES Trading SA to co-finance the rimeporide clinical trial in Duchenne, CHF 628,697 was recognized in 2015 to fund the production of Rimeporide and preparatory activities for the trial, CHF 656,863 are deferred to 2016 and will fund clinical trial activities for rimeporide.

** R&D income of CHF 25,409,1 for Cilenditide was recieved from ARES Trading SA in 2014 and recognized in our accounts in 2015

8. EXPENSES

a) Principal current R&D projects in rare diseases.
b) Development of Rimeporide in Duchenne muscular dystrophy.
c) Prospection & generation of new drug development opportunities for rare diseases.
d) Repositioning platform development to support the systematic discovery and evaluation of new projects.
e) Development of Cilengitide in Focal Segmental Glomerulosclerosis in partnership with Merck KGaA.
f) Reintroduction on the market of the FloWatch medical device for infants with cardiac defects.
g) General Foundation expenses in overall support of R&D activities.
h) Staff and travel costs recorded and allocated to the specific activities. The staff headcount represented three senior managers and three R&D program managers. In addition, EspeRare benefits from a number of consultants and volunteers. Total staff benefits for 2016 amount to CHF 658,993.57 (Salaries & Social charges amount to CHF 618,814.20, Travel Expenses amount to CHF 38,852.82 and Volunteers reimbursements amount to CHF 1,326.55). The allocation of salaries & social charges to the four R&D projects, repositioning platform and to the Foundation General Administration according to the percentage of the time spent by employee on the six activities.
i) All legal fees/advice for contract negotiation and finalization related to the Rimeporide project.

9. PROVISIONS

During 2015 the following provisions were incurred and other were carried over from past years:

Provisions	2016 CHF	2015 CHF
Rent 2013	7 200	7 200
Rent 2014	9 600	9 600
Rent 2015	9 600	600
Rent 2016 + Moved to new facilities	12 567	0
TOTAL	**38 967**	**24 400**

As per 'Eclosion Incubation Contract' = 20m^3 at CHF 500.– per month + CHF 300.– monthly infrastructure charge.

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 a potential liability that may occure, depending on the outcome of an uncertain future event. This 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 60 hours were incurred, representing a total of CHF 19,440.

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.

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

P.O. Box 347
CH-1211 Geneva 13

Telephone +41 58 249 25 15
Fax +41 58 249 25 13
www.kpmg.ch

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 as disclosed in pages 32 to 36 for the year ended 31 December 2016.

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, 27 March 2017

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

How can I support EspeRare?

EspeRare is a foundation recognized 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**, which allows Europe-an 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 fits 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

ASHOKA

Making more health
by Ashoka and Boehringer Ingelheim

G21

CTI – Start-up et entrepreneuriat, Promotion R&D, Soutien TST

HEALTH VALLEY
SWITZERLAND

DUCHENNE UK

AFMTÉLÉTHON
INNOVER POUR GUERIR

ALTR DOMANI - Onlus

Duchenne Parent Project
ESPAÑA

Children's National

MMV
Medicines for Malaria Venture

McKinsey&Company

cost
EUROPEAN COOPERATION
IN SCIENCE AND TECHNOLOGY

FONDATION Eclosion
Sciences de la Vie

EnvA
École nationale vétérinaire d'Alfort

Genetic Alliance

INSTITUT DE MYOLOGIE
INNOVER POUR GUERIR

HOSPITAL DE LA SANTA CREU I SANT PAU
UNIVERSITAT AUTÒNOMA DE BARCELONA

Avec le soutien de la
Loterie Romande

COMITÉ INTERNATIONAL GENÈVE
ICRC

ACTION DUCHENNE

MERCK

Microsoft

SIB
Swiss Institute of Bioinformatics

NATIONAL INSTITUTES OF HEALTH

TREAT-NMD
Neuromuscular Network

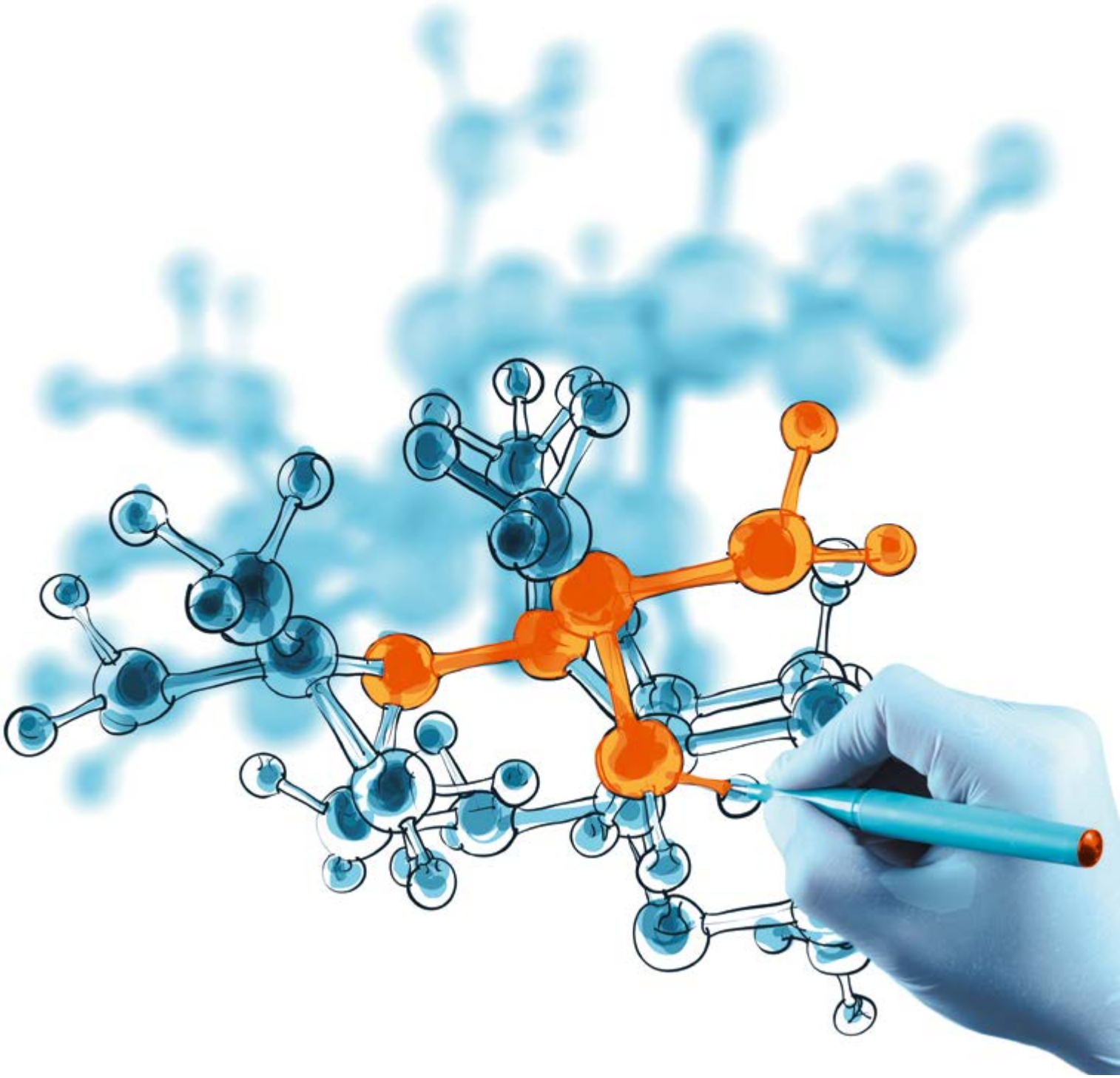
Great Ormond Street Hospital Charity

University of BRISTOL

UNIVERSITÉ DE GENÈVE

OSPEDALE SAN RAFFAELE

Campus Biotech Innovation Park
Avenue de Sécheron 15
CH-1202 Geneva - Switzerland
Phone +41 22 794 4004
Fax +41 22 794 4005
Email foundation@esperare.org
Website **www.esperare.org**



Design and infographics: Comstone, Geneva
Desktop publishing: Ink Drop, Geneva
Photos: Shutterstock, Esperare