ANNUAL REPORT 2014

esperare foundation

Advancing treatments for rare diseases
Together

« My cave »
painting of Eva, 11 years old, suffering from a rare neurodevelopmental disease

Design: ComStone – Portraits: Jean-Baptiste Delage – Imagebank: Shutterstock – Dreamstime

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 and the Executive Director

EspeRare was launched in April 2013 at International Rare Disease ***Research Consortium first congress.*** *Established in Geneva, Switzerland, it* ***is recognised by the Swiss authorities to be operating for the public benefit. In line with its nonprofit status, all revenues generated by the foundation through the development of therapeutic assets are reinvested for new rare disease programmes within its portfolio.***

MISSION

In collaboration with patient organisations, academia, governmental agencies, biotech and pharmaceutical companies, EspeRare uncovers the potential of existing molecules to address severe therapeutic unmet needs in rare diseases. Through the identification and validation of these therapeutic opportunities, it addresses the translational gap in rare disease drug development. Thus, giving a chance to these existing drugs to reach these patients.

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.

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

We live in a world where every minute a child is born with a rare disease that has no cure, not even a treatment. There is much that can be done to improve the lives of these children. EspeRare’s achievements to date have proven that disruptive models like ours can be a major catalyst in pursing that goal. We have completed our second year, and our niche in the world of accelerating access to new treatments for those who suffer is now clearly defined and has delivered conclusive outcomes.

In 2014, as a validation of our model, EspeRare has proven that it is important to peruse drug rescue in rare diseases. **Our efforts enable to demonstrate that a drug, lying in the drawer at a pharmaceutical company, has a potential to become an impactful treatment** for boys affected by a deadly myopathy. Commenting on this drug rescue opportunity, a leading cardiologist in Duchenne Muscular Dystrophy, Professor Duboc states: *“Rimeporide has demonstrated its potential to transform Duchenne muscular dystrophy from a life threatening to a chronic disease”*.

Beyond this hallmark success, we have taken several significant steps to scale our work and impact in rare diseases.

- EspeRare is e**xpanding its programme portfolio** and has started rescuing a second shelved drug for a degenerative condition that leads to renal failure. It also has identified an opportunity to develop an anti-malarial drug in a deadly metabolic disease and is preparing to launch research activities early 2015.
- The foundation is also **expanding its collaborations with pharmaceutical companies** and has been invited to join the “Making More Health” programme of Boehringer Ingelheim.
- With an endowment of the Loterie Suisse Romande and a partnership with the National Institutes of Health (USA), EspeRare has also started setting-up its informatics Drug Repositioning Platform.
- Both the president and the executive director have been very **active this year in a number of critical international consortia**. These include leadership roles in the European Commission Action for Cooperation in Science and Technology, ELSI 2.0, the Global Alliance for Genes and Health and the International Rare Disease Research Consortium (IRDIRC). IRDIRC is working to examine drug repurposing in rare disease overall as a way to accelerate therapeutic development for rare diseases and EspeRare is involved in that analysis.

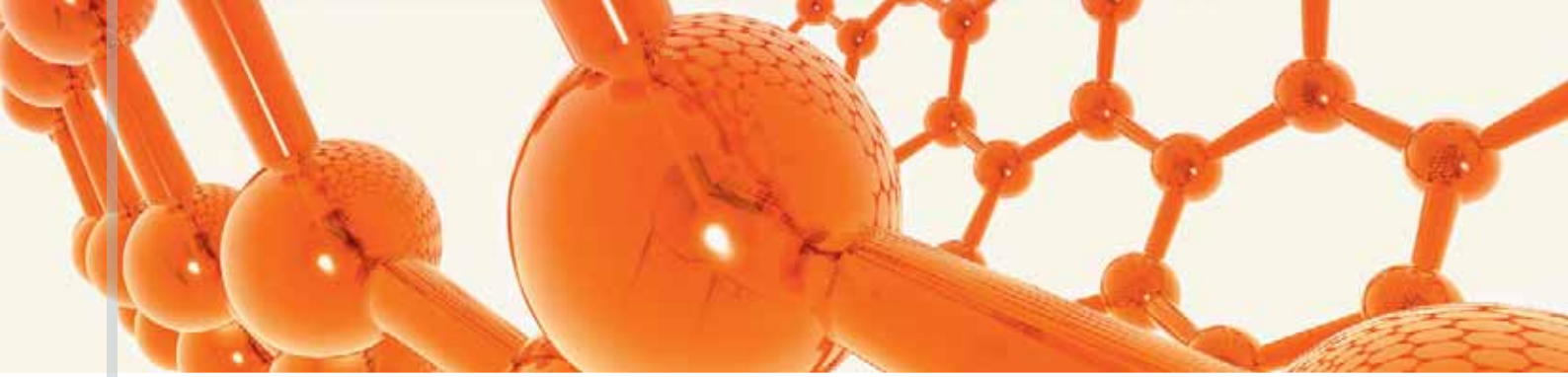
EspeRare’s promising path ahead is fuelling our determination to broaden our activities. **We are committed to pursue meaningful treatment opportunities, include patients at each step of the way, catalyse broad access to the medicine we develop, and ultimately driving measurable improvements in the lives of these children that deserve our attention and commitment.**

We deeply appreciate our partners and donors’ trust, who share our compassion for individuals and their families affected by rare diseases and expect us to deliver excellence in our work and careful stewardship of our therapeutic development programmes. We are also very grateful for all of the support we have received and have great hope that the new paradigm we are advancing will transform drug development in the field.

Together, focused on the goals, there is little we cannot do!

Sharon Terry
President

Caroline Kant
Executive Director



2014 highlights

Since it's launched in 2013, EspeRare has proven and is expanding its impact for children affected by rare diseases

This year EspeRare has **proven that it can give a second life to existing drugs for children affected by catastrophic rare diseases**. Its most advanced programme focuses on the development of a treatment in Duchenne muscular dystrophy, a deadly pediatric disease affecting 1 boy in 3600. Last year, the Foundation obtained the rights to develop Rimeporide, a dormant Merck Serono drug, for these children so desperately in need of a medicine. Since then, EspeRare has proven its ability to catalyse and fund the development of this unexplored yet promising medicine and has **reached the important milestone of validating Rimeporide's therapeutic potential** in research models of this disease. Based on these promising results, EspeRare is continuing its development and is preparing to test Rimeporide in boys affected by Duchenne (*see page 18*). As a recognition of these groundbreaking efforts, EspeRare and Merck Serono received a **"Social & Business Co-Creation: collaboration for impact" award** for this project, at the "Courage to Dare" 5th Zermatt Summit.

In addition, EspeRare is expanding its programme portfolio and has **started rescuing a second drug,** cilengitide in a degenerative condition that leads to renal failure and that is affecting children and adults alike. Cilengitide is a compound previously developed by Merck Serono in patients with brain tumors, and it's mode of action represents a possible treatment in this disease. To explore the therapeutic potential of cilengitide for those patients, EspeRare has established a partnership with Professor Moin Saleem from Bristol University that is conducting the first pre-clinical experimental investigations (*see page 20*).

In addition to these two ongoing projects, the Foundation is also expanding its collaborations with pharmaceutical companies and joined "Making More Health" programme of Boehringer Ingelheim.

EspeRare platform
R&D programmes

Peter Potter-Lesage becomes EspeRare's treasurer and board member

Translational Drug Rescue platform launch

Social & Business Co-Creation award at the Zermatt Summit

3rd programme in a rare metabolic disease

EspeRare included in the ASHOKA network, Caroline Kant becomes a fellow

JANUARY	FABRUARY	MARCH	APRIL	MAY	JUNE

With a partnership with the National Institutes of Health (USA) EspeRare has also started setting-up its Drug Repositioning Platform to support systematic identification and evaluation of untapped therapeutic opportunities in the rare diseases in its focus. (*see page 17*).

Furthermore, in June, as a tribute of EspeRare's novel venture philanthropic approach, ASHOKA, the global association that supports the world's leading social entrepreneurs who have system's changing solutions for the world has nominated EspeRare's CEO into its fellowship programme.

"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

"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

"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

Presentation of Rimeporide programme at the ICNMD congress

Experimental testing of Cilengitide for a renal disease

Therapeutic potential of Rimeporide in DMD demonstrated with preclinical package

AFM Téléthon grant obtained for Rimeporide clinical development

Boehringer Ingelheim invites EspeRare in the "Making More Health" programme

JULY	AUGUST	SEPTEMBER	OCTOBER	NOVEMBER	DECEMBER

ESPERARE GAINED RECOGNITION FOR ITS IMPACT AND SOCIAL ENGAGEMENT

January 2014

Citizen's Health COST action kick-off in Brussels

Cooperation in Science and Technology (COST) is one of the longest-running European frameworks supporting cooperation among scientists and researchers across Europe. EspeRare represented Switzerland in this action focused on Citizen's Health. Twenty-two countries are represented that aims at developing legal and scientific guidelines in the area of Citizen Health, in particular genetic testing, biobanking, health ethics and justice and public democratisation of research. ■

cost
EUROPEAN COOPERATION IN SCIENCE AND TECHNOLOGY

May 2014

EspeRare's CEO becomes ASHOKA's 11th fellow in Switzerland

Ashoka identifies, selects and supports the world's leading social entrepreneurs with innovative and system's changing solutions that have the potential to address the world most critical social challenges. Through the nomination of Caroline Kant as Ashoka fellow, EspeRare has been selected for its ground breaking positioning and approach in addressing rare diseases. ■

ASHOKA

June 2014

A winner of the Social & Business Co-Creation competition at the 5th Zermatt Summit "The Courage to Dare"

EspeRare together with Merck Serono are one of the three price winners of the "Social & Business Co-Creation: collaboration for impact" competition for its project "Advancing treatment for Duchenne". ■

ZERMATT SUMMIT

September 2014

Featured in L'Express (FR) special edition dedicated to sustainable economy: "These pioneers who are changing the world"

This edition dedicated to innovation, provides an overview of entrepreneurs at the heart of social innovation and portrays Caroline Kant, co-founder and executive director of EspeRare. ■

L'EXPRESS

November 2014

Invited into Boehringer Ingelheim "Making More Health" programme (DE),

In this context EspeRare explores the possibility to create a business partnership with this big pharmaceutical company and to benefit from the pro-bono support of experts within the company to foster the foundation future development. ■

Making more health
by Ashoka and Boehringer Ingelheim

December 2014

AFM Telethon (FR) invites Rimeporide in Duchenne in its strategic portfolio of programmes

AMF Téléthon is one of the largest patient organisation in the world. This front runner in funding rare diseases research since more than 50 years, is co-funding our programme in Duchenne. ■

AFMTÉLÉTHON
INNOVER POUR GUÉRIR

Addressing rare diseases

More than 25 million people in the US and 30 million people in Europe are affected by rare diseases

↓

50% are children

9 years on average is required for a correct diagnosis: the Diagnostic Odyssey

More than 7 000 rare diseases have been identified

80% of rare diseases have identified genetic origins

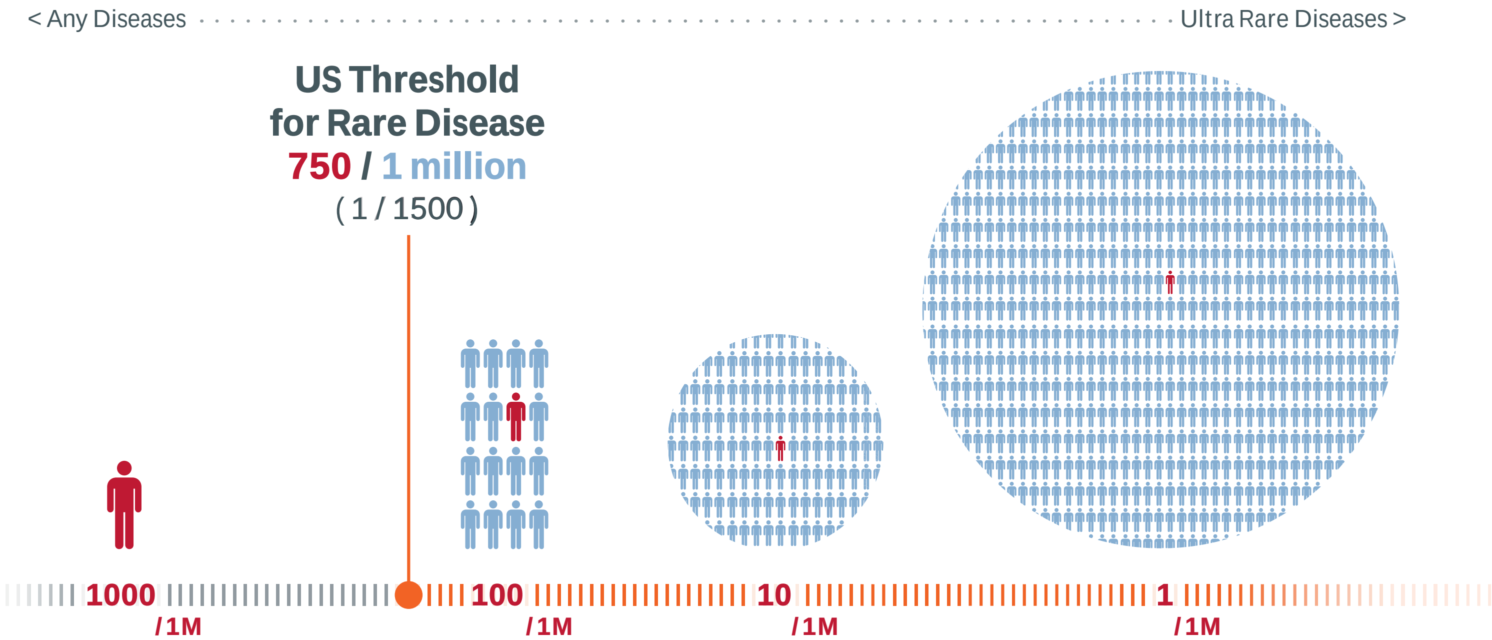
Only 5% of rare diseases have approved therapeutic solutions

Source: Orphanet and the US Orphan Drug Act

Frequency of Disease

Number of Patients per Million

(logarithmic Scale)



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

Patients are at the core of current progress in rare disease R&D:

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 part because of EspeRare's strategic partnership with Genetic Alliance, a network of more than 1,200 disease advocacy organisations.

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

1 Source: Orphanet and the US Orphan Drug Act

Advancing rare disease treatments

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

Repurposed drugs in rare diseases are generally being approved in only 3-7 years and at about 60% of the cost of typical drug development.

Along the drug development process, major hurdles prevent new treatments from reaching patients in need. In this context, repositioning existing drugs offers an opportunity to efficiently develop new treatments. Drug rescue and repositioning is the discovery and development of new therapeutic applications for existing or abandoned drugs.

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.

This approach is of interest to address medical needs in rare diseases as time associated with bringing repositioned drugs to patients is shortened and the chance of success is higher. While approximately 10% of new drug applications gain market approval, repurposed drugs approach approval rates is of about 30%. Additionally, the use of previous data significantly reduces the development costs of a new potential drug.

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

Focused on these untapped and de-risked opportunities, EspeRare identifies and develops existing drugs 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 remains economically attractive for commercial partners and beneficial for patients and the healthcare system at large. ■

ESPERARE'S IMPACT: BRINGING TOGETHER PATIENTS AND COMMERCIAL INTEREST TO ADDRESS RARE DISEASES

Several therapeutic opportunities to treat rare disease patients exist but are too often left in "drawers" of pharmaceutical companies or universities. These opportunities are never tested nor developed because biopharmaceutical companies are rarely willing to risk investing Research and Development (R&D) budget for this small market and lower potential of financial return. Academia on the other hand 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. To achieve its goals the foundation leverages its ability to:

a. Identify "dormant" repositioning opportunities with high therapeutic potential

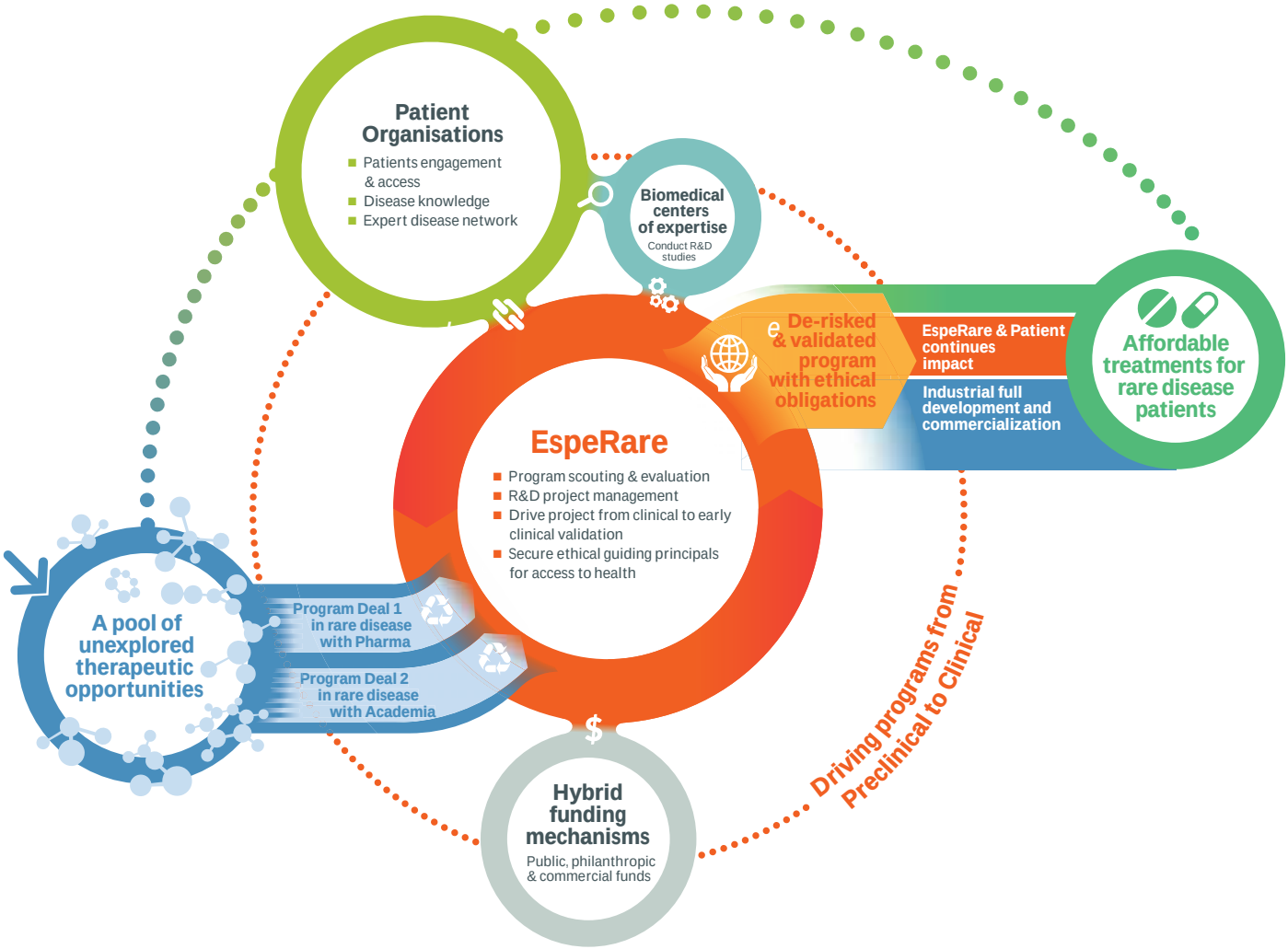
b. Onboard patient organisations to support patient to access to disease biomedical expert and facilitate drug development

c. Mobilise complementary public, philanthropic and commercial funds to finance R&D activities

d. Provide R&D and project management coordination to the drug development partners necessary to efficiently develop these opportunities

e. Partner with commercial biopharmaceutical organisation for late stage drug development and commercialisation

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 our 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 EspeRare lies in its unique ability to build a viable model that allows 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/integrates patient and commercial interests into a system that accelerates and de-risks drug development with the goal of bringing affordable new treatments to these underserved patients. ■



About the translational gap, a major roadblock for new treatments

ADDRESSING THE "VALLEY OF DEATH" IN TRANSLATIONAL RESEARCH

Therapeutic research and development require a global and integrated approach allowing continuity and integration of academic, clinical research, drug manufacturing and industrial efforts.

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 drug development expertise, the foundation coordinates all necessary R&D activities to address this gap.

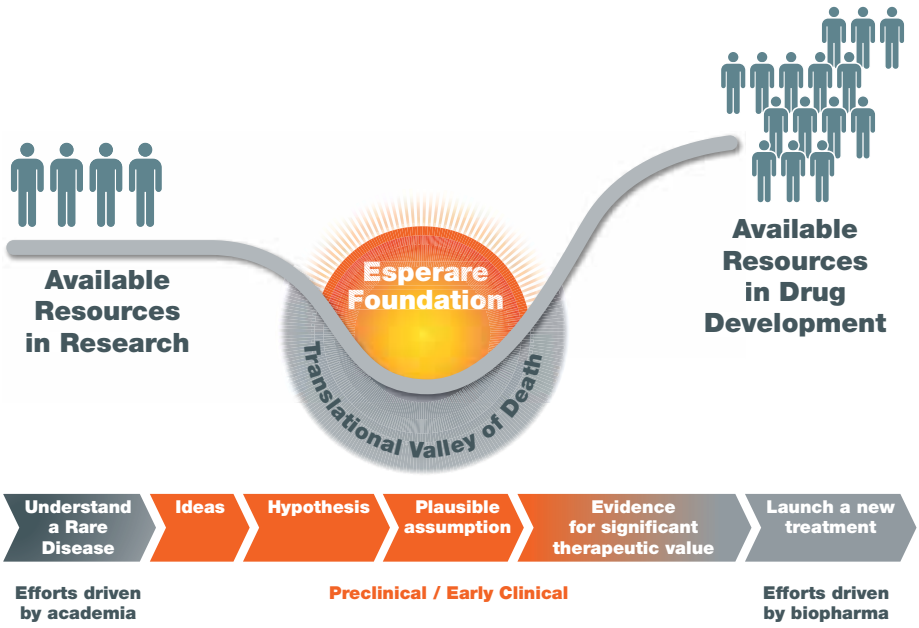
More specifically, EspeRare focuses on driving preclinical and early clinical development activities required to demonstrate human proof of concept of investigational drugs. For each of its drug development projects in a given rare disease the foundation develops a collaborative approach that:

- Integrates «Patient voice» through alliance with patient advocacy groups
- Mobilises research, clinical experts and biomedical centres of excellence to conduct preclinical and clinical development activities
- Engages industry partners ethically to manage transition into late clinical development and commercialisation
- Interacts directly with regulatory agencies and health authorities to best prepare path to approval and patient access to treatment

For each of its drug development programmes in rare diseases, EspeRare delivers product development partnerships that drive strong coordination with patient groups, clinical centres, academia, industry and regulators, ultimately overcoming the "valley of death" that prevents new treatments from reaching these patients.

Once proof of concept in humans is demonstrated and a conclusive data package generated, programmes can go back to the originator or are transferred to industry partners for 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.



ABOUT TRANSLATIONAL RESEARCH

...a scientific discipline that drives the translation of knowledge from basic sciences into the development of new treatments, ultimately helping to make findings from research useful for medical applications that enhance human health. In drug development these activities are conducted during preclinical validation until human proof of concept in early clinical development (until phase II).

EspeRare provides scientific and operational expertise to address the "valley of death" in translational research and drive the proof of concept of unexplored treatments for rare diseases.

> " **Bridging the gap between basic science and clinical development is critical for the successful development of more products for rare diseases. We, here in the Office of Orphan Products Development at FDA, were very interested to learn about EspeRare."**
>
> **Gayatri R. Rao, M.D., J.D.**
> Director for the FDA's Office of Orphan Products Development Chair of Paediatric Neurology, University College of London

Building our portfolio

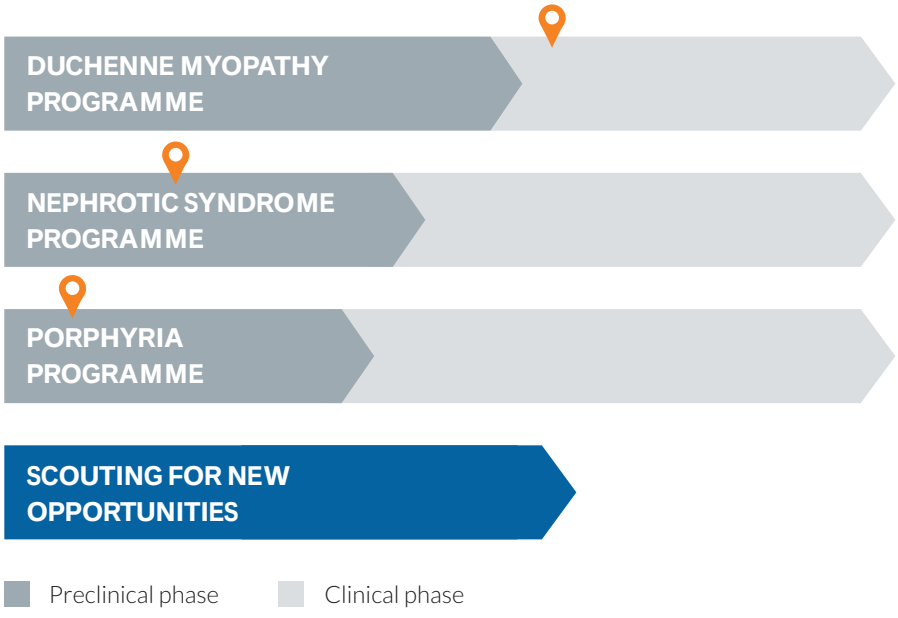
With its first programme, EspeRare has proven its ability to give a chance to dormant therapeutic opportunities. **After one and a half years, the foundation has now demonstrated the therapeutic potential of a shelved drug to treat children burden by debilitating muscular degeneration.** This first programme is also a validation of the strength of EspeRare's philanthropic model to drive and fund drug development in rare diseases (*see page 18-19*).

Beyond this first programme, the foundation is building a robust and diversified portfolio of programmes that have the potential to address critical unmet medical needs in EspeRare's rare diseases of focus. Towards this goal EspeRare has initiated a new project in a rare renal disease and is evaluating others with a number of partners.

EspeRare is looking to diversify its partners and develop its portfolio in rare diseases by:

- Working with pharmaceutical companies, academia and patient organisations to identify opportunities that fit EspeRare's development model and 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



ESPERARE'S UNIQUE ABILITY TO IDENTIFY DRUGS TO RESCUE OR REPOSITION IN RARE DISEASES

A two-way integrated *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:

1. A drug 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 Institutes of Health** (US) is providing personalised access to data on drugs developed worldwide.

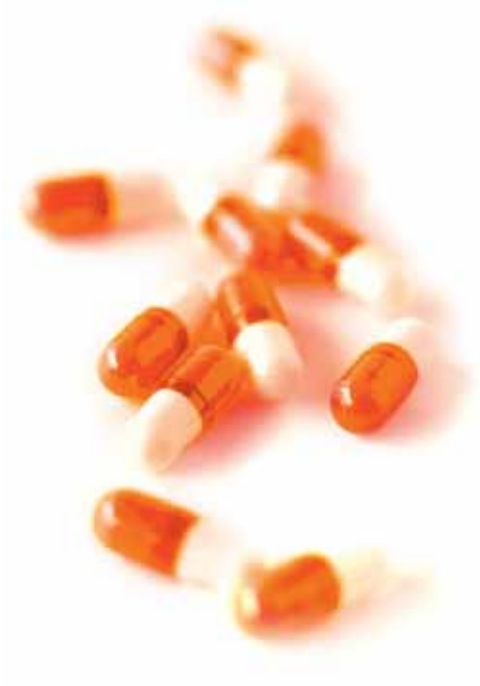
2. Rare disease biomedical maps: integrating biomedical data on the molecular pathophysiology of the 30 targeted rare diseases. The information is extracted from scientific literature. This understanding of the biological cascades involved in these diseases is improved thanks to the contributions from biomedical experts in EspeRare's network.

Wise selection of existing drugs with de-risked priorities within the Drug database and identification of new disease applications using the Rare diseases biomedical maps allow to uncover de-risked rescue or repositioning opportunities with sound therapeutic potential.

A first version of the Drug Repositioning platform was launched in March 2014. The capabilities of the platform are being enhanced and other data sources will be 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.

When possible, before initiating the full development of these new therapeutic opportunities discovered with the *in silico* approach, EspeRare conducts an interim *in vitro* validation assessment. To this end, the organisation collaborates with medical reference centres of a given disease to access patient samples (e.g.: blood or tissue specimens) and experimentally test, in these samples, the capacity of the selected drug(s) to positively modulate the targeted pathophysiological mechanisms. ■



GAUGERX, A COLLABORATIVE PROJECT WITH GENETIC ALLIANCE

This open access, interactive, web-based tool under development is integrating and translating available scientific knowledge on rare diseases to support drug development. GaugeRx 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)

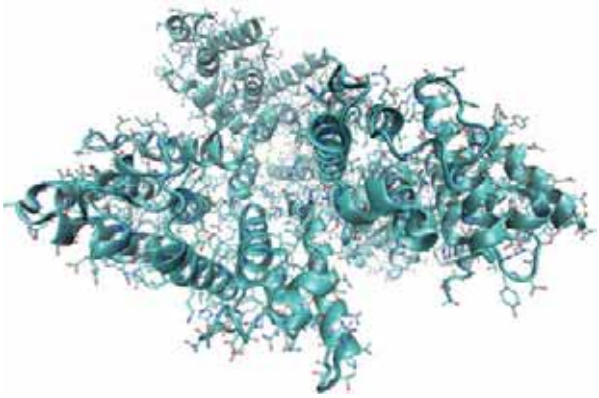
ABOUT DUCHENNE MUSCULAR DYSTROPHY (DMD)

Duchenne muscular dystrophy (DMD) is a rare genetic pediatric disease that affects approximately 1 in 3500 male births worldwide. It is a rapidly progressive form of muscular dystrophy caused by a mutation in a gene which encodes the dystrophin protein. Its absence causes progressive skeletal muscle degeneration leading to a loss of ambulation around the age of 10. Then progressive respiratory muscle weakness and cardiac failure both represent major life-threatening complications.

Today there is no cure for DMD boys. Several therapeutic attempts including gene therapy, transplantation of stem cells, exon skipping treatments as well as classical pharmacological approaches (anti-inflammatory and antifibrotic) are currently being investigated. The use of corticosteroid is the main pharmacological intervention, but it has limited efficacy and induces severe side effects such as diabetes and respiratory infections. A new treatment Translarna is now also marketed as a therapy that prolongs ambulation in 13% of DMD patients with a specific mutation.
However 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. ■

RIMEPORIDE IDENTITY CARD:

Name:	Rimeporide
Target:	Sodium-Proton (Na+/H+) Exchanger (NHE-1) inhibitor
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 generated in DMD animal model (mdx mice)
Opportunity:	Robust beneficial anti-inflammatory, anti-fibrotic and cardioprotective effects demonstrated in DMD and heart failure animal models.Therapeutic potential to prolong ambulation and delay cardiomyopathy in all patients with DMD; good safety profile in human.



The Dystrophin protein
by Dr. Jiri Mareda

> **“ Rimeporide has demonstrated its potential to transform Duchenne muscular dystrophy from a life threatening to a chronic disease.”**
>
> **Prof. Denis Duboc,**
> Cardiologist, Hôpital Cochin, Paris

VALIDATION OF RIMEPORIDE’S THERAPEUTIC POTENTIAL IN DMD ACHIEVED

Rimeporide is a safe, potent and selective NHE- 1 inhibitor which has shown beneficial effect in several animal models of heart failure and was already administered to several healthy adults.

Rimeporide represents an innovative and promising approach to address muscle degeneration and cardiomyopathy in Duchenne muscular dystrophy. In line with its model, EspeRare is allowing and accelerating the development of this new therapeutic opportunity by leveraging:

a. extensive data on pharmacology, toxicology, and human safety;
b. partnerships with patient organisations and medical diseases experts;
c. public and philanthropic grants to co-fund the development of the opportunity.

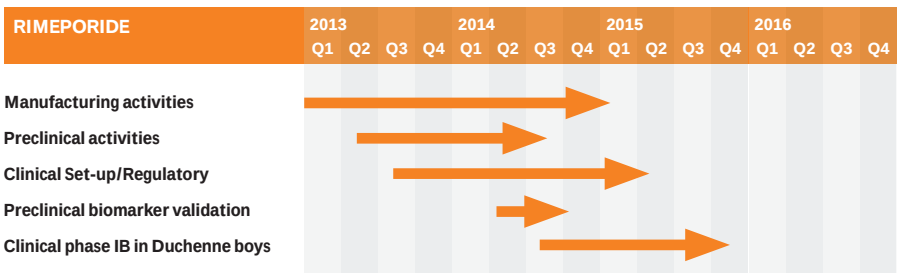
This year, EspeRare successfully conducted two non-clinical studies in collaboration with the Children National Medical Centre (USA) and the University of Geneva (Switzerland). These studies have demonstrated Rimeporide’s ability to significantly decrease levels of inflammation and fibrosis in a large panel of skeletal muscles and in the heart. Those results combined to prior results in heart failure provide strong evidence that Rimeporide has the potential to prolong ambulation and to delay progression of cardiomyopathy in all patients with DMD, regardless of the mutation they carry.

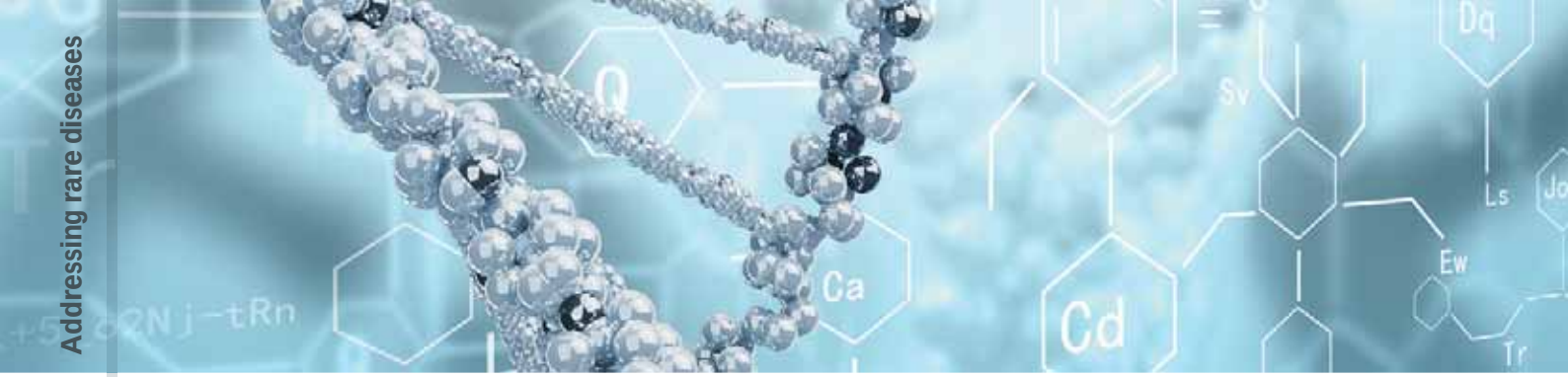
Since December 2014, there is now robust safety and efficacy evidence to support clinical development of Rimeporide in DMD young ambulant patients. This first study in Duchenne boys will start in 2015, in main European clinical centres and will be supervised by leading experts in the field (Prof. F. Muntoni, Prof. S.R. Mercuri, Prof. T. Voit). It will evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of Rimeporide in DMD.

In October 2014, EspeRare has filed an Orphan Drug Designation for Rimeporide in Duchenne to the European Medicines Agency (EMA). A positive opinion is expected in March 2015 and, if granted, will secure a 10- year data exclusivity in Europe.

PATIENTS’ GROUPS AND EXPERTS’ ALLIANCES TO STRENGTHEN RIMEPORIDE DEVELOPMENT STRATEGY

- ***Funds granted by French Telethon (AFM) & Swiss Technology & Innovation (CTI) to support ongoing research in animals and cells.***
- ***Key collaboration established with neuromuscular patient associations: PPMD (US) & AFM (France), Action Duchenne (UK), MD Campaign (UK).***
- ***Strategic partnership with clinical centres of Excellence : University College of London (UK), Association Institut de Myologie and Genethon (Paris, France), CHUV (Lausanne, Suisse), University Catholic of Roma (Italy)***





Second programme: Cilengitide in Focal Segmental Glomerulosclerosis (FSGS)

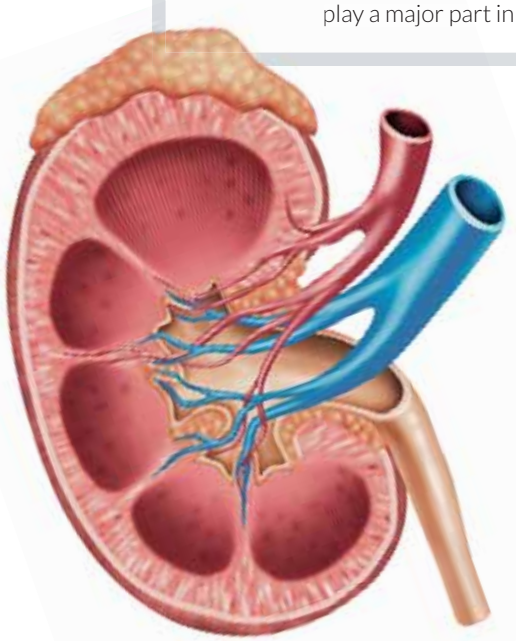
ABOUT FOCAL SEGMENTAL GLOMERULOSCLEROSIS

Focal segmental glomerulosclerosis is a rare disease that results in impaired renal function due to injury and scarring of the glomeruli which are 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.

Currently, there is no cure for this debilitating disease and the cause of FSGS is unknown. This is a lifelong chronic disease and the disease burden to patients is tremendous. In particular, it often requires management by dialysis and in some cases transplantation. This rare form of a nephrotic syndrome affects both children and adults with peaks at 6-8 and 20-30 years of age, respectively. The life expectancy of a 10 year-old child on haemodialysis due to end stage kidney disease is dramatically reduced. ■

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 more than 1600 adults (Phases I to III) for cancer and being evaluated non-clinically using human podocytes 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



CILENGITIDE, A REPOSITIONING OPPORTUNITY FOR A PHASE III DEPRIORITISED ASSET

Cilengitide is an investigational compound developed by Merck Serono. The small molecule is a potential first-in-class αvβ3 integrin inhibitor that was in clinical development in oncology until Phase III. The development of this drug candidate was halted in 2013 as cilengitide failed to meet its primary endpoint of significantly increasing overall survival when added to the current standard chemoradiotherapy regimen.

Published scientific data suggest that the inhibition of activation of αvβ3 integrin could potentially modulate the pathologic processes characterised by inappropriate motility of podocytes in FSGS. EspeRare has initiated a study to test the ability of cilengitide, to modulate the motility of podocytes in an experimental in-vitro model, using human cells. If demonstrated, such an effect could potentially translate into a reduced or halted decline of renal function and progression to end stage kidney disease in patients. In that context, cilengitide represents an attractive investigational candidate for a potential future treatment for FSGS.

PATIENT GROUPS AND EXPERT ALLIANCES TO STRENGTHEN CILENGITIDE DEVELOPMENT STRATEGY

- *Co-funding with Merck Serono (Switzerland)*
- *EspeRare is part of a European Nephrotic Syndrome Consortium (CoNeCon: comprised of partners from both industry and academia) and will present in February at the kick off*

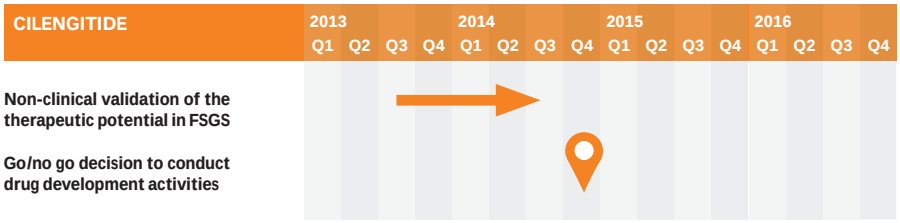
CURRENT NONCLINICAL STUDIES TO VALIDATE THE THERAPEUTIC RESCUE OPPORTUNITY

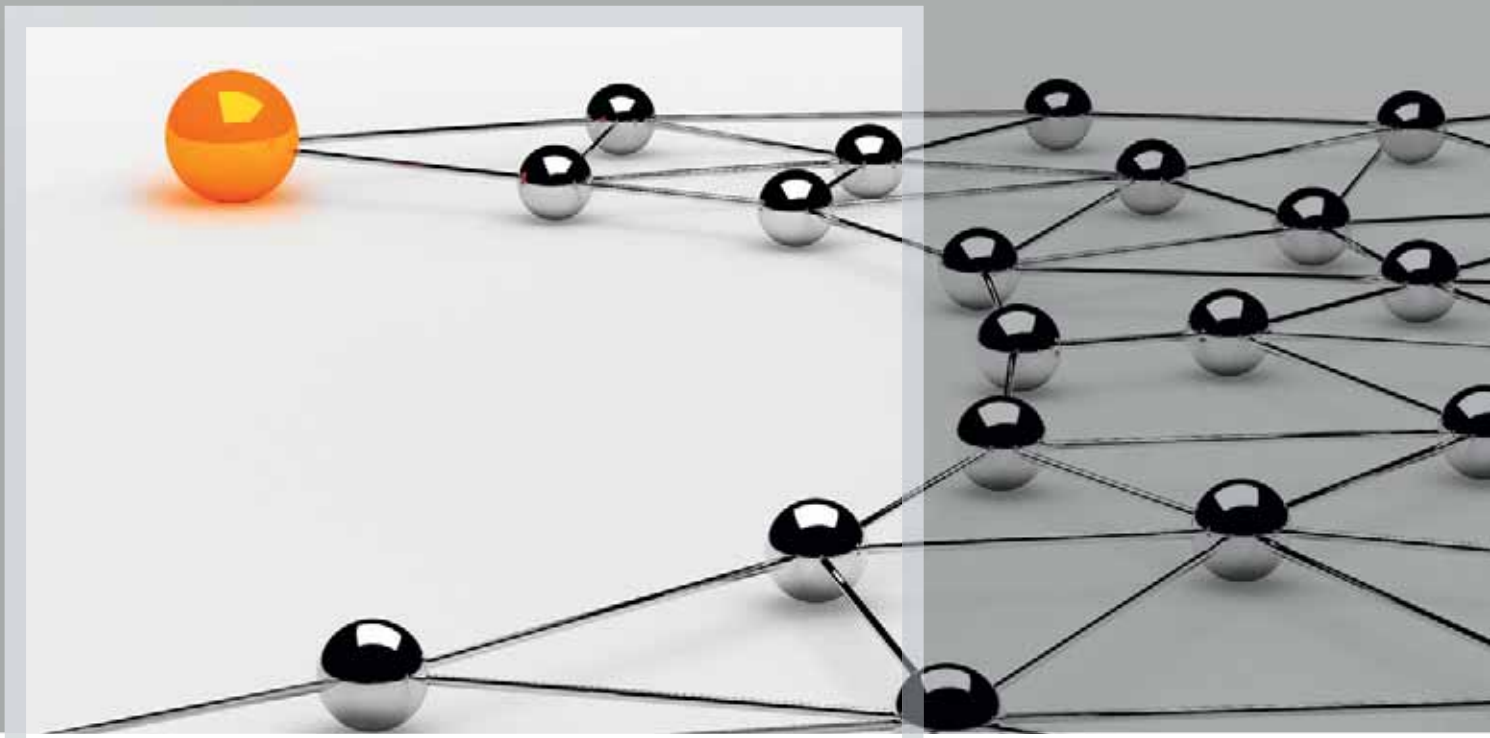
EspeRare is validating this drug rescue opportunity using a unique immortalised human podocyte cell line.

A STUDY IN COLLABORATION WITH PROFESSOR MOIN SALEEM AT BRISTOL UNIVERSITY (UK)

The research on cilengitide's therapeutic potential in experimental models of podocyte activation and motility is conducted under the leadership of Professor Moin Saleem, an expert in glomerular diseases and in particular nephrotic syndrome, at Bristol University, School of Clinical Sciences. He is also in charge of the UK FSGS patient registry.

This first assessment of the therapeutic potential of cilengitide in non clinical models of focal segmental glomerulosclerosis is set to be completed by Q2 2015, and is co-funded by Merck Serono.





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 its 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 and the CEO of Genetic Alliance, located in 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. ■

THE FOUNDATION BOARD

Monique A. Caillat

Béatrice Greco

Peter Potter-Lesage

Ewen Sedman

Sharon F. Terry - President

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 in neurology while heading the translational testing of investigational drugs. Since 2009, within the Platform of Global Health she has led novel and integrated translational research programmes in neglected diseases.

Beatrice's passion for innovation and her particular interest in applying science to address neglected diseases 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 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 steering committee of the International Rare Disease Research Consortium and an Ashoka Fellow.

HEAD OFFICE

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.

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 programme leader and successfully led several R&D programmes 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.

Caroline Kant-Mareda

Florence Porte-Thomé

TEAM

ILARIA DI RESTA

Ilaria has over 13 years 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.

MYRIAM EL GAALOUL

Myriam is a PharmD with 10-year experience in clinical development. In her career, she led early phase drug development programmes and clinical trials in diverse therapeutic areas (e.g. neurology, oncology, fertility, and rheumatology), in various environments (e.g. hospitals, pharmaceutical organisations, contract research organisations) and across nearly all continents. Myriam provides her clinical pharmacology and project management expertise to EspeRare.

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.

DIANE MELLETT

Diane is a dually qualified US and UK lawyer with over 20 years' experience in the Biotech and Pharma area. With her seasoned expertise in establishing drug development partnerships, she has supported EspeRare with collaborative and licensing agreements. Before working as an independent advisor to clients, she was General Counsel at Cambridge Antibody Technology plc.

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.

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 biotech. 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 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 the management of preclinical and translational activities of the foundation's programmes.

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 honors, 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

Stéhane Blot is heading the neurobiology laboratory of theVeterinary 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 addition, within Transgene, a world leader in gene therapy, he became in 2001 its research director working on projects in cancer immunotherapy and infectious diseases. Recently as a recognition for his impact in the rare disease drug development he has been named in 2014 the "Inspirational Stakeholder of the Year" at the 5th Annual Congress "World Orphan Drug Congress". In addition to his role, Dr Braun is advising EspeRare on the strategic development of Rimeporide in Duchenne.

DR. PIERRE CARLIER

Pierre Carlier, MD, PhD, CEA, is the Director of 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, in 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 as the NHGRI Director's Genome Advance. 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 clinical development in the CNS area within the pharmaceutical industry including experience in 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 is an advisor to EspeRare for the programme in Duchenne and subsequent programmes in neuromuscular diseases.

PROF. ANTOINE HADENGUE

Antoine Hadengue is a Professor of Gastroenterology and Hepatology, at the University Hospital 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 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 like an antiepileptic under development as an approved orphan drug, the repositioning of a compound developed for cancer to treat the rare disease African sleeping sickness, a treatment for a rare thyroid cancer. Prof. Ramaiah is now working since 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 like orphan cancers, 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 disease. 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, 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 and which allows molecules such as cilengitide to be tested as potential treatments for FSGS.

DR. LAURENT SERVAIS

Laurent Servais is a paediatrician and is 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 national centre of expertise in clinical myology in Paris. In addition of 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 the 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. After that he specialised in ion transport in the kidney under acidic conditions at the University of Mainz. For 16 years of experience in cardiovascular research at former Hoechst AG, heading a Research Team. Thereafter, he became the head of cardiovascular research at Merck KGaA Darmstadt and is now heading the drug repositioning activities at Merck Serono. Wolfgang provides its know-how into NHE biology and contributes with his cardiovascular biomedical expertise for EspeRare's project in Duchenne muscular dystrophy.

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 1 employee and 9 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 SFG Société Fiduciaire et de Gérance SA 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 2014

The year was characterised by a number of factors. Considerable donations were received or confirmed for the future, staff were recruited, planning was activated and, most important of all, ***Research & Development Project funding increased significantly to CHF 1,176,054*** (note 8 a-e), .as compared to CHF 429,159 in 2013.

Founding Capital

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

Donations

Donations recognised in 2014 amounted to CHF 1,312,622 including one from the Loterie Suisse Romande received in the final quarter of 2013 of CHF 150,000 for activities the following year and thus deferred to 2014.

A total of CHF 1,229,709 from Merck Serono was recognised in 2014 with a further 25,409 being deferred to 2015. Also recognised in 2014 was a contribution from AFM Telethon for CHF 82,912. In addition, Awards & Support of 162,208 were recognised from ASHOKA and the Loterie Romande. Finally, an amount of CHF 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).

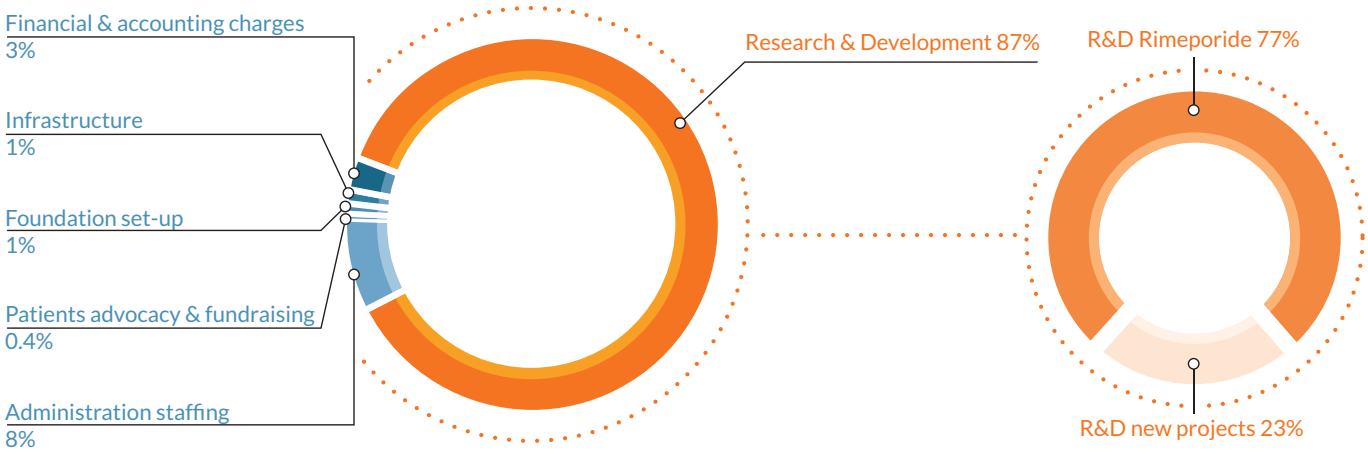
Staff

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 9 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 2014



THE FINANCIAL YEAR AHEAD TO DECEMBER 2015

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 and USD 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.

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 CHF 1.5 million in 2015, rising to around CHF 3 million for 2016.

Conclusion

The detailed financial tables that follow – Balance Sheet, Statement of Income & Expenditure – represent EspeRare in its second 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 2014

	NOTES	2014	2014	2013	2013
ASSETS		**CHF**	**EUR**	CHF	EUR
CURRENT ASSETS					
Cash & Cash Equivalents	2i				
BCGE Current Accounts		2 072 923,83	1 724 060,24	1 862 480,76	1 519 772,14
Prepaid & Receivables					
Accounts Receivable		0,00	0,00	27 000,00	22 031,82
Prepaid Expenses & Accrued Income		13 845,55	11 515,41	0,00	0,00
Withholding Tax & VAT Receivable		695,35	578,33	381,27	311,11
TOTAL CURRENT ASSETS		**2 087 464,73**	**1 736 153,97**	**1 889 862,03**	**1 542 115,08**
FIXED ASSETS					
Tangible Assets					
Computers & Equipment	2d	7 768,70	6 461,26	5 541,85	4 522,11
(less depreciation)		(4 366,75)	(3 631,85)	(1 847,28)	(1 507,37)
TOTAL FIXED ASSETS		**3 401,95**	**2 829,42**	**3 694,57**	**3 014,75**
TOTAL ASSETS		**2 090 866,68**	**1 738 983,39**	**1 893 556,60**	**1 545 129,82**
LIABILITIES					
CURRENT LIABILITIES					
Short Term Liabilities					
Suppliers		57 560,90	47 873,66	22 769,80	18 580,01
Employees Accounts		158,05	131,45	853,34	696,32
Social Charges		453,35	377,05	12 578,75	10 264,18
Total Short Term Liabilities		**58 172,30**	**48 382,17**	**36 201,89**	**29 540,51**
Provisions	2f	**190 900,00**	**158 772,40**	**17 080,00**	**13 937,17**
Deferred Income	7a	**25 409,19**	**21 132,94**	**150 000,00**	**122 399,02**
TOTAL CURRENT LIABILITIES		**274 481,49**	**228 287,51**	**203 281,89**	**165 876,70**
CAPITAL & RESERVES					
Foundation Capital	9	50 000,00	41 585,23	50 000,00	40 799,67
Operations Reserve	3	1 766 385,19	1 469 110,65	1 640 274,71	1 338 453,46
TOTAL CAPITAL & RESERVES		**1 816 385,19**	**1 510 695,88**	**1 690 274,71**	**1 379 253,13**
TOTAL LIABILITIES		**2 090 866,68**	**1 738 983,39**	**1 893 556,60**	**1 545 129,82**

For the ease of reference of our stakeholders, equivalent Euro figures have been provided at the official end-of-year rate of 1 ,2255 for 2013 and 1.20235 for 2014

ESPERARE STATEMENT OF INCOME & EXPENDITURE FOR THE PERIOD FROM JANUARY 1ST TO DECEMBER 31, 2014

	NOTES	2014 12 months CHF	2014 12 months EUR	2013 9 months CHF	2013 9 months EUR
INCOME					
R&D Income	2b/7a	1 312 621,59	1 091 713,39	2 241 000,00	1 828 641,37
R&D Services		0,00	0,00	25 000,00	20 399,84
Financial Income	2k	897,36	746,34	1 088,76	888,42
Other Income		6 064,50	5 043,87	202,47	165,21
Awards & Support	2b/7a	162 208,31	134 909,39	0,00	0,00
TOTAL INCOME		**1 481 791,76**	**1 232 412,99**	**2 267 291,23**	**1 850 094,84**
EXPENDITURE					
Research & Development Expenditure	2e				
R &D Projects	8a				
Rimeporide	8b				
Research & Development		503 591,83	418 839,63	169 869,51	138 612,41
Support Costs	8g	400 316,29	332 944,89	166 649,05	135 984,54
Legal Fees	8h	1 653,75	1 375,43	22 638,65	18 472,99
TOTAL R&D PROJECTS, RIMEPORIDE		**905 561,87**	**753 159,95**	**359 157,21**	**293 069,94**
NEW PROJECTS	8c				
Repositioning Platform	8d	135 316,34	112 543,22	3 000,00	2 447,98
Support Costs	8g	**56 981,59**	**47 391,85**	**67 002,05**	**54 673,24**
Cilengitide	8e	25 365,00	21 096,19	0,00	0,00
Support Costs	8g	52 829,33	43 938,40	0,00	0,00
Total New Projects		270 492,26	224 969,65	70 002,05	57 121,22
TOTAL RESEARCH & DEVELOPMENT EXPENDITURE		**1 176 054,13**	**978 129,60**	**429 159,26**	**350 191,15**
General Foundation Administration	8g				
Administration staffing & volunteers	8g	105 483,68	87 731,26	72 265,43	58 968,12
Patient Association Consultancy		5 057,21	4 206,10	39 584,80	32 300,94
Office Rental & Costs		12 849,02	10 686,59	10 205,99	8 328,02
Accounting & Audit Expenses		29 025,08	24 140,29	7 759,00	6 331,29
Other Expenses		9 586,23	7 972,91	18 732,18	15 285,34
General Legal Fees		179,26	149,09	11 459,28	9 350,70
Fundraising		70,00	58,22	752,50	614,04
Financial Charges		1 639,76	1 363,80	593,96	484,67
Exchange Differences	2c	12 325,21	10 250,93	29 207,23	23 832,91
Board meeting		892,23	742,07	5 449,61	4 446,85
Depreciation		2 519,47	2 095,45	1 847,28	1 507,37
TOTAL GENERAL ADMINISTRATION EXPENDITURE		**179 627,15**	**149 396,72**	**197 857,26**	**161 450,23**
TOTAL EXPENDITURE		**1 355 681,28**	**1 127 526,33**	**627 016,52**	**511 641,39**
RESULTS FROM OPERATING ACTIVITIES	3	**126 110,48**	**104 886,66**	**1 640 274,71**	**1 338 453,46**

NOTES TO FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2013

1. ORGANISATION

The EspeRare foundation ("EspeRare") is a Swiss Foundation, established as a not-for-profit legal entity, registered in Geneva under statutes dated 27 March 2013. It is managed by a foundation board, an executive director and 2 senior managers.

With its head-office in Geneva, the aim of EspeRare is to bring public and private sector partners together to both fund and provide managerial and logistical support to drive the identification and development of treatments for rare diseases. The foundation focuses on accelerating the cost-effective development of unexplored (re)positioning opportunities for rare neurological and immunological diseases. In partnership with patient 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 recognised 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 Standards
The accounting standards followed are those of the Swiss Code of Obligations, articles 957 to 964.

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. A reconciliation between donations received in cash and income recognised in the income and expenditure account is shown in note 7.

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 1.20235
1 USD = CHF 0.993636

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.

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) 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.

h) Fair Value
The fair value of cash, other assets, deferred income and accounts payable are not materially different from the carrying amounts.

i) Cash and Cash Equivalents
Cash and cash equivalents comprise cash balances of current accounts.

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

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

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

3. RESERVES

Operations reserve
The Operations Reserve represents excess of donations over expenditure for the period and is 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. The currencies giving rise to this risk are principally the Euro and the US Dollar.

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 2014 does not differ from their carrying amounts shown in the balance sheet.

5. COMMITMENTS

As at 31 December 2014, there were no significant capital expenditure commitments

6. SUBSEQUENT EVENTS

No events occurred subsequent to 31 December 2014 and prior to the approval of the financial statements that would require modification of or disclosure in the financial statements.

7. INCOME

a) Donations received at bank:

During 2014 the following donations were granted:

Donor	Currency	Total Grant	Recognised 2014 CHF	Deferred 2015 CHF	Notes
R&D Income					
ARES Trading SA (Merck Serono Affiliate)	EUR	1,000,000	1,204,300		I&EStatement - Rimeporide
ARES Trading SA (Merck Serono Affiliate)	EUR	20,889	25,409		I&EStatement - Cilengitide
ARES Trading SA (Merck Serono Affiliate)	EUR	20,889		25,409	Cilengitide - Research & development
AFM Telethon	EUR	68,000	82,912		Grant Rimeporide fully committed in 2014
TOTAL		**1,109,777**	**1,312,622**	**25,409**	**R&D Income**
Awards & Support					I&EStatement
ASHOKA	EUR	10,000	12,208		I&EStatement
Loterie Suisse Romande *	CHF		150,000		Deferred Income
TOTAL			**162,208**		**Awards & Support**
Off Balance Sheet:					
Commission of Technology and Information **	CHF		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 awarded & directly transferred to our academic partner the University of Geneva by CTI

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 & 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) 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 programme managers. In addition, EspeRare benefits from a number of consultants and volunteers. Total staff benefits for 2014 amount to CHF 617'395,99 (Salaries & Social charges amount to CHF 586'408,05, Travel Expenses amount to CHF 27'002,78 and Volunteers reimbursements amount to CHF 3'985,16).

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 finalisation related to the Rimeporide project.

9. 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.

10. GOVERNANCE

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

Members of the Board act on a voluntary basis and may not claim any financial compensation other than expenses incurred such as travel and accommodation. For activities over and above the normal requirements of the position, each Member may receive appropriate reimbursement and compensation. Payment of any such reimbursement or compensation is only permissible where it corresponds to a service carried out for the benefit of the Foundation. Employees paid by the Foundation such as the Executive Director and the R&D Director serve on the Board only in an advisory capacity and have no voting rights.

11. RISKS AND UNCERTAINTIES

EspeRare encounters certain risks and uncertainties in conducting its affairs. These risks and uncertainties have financial statement implications. In all instances, these have been considered in the financial statements, despite the fact that the outcomes of these uncertainties can not be predicted with absolute certainty. Management has concluded that provisions for these risks are appropriate, and any adverse resolution of these uncertainties will not have a material impact on the financial position or results of the foundation.

SFG

Report of the statutory auditor on the limited statutory examination to the Foundation Board of Fondation EspeRare, Plan-Les-Ouates

As statutory auditor, we have examined the financial statements (Balance Sheet, Statement of Income & Expenditure, and Notes to financial statements) of Fondation EspeRare, for the year ended 31th December 2014.

These financial statements are the responsibility of the Foundation Board. 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 company personnel and analytical procedures as well as detailed tests of company documents 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 company's articles of incorporation.

Geneva, March 25th, 2015

SFG Conseil SA

Ph. Schmuz
Licensed audit expert
(Auditor in charge)

E. Carmine
Licensed auditor

Encl. :

Financial statements including :
- Balance Sheet
- Statement of Income & Expenditure
- Notes to financial statements

S34/C76/B84-4620-rapport restreint 2014 - n°4322

How you can support EspeRare

FUNDING

Throughout our activities we are committed to raise and use public and private funding, in a socially responsible and nonprofit manner.

DONORS

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

Its capital is built through institutional and private donations, bequests, grants and also by the product of its R&D activities. In line with its nonprofit status, all revenues generated by the foundation through the development of therapeutic assets are reinvested for new rare disease programmes in its portfolio. Neither endowment nor share in net profits of the foundation shall be given or distributed to a director, employee or any other individual.

Please do not hesitate to contact us for further detailed information. ■

The foundation has joined the Transnational Giving Europe (TGE) network, a partnership of leading European foundations and associations that facilitates tax-efficient cross-border giving within Europe. The TGE network enables donors, both corporations and individuals, resident in one of the participating countries, to financially support non-profit organisations in other member countries, while benefiting directly from the tax advantages provided for in the legislation of their country of residence.

THEY SUPPORT US

AFMTÉLÉTHON
INNOVER POUR GUÉRIR

Making more health
by Ashoka and Boehringer Ingelheim

Children's National

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

cost
EUROPEAN COOPERATION IN SCIENCE AND TECHNOLOGY

FONDATION Eclosion
Sciences de la Vie

Genetic Alliance

INSTITUT DE MYOLOGIE
INNOVER POUR GUERIR

Avec le soutien de la
Loterie Romande

MMV
Medicines for Malaria Venture

MERCK

Microsoft

NATIONAL INSTITUTES OF HEALTH

TREAT-NMD
Neuromuscular Network

University of BRISTOL

UNIVERSITÉ DE GENÈVE

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**