ANNUAL REPORT
2015

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 sleeved treatments for debilitating rare diseases.

> **“ If opportunity doesn’t knock, build a door.”**
>
> **Milton Berle**

Dear Friends,

It is hard to believe, but EspeRare is three years old! In this short time, we have only felt a strong increase in interest and need for the niche in which we have placed our efforts. While there is a tsunami of interest in rare diseases, and even in drug repurposing, all of the other activities are in the for-profit space. Our mission is comprehensive: not only do we want to repurpose existing drugs for rare conditions, but we are also concerned that access to these drugs is fair and equitable. We are concerned that current trends in rare diseases show astronomical prices being set and accepted by some markets around the world. The EspeRare model was developed as an alternative to this costly approach that is starting to burden health economics and creating access to medicine challenges.

We are convinced that accelerating the process of moving molecules that have undergone initial development into another indication is a critical and less risky path to alleviating the burden of these diseases. They are rare, and affect only small populations, but taken collectively they represent a major healthcare burden as they affect more than 1 in 10 people worldwide.

We are very excited to have reached a point where we have validated the relevance of our unique model with our first R&D programme: the rescue of Rimeporide, a drug that was left abandoned by a pharmaceutical company and for which we have obtained Orphan Drug Designation this year in Duchenne muscular dystrophy. Thanks to our highly collaborative and philanthropic model, not only have we given a chance to this drug to reach those children in need by combine public, philanthropic and private funding but we are proud to report that we are now investigating this drug in boys affected by Duchenne in four European clinical reference centres.

EspeRare has received important recognition in this past year. Caroline Kant, our CEO, was named Swiss Woman Entrepreneur of the Year. This recognition, from the Club of Female Entrepreneur, recognizes her tremendous vision in giving birth to a nonprofit organisation to repurpose interventions, decreasing the enormous amount of time and money it generally takes to alleviate the suffering of individuals affected by rare diseases. The Swiss economic journal Bilan also recognised EspeRare as a top 8 Swiss start up for 2015.

As we have validated the relevance of our novel model, we are now shifting into an expansion phase. We are scaling up with the development of a portfolio of therapeutic programmes in multiple rare diseases. As part of a longstanding partnership with Ashoka, McKinsey has worked with Caroline and her team to enhance the delivery of our unique approach and maximise our impact for the patients we serve. To this end, McKinsey supported us in thinking through our business model and defining our growth priorities.

Personally, as I work in the rare disease world, particularly in a leadership role in organisations such as the International Rare Disease Research Consortium and the Accelerating Medicines Partnership, I know there is a need for EspeRare because it can implement the model that great strategists are formulating. We look forward to stronger and more energetic collaborations with donors, partners, and patients in the coming year.

Sincerely,

Sharon Terry
President

2015 highlights

JAN-FEB 2015

EspeRare selected as a Top Swiss start-up with an innovative business model

Featured by the economic journal Bilan in January for its innovative business model, EspeRare is also presented in the magazine edition of February in the top 8 Swiss start-ups, among 50 promising start-ups from all industries in which one should invest. ■

MAY 2015

The Rimeporide drug receives the Orphan Drug Designation in Duchenne Muscular Dystrophy (DMD)

The European Medicines Agency has granted the Orphan Drug Designation to Rimeporide for DMD, a life-threatening muscle disease affecting boys early in childhood. This designation is a key recognition of the therapeutic potential of EspeRare's leading drug under development, which is currently being tested in boy's affected by this devastating disease. ■

JULY 2015

EspeRare part of a strategic task force to address rare diseases

To reach its objective to diagnose most rare diseases and to find 200 new treatments for rare diseases by 2020, the International Rare Diseases Research Consortium (IRDiRC) created a data mining and repurposing task force to enhance collaborations and exploit tools to accelerate the development of new treatments. The foundation's CEO was invited to become a member of this group and provide her expertise and experience in this field. ■

AUGUST 2015

AFM-Téléthon renews its support to EspeRare's therapeutic development efforts for Duchenne

The French leading patient organisation has renewed its financial support to EspeRare's programme in Duchenne. This grant is co-financing clinical trial activities currently being initiated in several hospitals in Europe. The AFM has also invited the Rimeporide programme into its strategic portfolio, which gives access to AFM's network of biomedical experts to best advance Rimeporide for boys burdened by such debilitating disease. ■

> “ The voyage of discovery is not in seeking new landscapes but in having new eyes.”
>
> Marcel Proust

SEPTEMBER 2015

CFE Swiss Woman Entrepreneur Award granted to EspeRare’s CEO

This award highlights the exceptional entrepreneurial work of a business woman in Switzerland. By winning this price, Caroline Kant gains a strong recognition for her efforts in driving forwards the novel business model of EspeRare. “I am very proud that a mission-driven business was chosen for this year’s award, this shows that in today’s economy, social entrepreneurship is starting to gain impact recognition.” commented EspeRare’s CEO. ■

C · F · E
CLUB DE FEMMES ENTREPRENEURES

OCTOBER 2015

Rimeporide in Duchenne presented at the 20th WMS Congress

EspeRare actively participated in the 20th International World Muscle Society Congress in Brighton (UK) with a poster presenting the rimeporide compound and its possible applications in Duchenne Muscular Dystrophy. ■

WMS
World Muscle Society

DECEMBER 2015

McKinsey supports the foundation enhancing its impact for patients

McKinsey supported EspeRare to think through its business model by defining its innovative value proposition and growth priorities. As part of a longstanding partnership with Ashoka, McKinsey has worked with Esperare to enhance the delivery of its highly distinctive approach and to maximize its impact for patients. ■

McKinsey&Company

DECEMBER 2015

EspeRare becomes a SIB affiliate

The Swiss Institute of Bioinformatics is a non-profit coalition of over 60 bioinformatics research and service groups in Switzerland. EspeRare has been invited to join this network as an affiliated institution. With this partnership, the foundation will be able to collaborate and leverage world-class bioinformatics collaborations and infrastructure that will support the development of its drug repositioning platform for rare diseases. ■

SIB
Swiss Institute of Bioinformatics

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 in the US.[1]

Rare diseases are chronic, progressive, degenerative and often life-threatening. Because of their low prevalence and their high level of complexity, they need special combined efforts for their management.

EMPOWERED ADVOCACY ORGANISATIONS IN RARE DISEASES

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

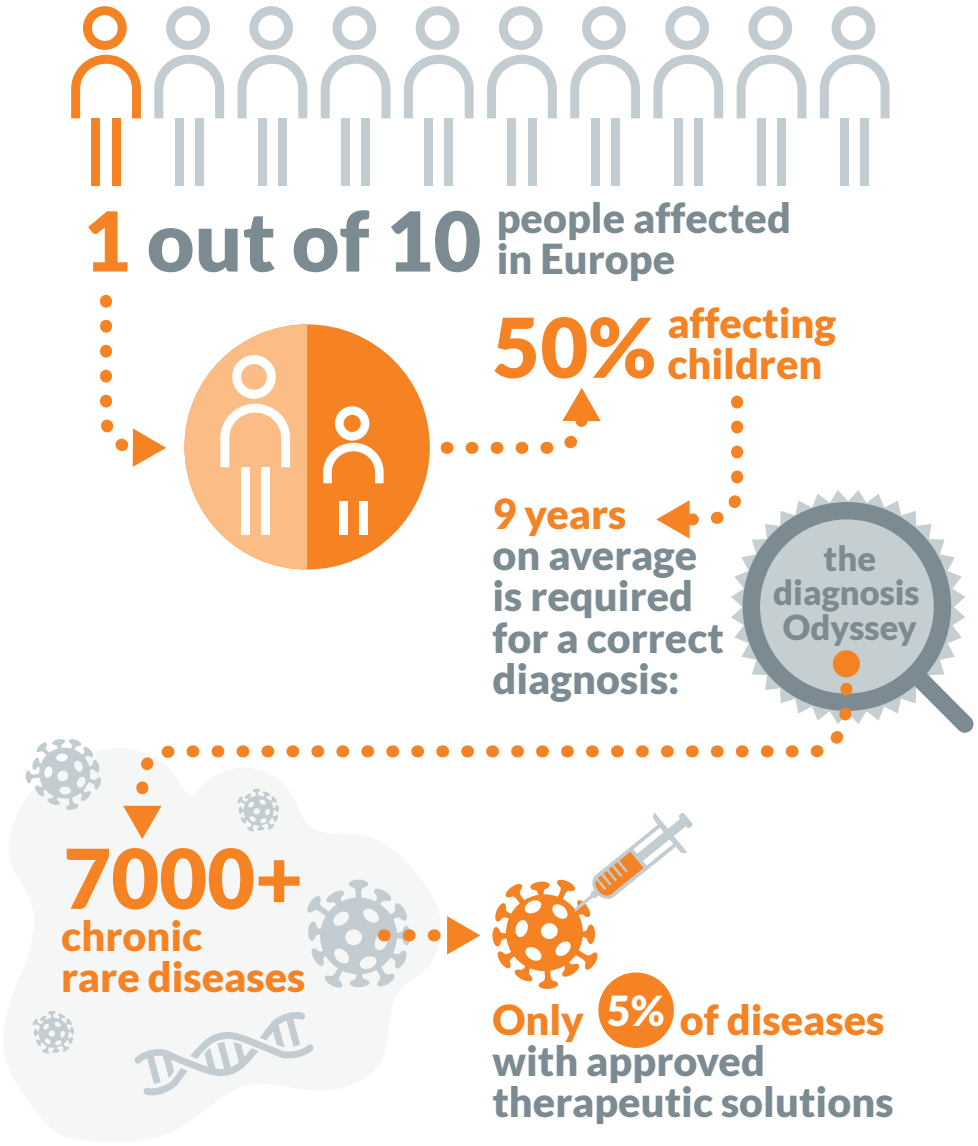
- Given the scarcity and fragmentation of medical expertise, patients are highly knowledgeable and have a strong influence on drug development
- Through support, research, fundraising and lobbying, they actively develop expert networks, manage disease related knowledge and engage in and support biomedical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

1 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 1200 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

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

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

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 drugs 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 often 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 the network of experts required in thousands of diseases, the foundation has selected around thirty diseases on which it first focuses its efforts. These diseases have been selected based on multiple criteria's, 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 tests, 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:

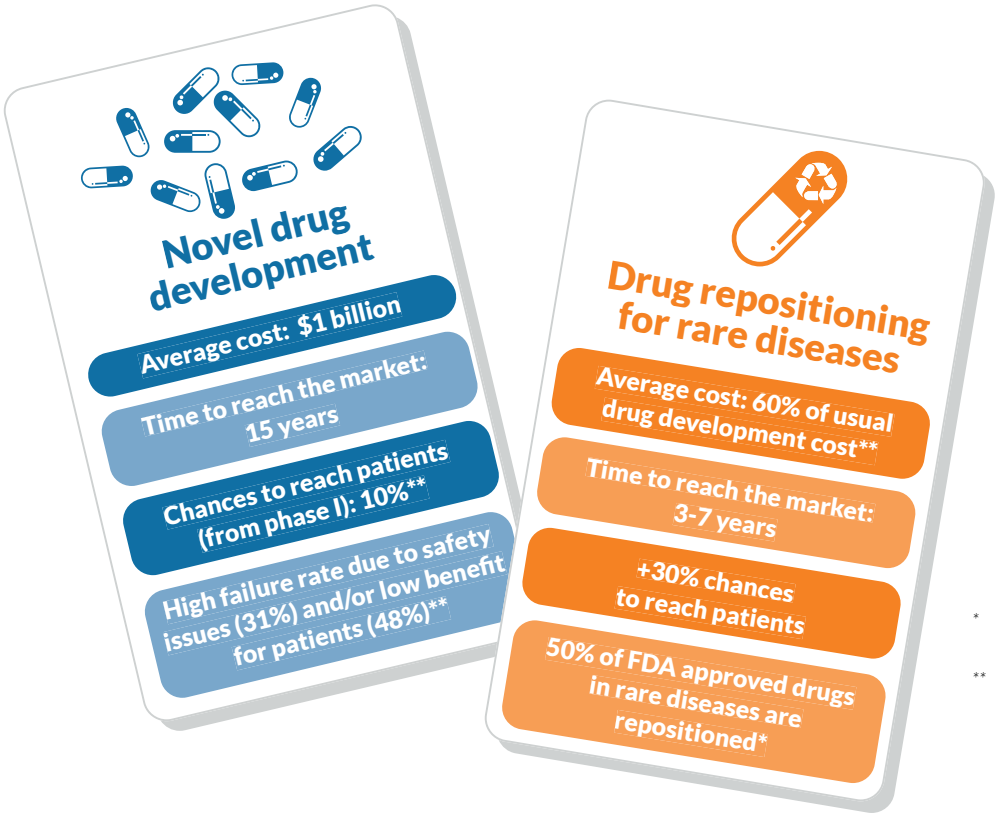
- Existing drugs are already known to exert a biological response in humans and this response may become beneficial for other health conditions.
- Many steps in the drug development process such as drug bioactivity and good safety profile in humans have already been demonstrated during the initial development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

However, repositioned drugs cannot be commercialised at high prices as compared to de novo therapeutics. Thus, so far, despite these clear therapeutic appeals 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 offers 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 remains 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: Anne Pariser, Director at CDER*

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

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.

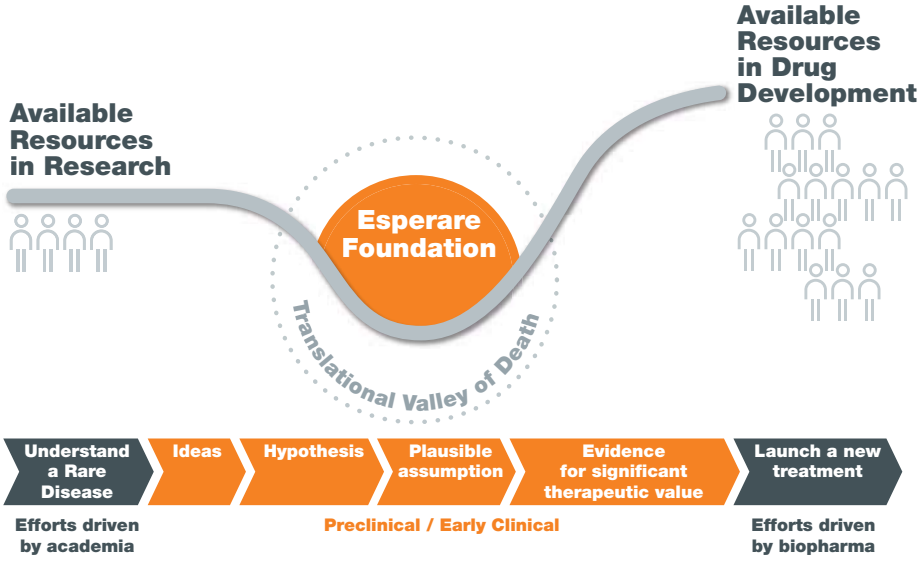
Using its collaborative approach and solid industrial drug development expertise, the foundation coordinates all necessary R&D activities to address this gap.

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

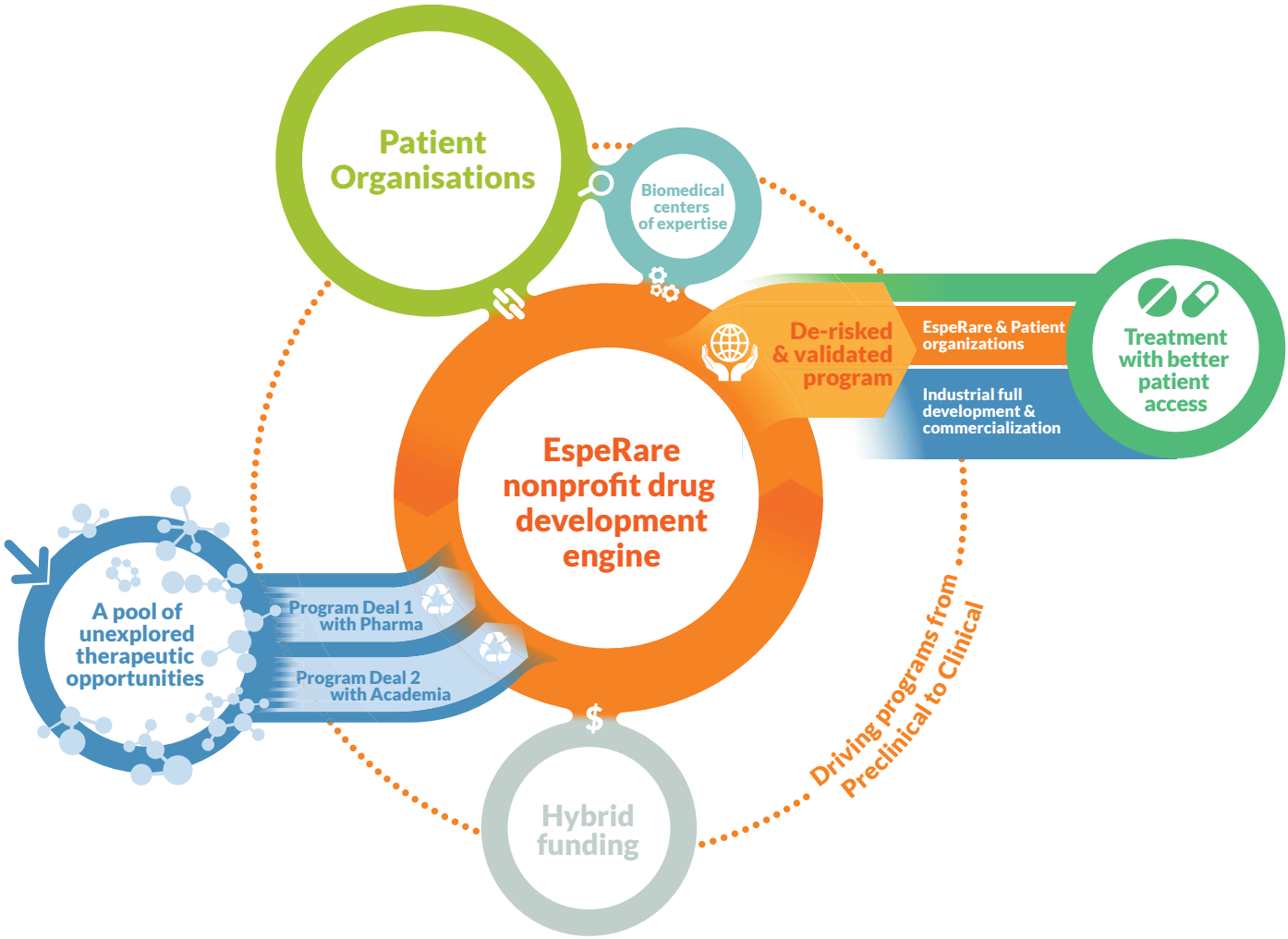
- Integrate «Patient voice» through alliance with patient advocacy groups
- Mobilise research and clinical experts and biomedical centres of excellence to conduct preclinical and clinical development activities
- Ethically engage industry partners to manage transition into late clinical development and commercialisation
- Interact directly with regulatory agencies and health authorities to best prepare path to approval and patient access to treatment

Once proof of concept in humans is demonstrated 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 health, thus safeguarding the ethical principles of a drug initially developed within a philanthropic structure.



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. 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 these opportunities.

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 highly networked, 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 pieces 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 accelerate and de-risk 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 two and a half years, the foundation has now demonstrated the therapeutic potential of Rimeporide, a shelved drug that EspeRare is now developing in children affected by this debilitating disease.** This first programme is also a validation of the strength of EspeRare's philanthropic model to drive and fund drug development in rare diseases (*see pages 12-13, 16-17*).

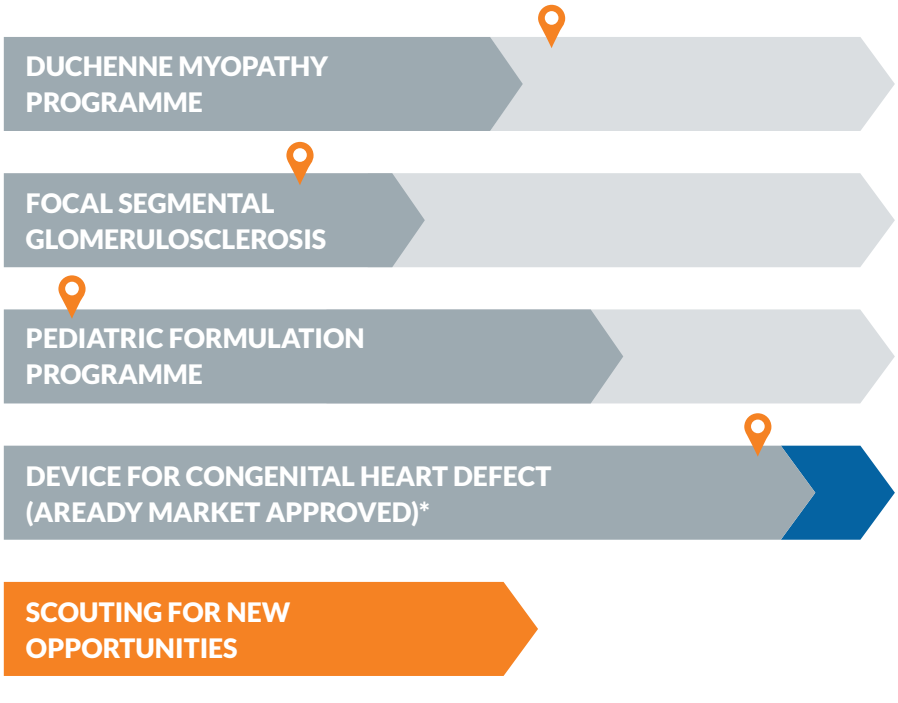
Beyond this first programme, the foundation is building a robust and diversified portfolio of programmes that has the potential to address critical unmet medical needs of children affected by rare diseases. Towards this goal EspeRare is developing another existing treatment in a rare renal disease (*see page 18-19*) and is looking to re-launch an existing therapeutic device for infants affected by severe cardiac defects.

EspeRare is looking 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 high unmet medical need disease scope
- 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

- Preclinical phase
- Clinical phase
- On the market



** EspeRare is looking to support the production and distribution of an already market approved device.*

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 that includes the:

1. **Treatment database:** compiling 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. A collaboration with the **National Institute of Health** (US) is providing access to data on drugs developed worldwide.

2. **Rare disease analytics system:** integrating biomedical data on the molecular pathophysiology of its 30 targeted rare diseases. The information is extracted from scientific literature and specialised databases. This understanding of the biological cascades involved in these diseases is validated and enhanced by biomedical experts in EspeRare's network.

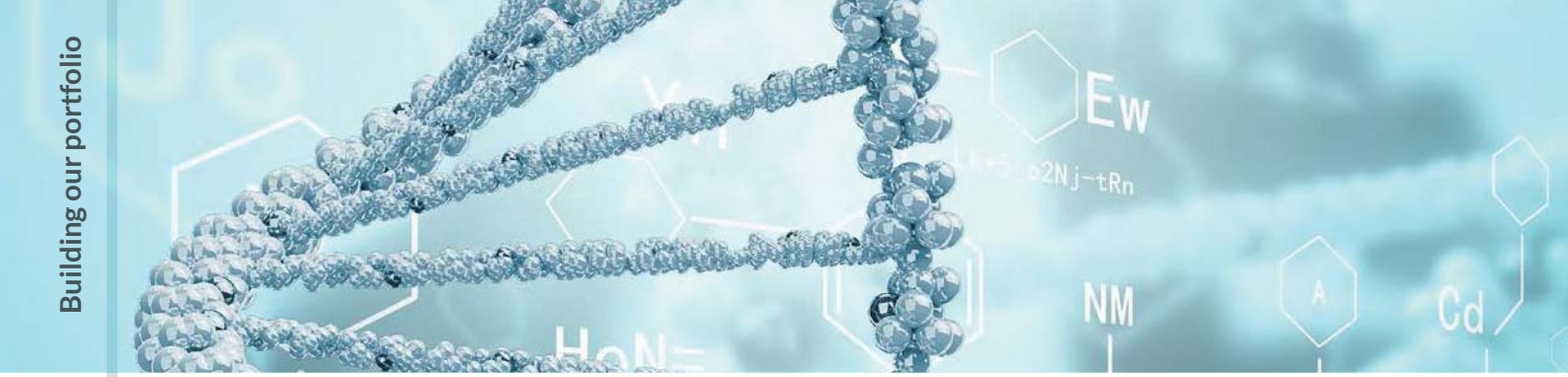
By combining wise selection of existing de-risked drugs within its Treatment database and identification of new disease applications using the Rare disease analytics system, our **Drug Repositioning platform** enables EspeRare to rescue drugs or to uncover repositioning opportunities with strong therapeutic 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 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.



First programme: Rimeporide in Duchenne Muscular Dystrophy (DMD)

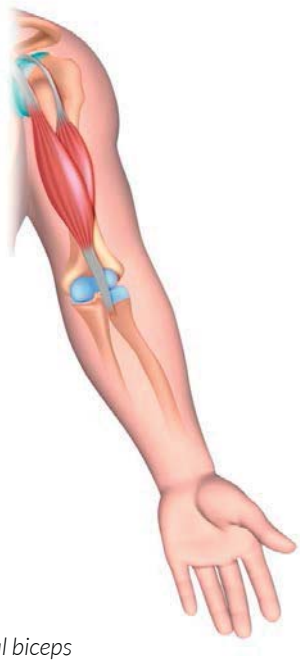
ABOUT DUCHENNE MUSCULAR DYSTROPHY (DMD)

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

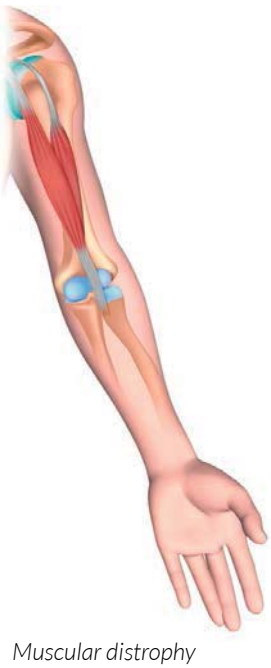
Patients affected by DMD have progressive loss of muscle function and weakness in their early childhood. This progressive muscle wasting typically leads first to loss of ambulation around 10 years of age. It eventually spreads to the arms, neck and other areas. Later in the twenties, this progresses 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 upon chronic use such as increased risks for diabetes, fractures, oedema and respiratory infections. 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. ■

> **“ 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



Normal biceps



Muscular distrophy

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

Rimeporide represents a novel investigational treatment that has the potential to delay the long term accumulation of muscle degeneration and cardiomyopathy in 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 and in the heart in a dystrophic mice model.

2015

Orphan Drug designation granted by the European Medicines Agency (EMA) for Rimeporide in DMD and filing of the clinical trial application for European countries.

2016 and beyond

Patients are being enrolled in a phase Ib clinical trial. Leading European neuro-paediatricians will enroll up to 20 patients with DMD during 2016 at the Armand Trousseau Hospital/ I-motion (Paris, France), the Great Ormond Street Hospital (London, UK), the Santa Creu i Sant Pau (Barcelona, Spain) and the San Raffaele Hospital (Milan, Italy).

Along the development path, EspeRare will strive to ensure that patients that are expected to benefit from the medication will have access to it. According to current development plans, Rimeporide aims to be marketed by 2020-2021.

> "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 big step forward for the treatment of DMD, alone or in combination with other available treatments. In particular, Rimeporide has the potential to address the 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:

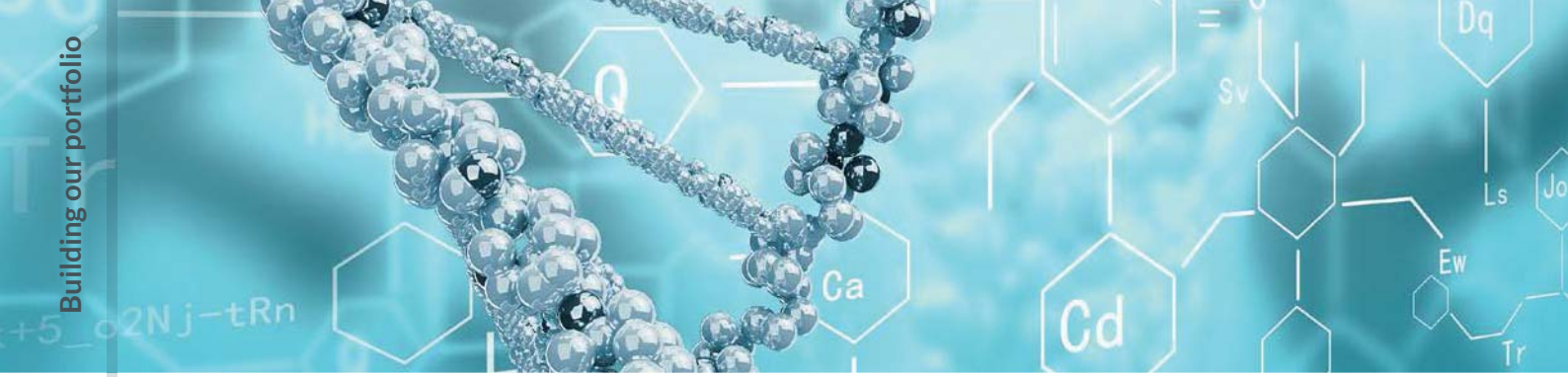
Name:	Rimeporide
Target:	Sodium-Proton (Na+/H+) Exchanger (NHE-1) inhibitor
Originator:	Merck Serono
Original indications:	Chronic Heart Failure (inactive development)
Drug development phase:	Administered to more than 150 healthy adults and Chronic Heart Failure patients (7 phase I trials)
Opportunity:	Therapeutic potential to prolong ambulation and delay cardiomyopathy in all patients with DMD; good safety profile in human.

A SOLID NETWORK OF PATIENT GROUPS AND DISEASE EXPERTS TO ADVISE AND STRENGTHEN RIMEPORIDE DEVELOPMENT STRATEGY : TREAT NMD ADVISORY COMMITTEE

R&D funding: French Telethon (AFM) & Swiss Technology & Innovation (CTI) supports ongoing research in nonclinical studies and Merck Serono is supporting the clinical development.

Key collaboration established with neuromuscular patient associations: AFM (France), PPMD (Spain), Action Duchenne (UK), MD Campaign (UK).

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



Second programme: Cilengitide in Focal Segmental Glomerulosclerosis (FSGS)

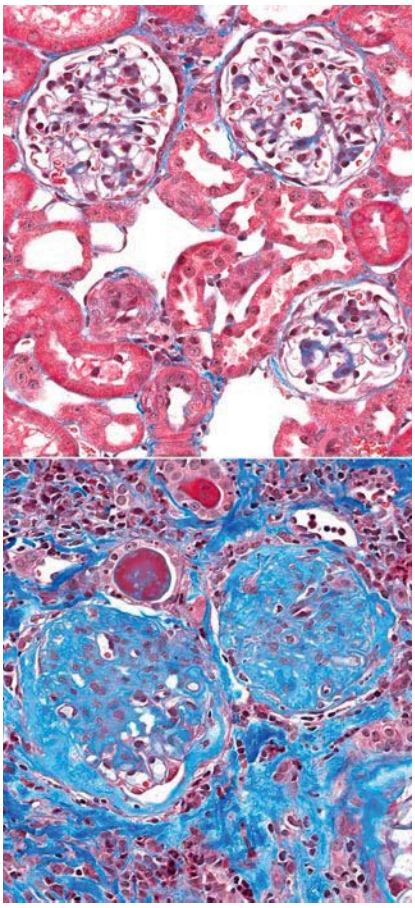
ABOUT FOCAL SEGMENTAL GLOMERULOSCLEROSIS

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.

Focal segmental glomerulosclerosis is a disease that results in impaired renal function due to injury and scarring of the glomeruli, the filtration units within the kidney. The ability of the glomeruli to act as filters depends on them having an intact physical filtration barrier, which is made up of tightly associated specialised cells called podocytes. The underlying mechanism of disease is podocyte injury and the consequential loss of the physical integrity of the filtration barrier.

The damaged glomeruli allow proteins, which would not normally do so, 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 and 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. ■



Normal healthy glomeruli (left) with glomerulosclerosis (right) a condition with fibrosis (scar) of the glomeruli (blue stain). The thin loops of blood vessels are replaced by the blue scar tissue.

(Source: Shutterstock)

Cilengitide is a safe, potent and selective αvβ3 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 represents an innovative and promising approach that targets podocyte loss in FSGS patients and that has the potential to translate into a reduction or arrest of the decline of renal function.

BACKGROUND

2013

EspeRare obtained the rights to study cilengitide in FSGS in 2013

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

Completion of the *in vitro* study to assess the potential of cilengitide in FSGS

In 2015, Prof. Saleem's team at Bristol University (UK) completed an in vitro study aimed at testing the ability of Cilengitide to modulate FSGS-induced podocytes' change of shape and motility. Cilengitide was found to be non-toxic to podocytes and was able 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 onwards

EspeRare is looking to explore the potential to **use Cilengitide in FSGS and other renal diseases**, rare or not, where αvβ3 integrins have been found to be 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

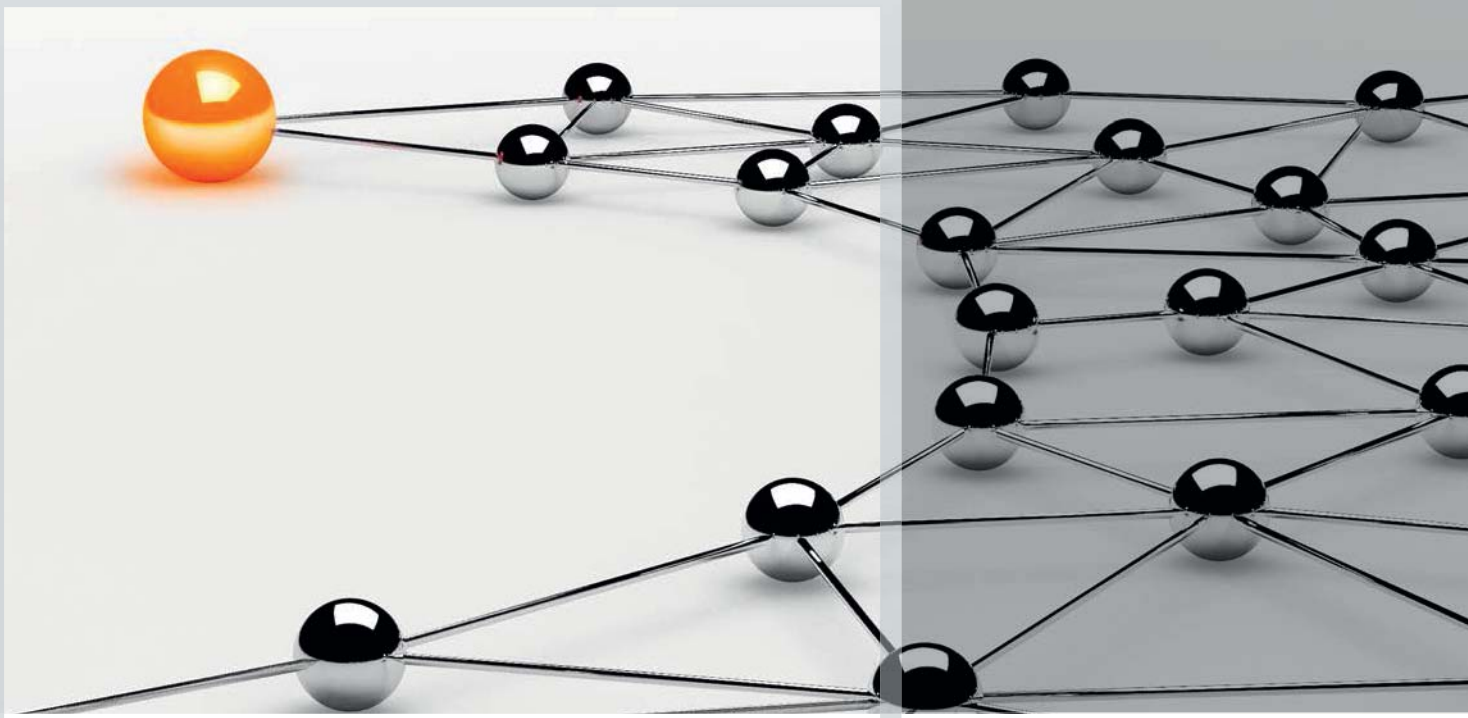
CILENGITIDE IDENTITY CARD:

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 1600 patients (adults and children, Phases I to III) for cancer and being evaluated non-clinically for FSGS
Opportunity:	Good safety profile in humans. Cilengitide has proven activity on αvβ3 integrin, a molecule whose inappropriate activation is thought to play a major part in the progression of FSGS

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

R&D funding: co-funding with Merck Serono (Switzerland), pending applications for public and patient associations funding.

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



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 nonprofit status, board members act on a voluntary basis and are key opinion leaders in the healthcare and rare disease space. The President is Sharon Terry, a pioneer of patient empowerment and citizen health, furthermore 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 scientific advisory boards are also constituted to support the strategic development. In the start-up phase, the Executive Director and the R&D Director manage a number of part-time employees, consultants and volunteers to deliver on EspeRare's objectives. ■

"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-Mareda
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. As Board Member, she is the General Counsel of the foundation.

With over 20 years of experience in the regulated industries in Europe and the US, 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 patient and healthcare provider interactions through medical mediations and her membership on the Geneva health ethics committee.

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 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 is providing to Esperare his expertise in financial representation and strategic business planning, financial and fundraising analysis, and 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 brings wide-ranging leadership expertise across the whole pharmaceutical R&D value chain.

Ewen 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 holds a combined honours degree in Physiology and Pharmacology.

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. In this context, she has also developed "Registry for All" and biobanking capabilities.

She is the founding CEO of PXE International, a research advocacy organisation for the rare genetic condition pseudoxanthoma elasticum. She is also the author of numerous peer-reviewed articles and among others, she is 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.

Monique A. Caillat

Béatrice Greco

Peter Potter-Lesage

Ewen Sedman

Sharon F. Terry - President

HEAD OFFICE

Caroline Kant-Mareda

Florence Porte-Thomé

CAROLINE KANT-MAREDA

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 is also a founder and represents the executive committee on EspeRare's board.

She brings broad know-how and international expertise in translational research, public-private partnerships, and product development within the pharmaceutical and information technology industries. Before founding EspeRare, Caroline built and managed a R&D department at Merck Serono. Prior to that, in the United States, she helped launch 3C Interactive, a software Silicon Valley company. Caroline holds degrees in molecular neurobiology and product development. Caroline in an ASHOKA fellow and was appointed CFE Swiss women entrepreneur of the year in 2015.

By establishing the EspeRare foundation, Caroline realises her dream of dedicating herself to address rare diseases in honour of her daughter, and for all children suffering with 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 the 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 paediatric 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 is an accounting and controlling specialist. With several years working for Dell Computer, Hewlett-Packard and Swisscom, she has been leading accounting and software setup projects for real estate entities, industry, NGOs and telecoms. She's actually engaged into humanitarian causes, for an ideal of a "better world". Having a strong IT literacy, she has been developing web mastering skills, and photography as a semi-pro leisure in the last past years. At EspeRare she links ledger accounting to reporting and auditing.

ILARIA DI RESTA

Ilaria has over 13 years of experience in clinical development. She has been responsible for the design and implementation of clinical trials in several therapeutic areas, with a particular focus on rare paediatric diseases. As an expert in clinical site coordination, Key Opinion Leader management and clinical study quality management, Ilaria is providing her clinical operation and project management expertise to the foundation.

HANANE GHEIT

Hanane is specialised in orphan and paediatric drug development in different areas such as metabolic diseases and neuro-oncology. She has been running the implementation and the coordination of international phase II/III clinical trials in clinical referral centres for rare diseases. She has participated in EU Health programs in paediatrics including a work package dedicated to the early evaluation of new anti-cancer compounds in children. Hanane provides her clinical operational expertise to EspeRare.

AGNÈS JAULENT

Agnès studied for her PhD in chemistry at Imperial College London and then completed her post doctoral studies at the LMB (Laboratory for Molecular Biology) in Cambridge, UK. She then joined a biotech company, Isogenica, a CRO that specialises in offering discovery services to the pharma industry in the fields of peptide, protein and antibody research. Agnès is an expert in all fields pertaining to peptide chemistry and bring this experience to EspeRare as a project manager.

GWENAËLLE LAPORTE

Gwenaëlle has several years of experience in commercial support and marketing in various industries and as a project management officer. She is fluent in English, French and German. With her board experience, she brings a diversified support to EspeRare's executive team.

CÉDRIC MERLOT

Cédric is the CEO of Drugdesigntech which he founded in 2007. After a few years at Sanofi-Aventis in the molecular modelling group, he joined Serono and had increasing responsibilities in the Scientific Computing department, with a focus on data management for small molecules and biologics and computer-assisted drug design for small molecules.He applies bioinformatics and data management expertise to support the development of the foundation Translational Platform.

SANDRA MILLET

Sandra worked for 4 years in the field of communication and organisational development, within the Research & Development function at Merck Serono. As a project manager in the ETAI communication group, she launched and developed business events and trade fairs for the manufacturing industry in Europe. Sandra holds a Master in business and commerce, and recently obtained a Master in Human Resources and Change Management. She brings to the Foundation her solid marketing and communication expertise.

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. Prior to establishing her consulting practice, Sylvie worked within the Index Ventures Life Sciences team. She also spent 4 years as a strategy consultant with Mckinsey and Company. She provides 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. His expertise includes the manufacturing of small molecules, biologics and Life Cycle Management in large pharmaceutical companies and biotechs. He brings this solid expertise of drug manufacturing processes to support EspeRare's drug development programmes.

ANDREW SLADE

Andrew holds a Ph.D. in molecular biology and postgraduate diploma in clinical research. He has a 15 year experience in preclinical and early clinical development,and a strong regulatory and drug manufacturing background. He benefits from an international exposure in large multinational organisations, with an extensive network of preclinical and clinical contacts across several therapeutic areas.

At EspeRare, Andrew is currently responsible of the management of preclinical and translational activities of the foundation's programmes.

DUC TRAN

Duc Tran brings 18 years of experience in drug discovery and drug development working for large pharmaceutical companies and start-ups in cardiovascular, anti-infective, CNS and reproductive medicine disease areas delivering a large number of projects into clinical development, up to PhIIa Proof of Concept. Duc holds degrees in organic and bioorganic chemistry and is a registered Project Manager. He provides EspeRare with his expertise in non-clinical, early clinical and manufacturing in support of the foundation's R&D activities.

SCIENTIFIC ADVISORS

PROF. GHASSAN BKAILY

Ghassan Bkaily, Ph.D., is a Professor at the Faculty of Medicine of Sherbrooke University. His research focuses on the role biochemical processes of 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 published numerous scientific papers and book chapters. His work received several awards and honours, such as the most outstanding pharmacology research paper of the Pharmacological Society of Canada (2004). Ghassan provides expertise in the mechanism of action of Rimeporide in the context of cardiomyopathy.

PROF. STÉPHANE BLOT

Stéphane Blot is heading the neurobiology laboratory of the Veterinary School of Alfort (ENVA), France. This unit is supported by the French Association against Myopathies. As a teacher-researcher, Prof. Blot gives theoretical and clinical lessons to veterinary students, trainings in neurology and neurosurgery and supervises PhD students. In parallel he participates among others to the instruction of students preparing the myopathology diploma of the French Institute of Myologie. Stéphane 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

Since 10 years, Serge Braun, Ph.D, 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 an effective research environment for new treatments in rare diseases. He has an extensive background in neuromuscular biomedical research in France and in the United States.

In 2001, he became Head of Research at Transgene, worldwide leader in gene therapy, and worked on cancer immunotherapy and infectious diseases projects. In recognition of his impact in rare disease drug development, he was named "Inspirational Stakeholder of the Year" at the 5th Annual "World Orphan Drug Congress". In addition to this role, Dr Braun has an extensive background in neuromuscular biomedical research and he is advising EspeRare on the strategic development of Rimeporide in Duchenne.

DR. PIERRE CARLIER

Pierre Carlier, MD, PhD, CEA, has been heading the NMR laboratory of the Myology Institute in Paris for more than 10 years. This leading specialist in magnetic resonance imaging and spectroscopy of muscle is focusing with his team on developing truly quantitative imaging measurements, essential to ensure the clinical relevance of high-technology imaging procedures. Developing and refining these quantitative techniques may enable the detection of very early and pre-clinical signs of a positive response to treatment, thus making MRI and MRS potentially attractive outcome measures in trials. Pierre is engaged in numerous research projects to further develop MRI&S as a non-invasive diagnostic tool and outcome measure. He provides EspeRare with his expertise in the imaging of muscles using NMR and MRI imaging techniques.

PROF. JOEL DUDLEY

Joel Dudley, PhD, is Assistant Professor of Genomic Sciences and Director of Biomedical Informatics at Icahn School of Medicine at Mount Sinai, New York. His published research covers topics in bioinformatics, systems medicine, personal and clinical genomics, drug and biomarker discovery. His computational drug repurposing work gained recognition by the NIH NHGRI for this contribution to Genome Advancement. He is also co-author of the book Exploring Personal Genomics from Oxford University Press, the first major text on personal genome analysis and interpretation. His current research aims to integrate and apply information from molecular profiling, clinical practice, and wearable sensors to realise the vision for a real-time learning healthcare system. In 2014, he was named one of the 100 Most Creative People in Business by Fast Company magazine. His is providing his leading computational drug repurposing expertise to support EspeRare drug rescue efforts and platform development.

DR JULIAN GRAY

Julian Gray has 25 years of experience in clinical development in the CNS area within the pharmaceutical industry, including drug development in Duchenne muscular dystrophy and other rare central nervous system indications. Dr Gray was the Medical Director at Santhera where he ran part of the clinical development for Idebenone. He combines qualifications and experience in neurology and pharmaceutical development with relevant experience in rare diseases. Julian also provides drug development training through his proprietary web-based drug development academy programme. Julian serves as the Medical responsible for the Duchenne programme and subsequent programmes in neuromuscular diseases.

PROF. ANTOINE HADENGUE

Antoine Hadengue is a Professor of Gastroenterology and Hepatology, at the University Hospitals of Geneva, Switzerland. Graduated from Paris Descartes Faculty of Medicine and specialised in gastroenterology and liver cellular biology, he first focused on hepatic pathophysiology research. Since 1994, he managed clinical activities, research works 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, Switzerland. Antoine provides his clinical expertise in support of EspeRare drug development efforts in metabolic diseases.

PROF. CONRAD HAUSER

Conrad Hauser is a physician specialised in Dermatology, Venereology, Allergy and Clinical Immunology. From 1993 to 2008, he was chief of the Department of Dermatology of Western Switzerland (Bern) and chief of the Allergy Unit, division of Immunology and Allergology, within the Geneva state hospital and medical school. In 2008, he joined the Merck Serono pharma company as a Senior Medical Director, and held the position of head of early development & head of biomarker strategy, global clinical development Unit Rheumatology. He provides his expert biomedical understanding in immunology to the foundation.

PROF. JIRI MAREDA

After obtaining a PhD in physical organic chemistry at the University of Geneva, Jiri Mareda worked as the research associate at the University of Pittsburgh, where he fully specialised in computational and theoretical chemistry. He was then teaching for more than 28 years organic chemistry to chemistry, pharmacy, and biology students at the University of Geneva. He was also giving advanced physical-organic courses for master and doctoral students at the Chemistry department.

Jiri now provides an insight at the molecular and chemical levels to help tackle challenges that EspeRare undertakes.

PROF. RAMAIAH MUTHYALA

With around 30 years of experience in the pharmaceutical industry, he was involved in commercial successes such as an antiepileptic under development approved as orphan drug, the repositioning of a compound developed for cancer to treat the rare disease African sleeping sickness or a treatment for a rare thyroid cancer. Prof. Ramaiah has been working for 10 years as Associate Professor in the Department of Experimental Clinical Pharmacology and as Adjunct Associate Professor for the Department of Medicine of Minnesota University. His research activities extend to rare diseases such as orphan cancers and neurological diseases, with a focus on the identification and repositioning of drugs for orphan diseases. He is a strategic advisor for the foundation's drug repositioning approach.

DR KANNEBOYINA NAGARAJU

Kanneboyina Nagaraju, PhD, DVM, is an immunologist with an expertise in molecular mechanisms of target tissue injury in muscle diseases. He is a principal investigator at Children's Research Institute Center for Genetic Medicine Research at Children's National Medical Center and a tenured Professor of Integrative Systems Biology and Paediatrics. One of the main focuses of Dr. Nagaraju's laboratory is to develop and validate animal models for neuromuscular diseases. With his team, he runs routinely preclinical drug testing on neuromuscular disease models especially in the mdx mouse model of Duchenne muscular dystrophy. He is a preclinical advisor to EspeRare Duchenne programme.

PROF. MOIN A. SALEEM

Moin A Saleem, FRCP, Ph.D. is Professor of Paediatric Renal Medicine at the Academic Renal Unit, Southmead Hospital, Bristol and Children's Renal Unit, Bristol Children's Hospital. He has more than 20 years' experience in fundamental research, especially focusing on understanding the fundamental mechanisms of kidney filtration, in order to understand the basis of glomerular diseases.

As part of his research into the basic biology of the podocyte, the glomerular cell primarily responsible for the complex function of filtration, he developed a technique for growing human podocytes in the laboratory. This has been a major methodological advance which allows molecules such as cilengitide to be tested as potential treatments for Focal Segmental Glomerulosclerosis.

DR. LAURENT SERVAIS

Laurent Servais is a paediatrician and the director of the clinical research department at the Institute of Myology in Paris. He is graduated from Louvain Medical School in Brussels where he obtained his PhD in Neuroscience in 2005. With 15 years of experience in rare diseases clinical research, he currently leads the department of Clinical Research within the French national centre of expertise in clinical myology in Paris. In addition to caring for patients with neuromuscular diseases within his medical practice, Laurent focuses on the development of clinical outcome measures and clinical trials in muscular dystrophies. Laurent and his team bring medical expertise to the clinical strategy of EspeRare's programme in Duchenne muscular dystrophy.

PROF. NICOLAS J.C. SIMON

Nicolas J.C. Simon, MD, PhD, is a Professor and Chairman of the Department of Pharmacology at Aix-Marseille University, School of Medicine Director of the Clinical Pharmaco-Toxicology Unit and Addiction medicine specialist at Sainte Marguerite Hospital, Marseille. Nicolas is specialised in pharmacokinetics and in addictology, he chaired the French Pharmacology and Therapeutic Society (SFPT) and is a member of several medical organisations. Nicolas produced more than 80 publications in various journals including the Clinical Pharmacokinetics. Nicolas brings EspeRare his expertise in pharmacokinetics and in the modelling of translational data to better optimise its drug development strategy.

WOLFGANG SCHOLZ

Wolfgang Scholz, MD, completed his medical education at the Universities of Mainz and Frankfurt. He specialised in ion transport in the kidney under acidic conditions at the University of Mainz. 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. Wolfgang provides his know-how into NHE biology and contributes with his cardiovascular biomedical expertise to EspeRare's project in Duchenne muscular dystrophy.

DR. ELIA STUPKA

Dr. Elia Stupka is a bioinformatics leading expert who started his genomics career as part of the core Human Genome Analysis Team and Ensembl group in the UK, where he participated in the human genome project. He was also Scientific Director at the University College London, where he began applying Next Generation Sequencing approaches to both rare and complex disease projects and exploring epigenomics approaches to identify novel biomarkers. He led the development of the first Translational Genomics and Bioinformatics Center in Italy at San Raffaele Hospital Research in Milan. He currently is the Director of Genomics and Computational Biology at Boehringer Ingelheim. Elia is providing his computational biomedical expertise to develop EspeRare proprietary data analytics platform.

"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 and international governmental and public bodies. These funds are used to finance the EspeRare portfolio to accelerate the cost-effective development of unexplored therapeutic opportunities for rare neurological and immunological diseases. In partnership with patient organisations, EspeRare addresses the key translational gaps and clinical development challenges, acting as a trusted partner for pharmaceutical companies, academic 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 a senior manager with 2 employees and 12 consultants. 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 is 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 2015

The year was characterised by a number of factors. The capital and reserve was committed, further considerable donations were received or confirmed for the future, staff were recruited, planning was activated and, most important of all, **Research & Development Project funding represented 76% of total expenses and amounted to CHF 1,221,561** (note 8 a-e), quite stable as compared to CHF 1,176,054 in 2014.

Significantly, in January 2015, the Swiss National Bank discontinued the minimum floor exchange rate between Swiss Francs and Euros. As such, during 2015, the EUR-CHF rate dropped from 1.202350 to 1.087400, representing a partially realised exchange loss of CHF 186,159. The decrease of GBP-CHF and USD-CHF rates have occasioned only minor losses. The total foreign currency loss thus amounts to CHF 188,589 for 2015 (2014: CHF 12,325).

Additionally the foundation incurred an excess of expenditure over income in 2015 of CHF 461,758 that is mainly due to expenses incurred for higher-cost activities leading to the entry of the Rimeporide programme into clinical development for Duchenne muscular dystrophy.

Founding Capital

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

Donations

Total donations recognised in 2015 amounted to CHF 1,114,698. R&D income came to CHF 804,698 including an amount of CHF 25,409 deferred from 2014. A total of CHF 1,285,560 was received from Merck Serono in 2015 with CHF 654,106 recognised this year and a further CHF 656,863 being deferred to 2016 to finance clinical trial activities of Rimeporide in Duchenne muscular dystrophy.

Also recognised in 2015 was a contribution from AFM Telethon for CHF 150,592.

In addition, Awards & Foundation Support income of CHF 310,000 was recognised from a Geneva foundation and the Foundation Tell & un tel. (Note 7).235,000 was paid directly by Swiss CTI to our academic partner the University of Geneva and is recorded in the notes as an off-balance-sheet item. (note 7).

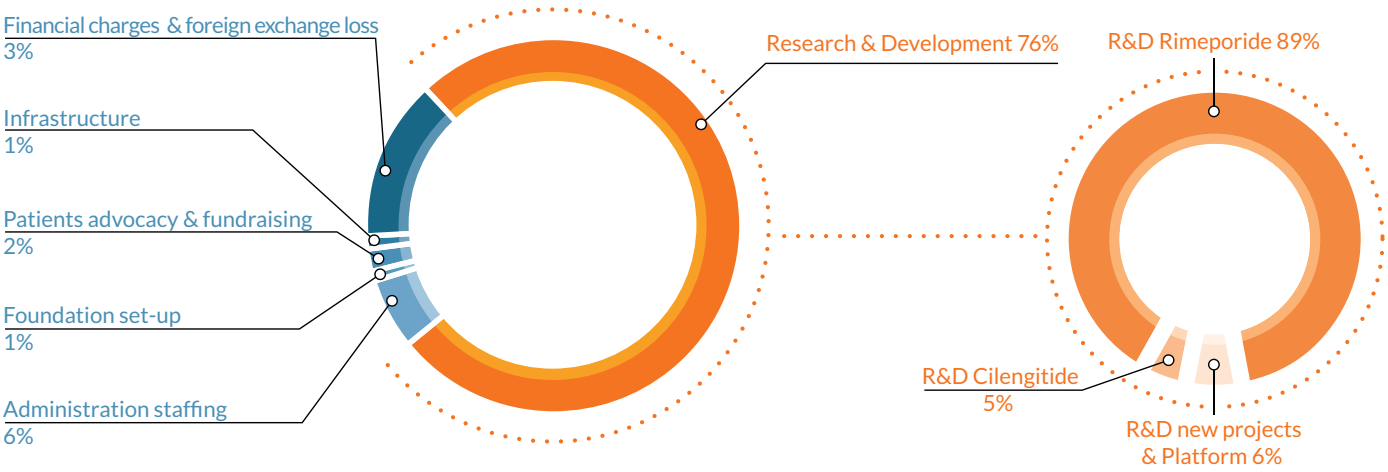
Staff

At year-end the senior management team consisted of a Chief Executive Officer, Chief Scientific Officer, and 1 staff member. Furthermore, EspeRare has a team of 12 consultants and counts 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 8d). ■

SNAPSHOT OF ESPERARE EXPENDITURE 2015



THE FINANCIAL YEAR AHEAD TO DECEMBER 2016

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, a new internal accounting structure has been implemented and KPMG International 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 2016. By the end of 2017 it is expected that EspeRare's first programme will be out-licensed to a commercial partner, this transaction is expected to bring in capital that will be used to fund the expansion of the foundation programme portfolio in rare diseases, including financing the "expensive" clinical development of 2 new programs. 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 this additional income will be mobilised in alignment with the foundation fundraising strategy and will enable the expansion of EspeRare's impact on the patients burden suffering for rare diseases.

Conclusion

The detailed financial tables that follow – Balance Sheet, Statement of Income & Expenditure – represent EspeRare in its third 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 at the service of its major goal: the discovery and development of new medicines for the treatment of rare diseases. ■

ESPERARE BALANCE SHEET TO 31 DECEMBER 2015

	NOTES	2015	2014
ASSETS		**CHF**	CHF
Current Assets			
Cash & Cash Equivalents	2i	420,00	-
BCGE Current Accounts	2i	2 209 701,24	2 072 923,83
Prepaid & Receivables			
Accounts Receivable		-	13 845,55
Withholding Tax & VAT Receivable		8 322,13	695,35
TOTAL CURRENT ASSETS		**2 218 443,37**	**2 087 464,73**
Non-current assets			
Computers & Equipment	2d	7 768,70	7 768,70
(less depreciation)		(6 956,32)	(4 366,75)
TOTAL NON-CURRENT ASSETS		**812,38**	**3 401,95**
TOTAL ASSETS		**2 219 255,75**	**2 090 866,68**
LIABILITIES			
Current Liabilities			
Suppliers		125 097,24	57 560,90
Employees Accounts		-	158,05
Social Charges		2 353,20	453,35
Due VAT		11 600,00	-
Provisions	2f/9	26 400,00	190 900,00
Accruals	2g	42 315,00	-
Deferred Income		656 863,00	25 409,19
TOTAL CURRENT LIABILITIES		**864 628,44**	**274 481,49**
CAPITAL & RESERVES			
Foundation Capital	10	50 000,00	50 000,00
Operations Reserve	3	1 766 385,19	1 640 274,71
Net excess of (Expenditure)/Income		(461 757,88)	126 110,48
TOTAL CAPITAL & RESERVES		**1 354 627,31**	**1 816 385,19**
TOTAL LIABILITIES AND CAPITAL		**2 219 255,75**	**2 090 866,68**

For the ease of reference of our stakeholders, equivalent Euro figures have been provided at the official end-of-year rate of 1.20235 for 2014 and 1.087400 for 2015

CASH FLOW AS AT 31 DECEMBER 2015

	2015	2014
OPERATING ACTIVITIES	**CHF**	CHF
Net excess of (Expenditure)/Income	(461 757,88)	126 110,48
+Depreciation	2 589,57	2 519,47
+decrease (increase) in Prepaid and Receivables	6 218,77	13 535,72
+increase (decrease) in Short term Liabilities	80 878,14	21 970,41
+increase (decrease) in Provisions	(164 500,00)	173 124,65
+increase (decrease) in Accruals	42 315,00	-
+increase (decrease) in Deferred income	631 453,81	(124 590,81)
Cash from operating activities (operating cash flow)	**137 197,41**	**212 669,92**
INVESTING ACTIVITIES		
Outflows for purchase of tangible fixed assets	-	(2 226,85)
Cash inflow/drain from investing activities	**-**	**(2 226,85)**
Cash inflow/drain from financing activities	**-**	**-**
NET CASH	**137 197,41**	**210 443,07**
Cash and cash equivalents at begining of period	2 072 923,83	1 862 480,76
Cash and cash equivalents at end of period	2 210 121,24	2 072 923,83
NET CASH	**137 197,41**	**210 443,07**

ESPERARE STATEMENT OF INCOME & EXPENDITURE FOR THE PERIOD FROM JANUARY 1ST TO DECEMBER 31, 2015

	NOTES	2015	2014
INCOME		**CHF**	CHF
Donations received	2b/7a	804 698,48	1 312 621,59
Financial Income	2k	2 134,06	897,36
Other Income		329 990,73	167 861,01
TOTAL INCOME		**1 136 823,27**	**1 481 379,96**
EXPENDITURE			
Research & Development Expenditure	2e		
R &D Projects	8a		
Rimeporide			
Research & Development	8b	695 136,14	503 591,83
Support Costs	8g	398 333,74	400 316,29
Legal Fees	8f	-	1 653,75
TOTAL R&D PROJECTS, RIMEPORIDE		**1 093 469,88**	**905 561,87**
NEW PROJECTS	8c		
Repositioning Platform	8d	-	135 316,34
Support Costs	8g	80 381,15	56 981,59
Cilengitide	8e	32 254,85	25 365,00
Support Costs	8h	15 454,98	52 829,33
TOTAL NEW PROJECTS		**128 090,98**	**270 492,26**
TOTAL RESEARCH & DEVELOPMENT EXPENDITURE		**1 221 560,86**	**1 176 054,13**
GENERAL FOUNDATION ADMINISTRATION	8d		
Administration staffing & volunteers	8g	97 622,59	105 483,68
Patient Association Consultancy		335,05	5 057,21
Office Rental & Costs		14 052,87	12 849,02
Office Rental		11 508,00	10 486,00
Office Costs		2 544,87	2 363,02
Accounting & Audit Expenses		26 754,74	29 025,08
Audit Expenses		26 754,74	16 719,08
Accounting Expenses		-	12 306,00
Other Expenses		5 071,39	8 539,23
General Insurance		260,40	260,40
IT Expenses		151,60	1 999,75
Communications		4 659,39	6 279,08
General Legal Fees		2 322,04	179,26
Fundraising		31 707,32	705,20
Fundraising direct costs		10 365,53	-
Advertising Costs		9 542,84	1 047,00
Other Operating Expenses		11 798,95	(411,80)
Financial Charges		2 733,41	1 639,76
Exchange Differences	2c	188 589,46	12 325,21
Board meeting		5 241,85	892,23
Depreciation		2 589,57	2 519,47
TOTAL GENERAL ADMINISTRATION EXPENDITURE		**377 020,29**	**179 215,35**
TOTAL EXPENDITURE		**1 598 581,15**	**1 355 269,48**
NET EXCESS OF (EXPENDITURE)/INCOME	3	**(461 757,88)**	**126 110,48**

NOTES TO FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2015

1. ORGANISATION

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

With its head-office in Plan-les-Ouates, Geneva, the aim of EspeRare is to bring public and private sector partners together to both fund and provide managerial and logistical support to drive the identification and development of treatments for rare diseases. The foundation focuses on accelerating the cost-effective development of unexplored (re)positioning opportunities for rare neurological and immunological diseases. In partnership with patient organisations, EspeRare addresses the key translational gaps and clinical development challenges, acting as a trusted partner for pharmaceutical companies, academic 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 monitored 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 an 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 statement of income and expenditure. Non-monetary assets and liabilities that are measured in terms of historical cost in a foreign currency are translated using the exchange rate at the date of the transaction.

The following exchange rates were used at year-end:

1 EUR = CHF 1.087400
1 USD = CHF 1.001012
1 GBP = CHF 1.475340

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 EsperRare 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 on a mid-term (3 years).

g) Accruals

An accrual is recognised in the balance sheet when EspeRare has a fair certitude that an outflow of economic benefits will be required to settle the obligation in the short term (1 year).

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. On 15 January 2015, the Swiss National Bank discontinued the minimum floor exchange rate between Swiss Francs and Euros As such, during 2015, the EUR-CHF rate dropped from 1.202350 to 1.087400, representing a loss of CHF 186'159. The decrease of GBP-CHF and USD-CHF rates have occasioned only minor losses. The total foreign currency loss amounts to CHF 188'589 for 2015 (2014: 12'325)

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 2015 does not differ from their carrying amounts shown in the balance sheet.

5. COMMITMENTS

As at 31 December 2015, there were no significant capital expenditure commitments.

6. SUBSEQUENT EVENTS

No events occurred subsequent to 31 December 2015 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 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	0	25,409		I&E Statement - Cilengitide deferred in 2014
AFM telethon	EUR	143,231	150,592	150,592		Grant Rimeporide fully committed in 2015
TOTAL		**1,364,120**	1,436,152	**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
TOTAL		**310,000**	310,000	**310,000**		**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 to fund Rimeporide clinical trial activities.

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

b) As a comparison during 2014 the following donations were granted:

Donor	Currency	Total Grant	Received 2014 CHF	Recognised 2014 CHF	Deferred 2015 CHF	Notes
R&D Income						
ARES Trading SA (Merck Serono Affiliate) *	EUR	1 000 000	1 204 300	1 204 300		I&E Statement - Rimeporide
ARES Trading SA (Merck Serono Affiliate)**	EUR	41 777	50 231	25 409	25 409	I&E Statement - Cilengitide
AFM telethon	EUR	68 000	82 912	82 912		Grant Rimeporide fully committed in 2014
TOTAL		**1 109 777**	1 337 443	**1 312 621**	**25 409**	**R&D Income**
Awards & Foundation Support						
ASHOKA	EUR	10 000	12 024	12 024		Award fully committed in 2014
Loterie Romande *	CHF	150 000		150 000		I&E Statement - Repositioning Platfrom
TOTAL			12 024	**162 024**		**Awards & Support**
Awards & Foundation Support						
Commission of Technology and Information **	EUR	194 451		235 000		Rimeporide - Research & Development

* Donation from Loterie Romande of CHF 150,000 was received in 2013 and recognized in our accounts in 2014
** Grant directly transferred to academic partner at University of Geneva

8. EXPENSES

a) Principal current R&D projects in rare diseases
b) Development of Rimeporide in Duchenne muscular dystrophy in partnership with Merck KGaA
c) Prospection & generdrug 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) General Foundation expenses in overall support of R&D activities
g) Relates to staff and travel costs that are recorded and allocated to the specific activities. The staff headcount represented 2 senior managers and two R&D program managers. In addition, EspeRare benefits from a number of consultants and volunteers. Total staff benefits for 2015 amount to CHF 591'792.46 (Salaries & Social charges amount to CHF 562'986.50, Travel Expenses amount to CHF 27'345.90 and Volunteers reimbursements amount to CHF 1460.06).
The allocation of salaries & social charges to the two R&D projects, repositioning platform and to the Foundation General Administration according to the percentage of the time spent by employee on the three activities.
h) 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	2015		2014	
	EUR	CHF	CHF	EUR
Rent 2013	7,200	6,621	7,200	6,621
Rent 2014	9,600	8,828	9,600	8,828
Rent 2015	9,600	8,828		
TOTAL	26,400	**24,278**	**16,800**	**15,450**

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.

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
Internet 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 28 to 32 for the year ended 31 December 2015. The limited statutory examination of the prior year financial statements was performed by another auditor.

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, 14 March 2016

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

How can I support EspeRare?

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

The foundation is also a member of the Transnational Giving Europe (TGE) network, which allows European citizen 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

Supporting us financially or through volunteering action, 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 the disease of your choice and accelerate the development of a new treatment.

I WANT TO ESTABLISH A CORPORATE PARTNERSHIP

If you would like to commit fundraising activities or a corporate donation to EspeRare mission, we can define with you the most appropriate way to make this happen.

We are happy to give you further information and answer your questions:

Individuals: donate@esperare.org
Corporate organisations: partnership@esperare.org

THEY SUPPORT US

AFMTÉLÉTHON
INNOVER POUR GUERIR

Making more health
by Ashoka and Boehringer Ingelheim

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

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

ACTION DUCHENNE

MERCK

Microsoft

SIB
Swiss Institute of Bioinformatics

NATIONAL INSTITUTES OF HEALTH

TREAT-NMD
Neuromuscular Network

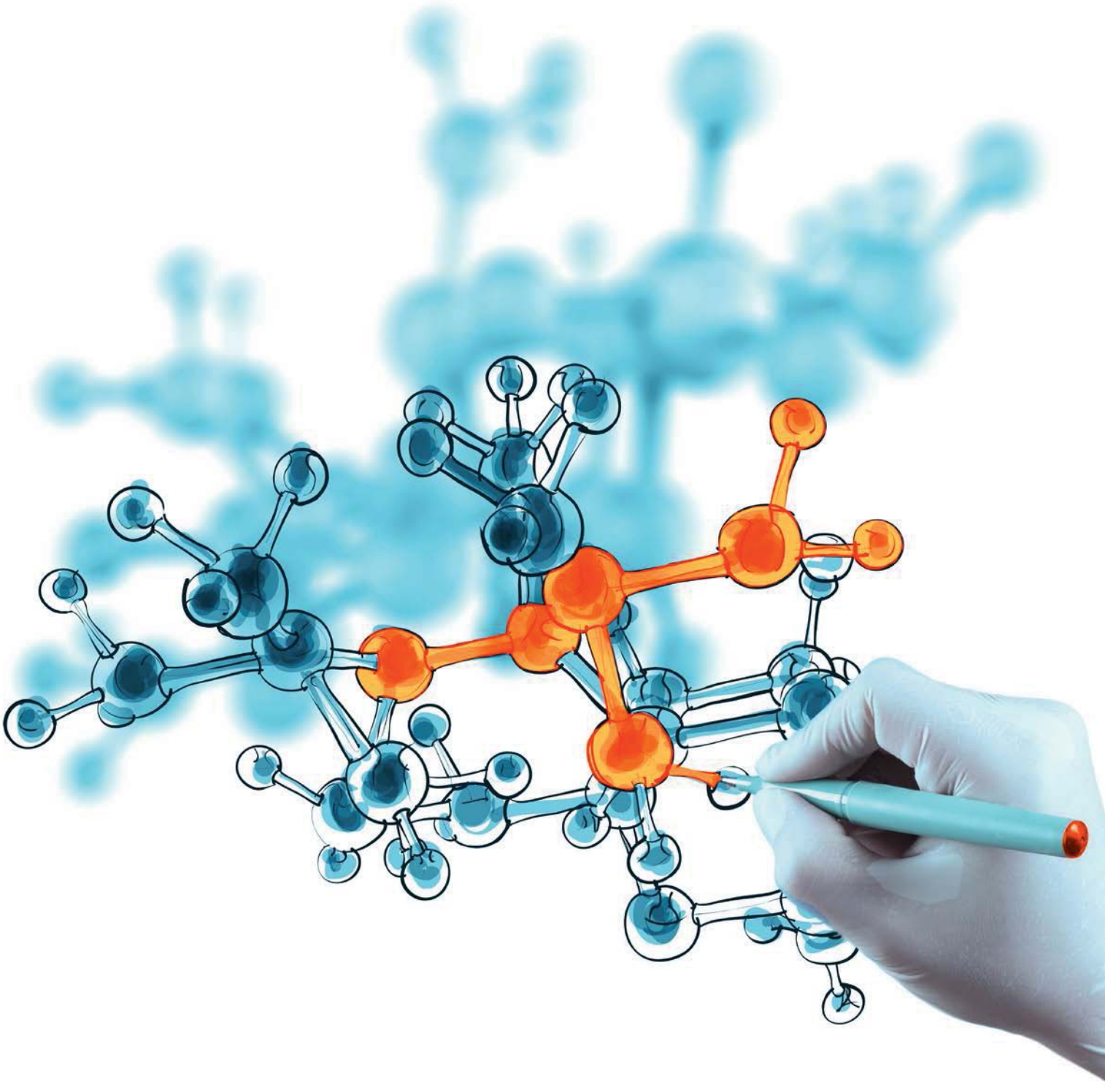
Great Ormond Street Hospital Charity

University of BRISTOL

UNIVERSITÉ DE GENÈVE

OSPEDALE SAN RAFFAELE

c/o Eclosion
14 chemin des Aulx
CH - 1228 Plan-les-Ouates, 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
Photos: Shutterstock, ingmedia