English

PEOPLE AND IDEAS FOR INNOVATION IN HEALTHCARE

Chiesi

Annual Report 2016

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www.chiesi.com

01 Introduction

[Our Mission]

Our aim is to be recognised as a research-focused international Group, able to develop and commercialise innovative pharmaceutical solutions to improve the quality of human life

We wish to maintain a high quality entrepreneurial team characterised by self-confidence and a collaborative spirit.

Our goal is to combine commitment to results with integrity, operating in a socially and environmentally responsible manner.

Chiesi

AT A GLANCE

Chiesi is an international, research-focused company, based in Parma, Italy.
Through our ***80 years*** in business, we have established a strong heritage in producing innovative pharmaceutical solutions to improve the quality of human life. We are committed to delivering outstanding results with integrity, operating in a socially and environmentally responsible manner.

Our focus is on **three core therapeutic** areas:

THERAPEUTIC AREA
Respiratory

€ 966
Sales mio €

THERAPEUTIC AREA
Neonatology

€ 233
Sales mio €

THERAPEUTIC AREA
Rare Diseases & Special Care

€ 361
Sales mio €

Our **pioneering work in research and development**, and in producing treatments that address unmet needs in these and other areas continues to pay off. **In 2016, the company continued to grow across all measure**.

Turnover 2016

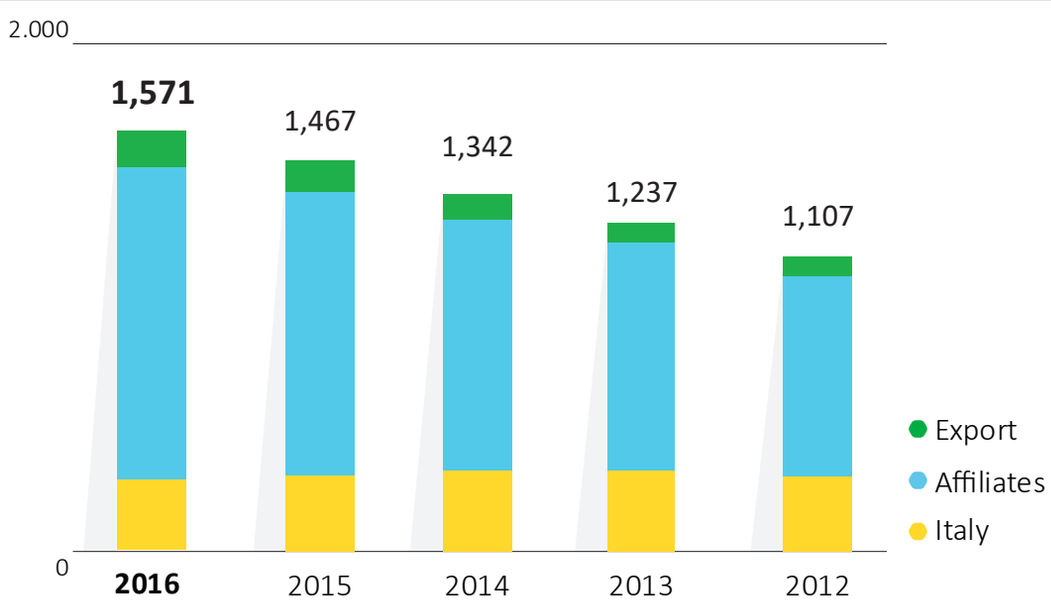
(IN MILLIONS OF EURO)

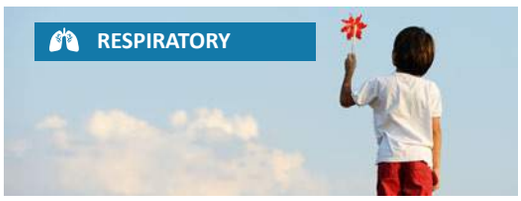
Global
1,571
Growth on **2015** 7%

Europe
1,037
Growth on **2015** 4.9%

US
252
Growth on **2015** 10.6%

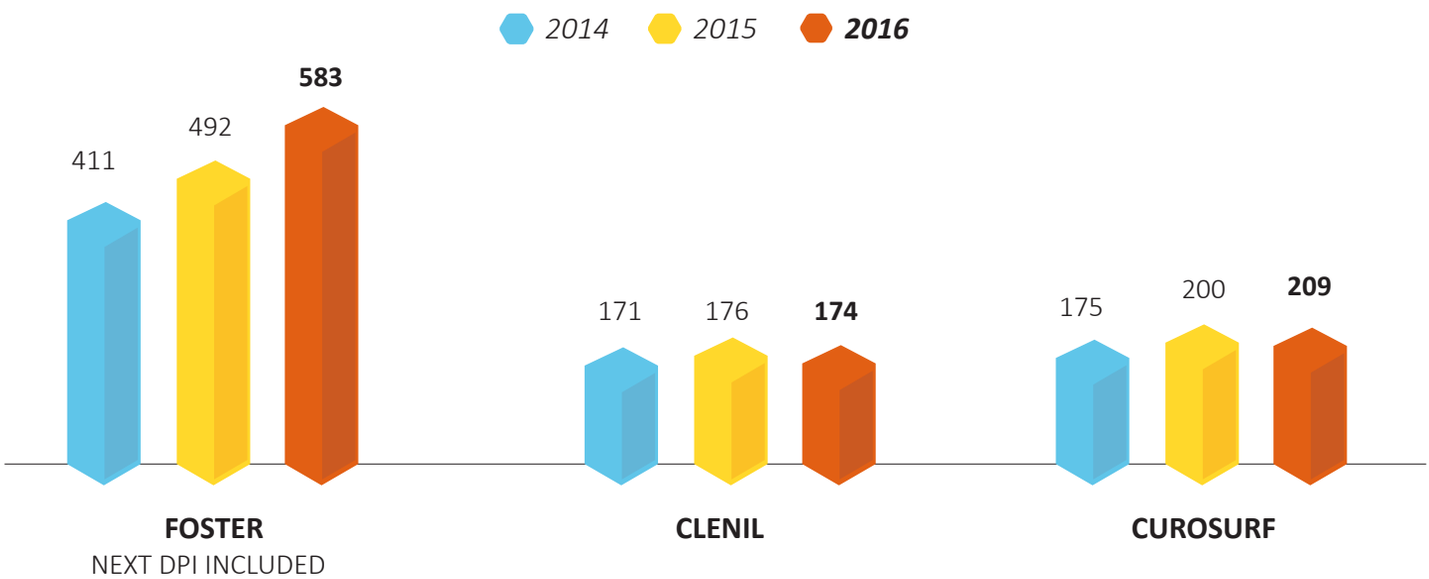
Emerging Markets and IMDD
286
Growth on **2015** 10.5%

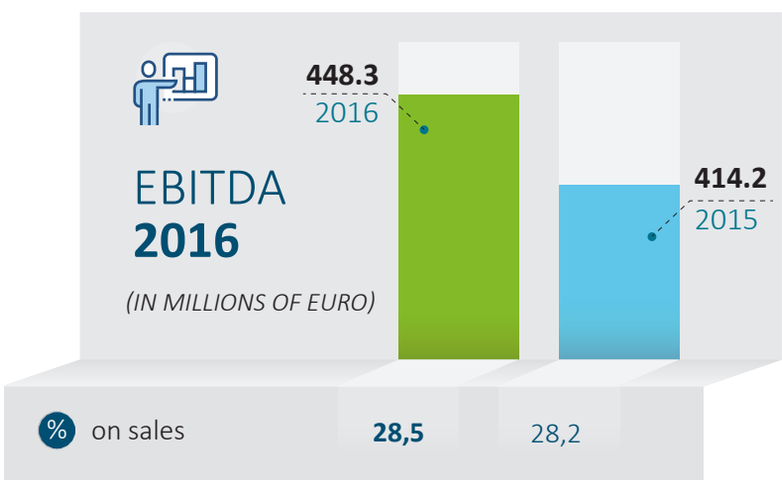




Main products

(IN MILLIONS OF EURO)





PORTFOLIO

51

active research and development projects

Employees worldwide

3,900 2013

4,100 2014

4,500 2015

4,813 2016

671
employees in R&D, including regulatory activities

694
employees in manufacturing

2016 Milestones

ACQUISITIONS IN EUROPE

Atopix Therapeutics Limited

The Group has acquired **Atopix** – a UK company with a new research project for severe asthma, enhancing Chiesi's portfolio in the respiratory therapeutic area.

Chiesi Spain
has acquired Lipograsil from Zambon Group

A Range of dietary supplements for weight control based on vegetable and micronutrient ingredients, placing itself in a key segment of the Spanish OTC area with a strong and already consolidated market.

COMMERCIAL AGREEMENTS

Chiesi Italy

Chiesi Italy, the Italian affiliate of the Chiesi Group, has concluded a distribution agreement as exclusive sales concessionaires, for Italy, with **Marco Antonetto Farmaceutici**, which has some major brands in the consumer healthcare landscape.

The Medicines Company, USA

2016 saw Chiesi make the single biggest business development deal in our Group's history, with the acquisition of the worldwide rights to three cardiovascular products from US-based **The Medicines Company**. This strategic investment is designed to reinforce our presence in the US market and support our aim of becoming a recognized leader in hospital and adjacent specialties in the US.

+4.9 %

The European affiliates have shown a general turnover increase of **4.9%**, reaching the **one billion milestone** for the first time

New Products

2016 saw the European Medicines Agency (EMA) submission of the dossiers requesting the Market Authorization of two new drugs in the respiratory and rare disease pipeline:

Lamzede® (velmanase alpha) the first new biological entity and the second biotechnological product (after *Holoclar®*) for which Chiesi has submitted a request for the Marketing Authorization with a centralized procedure. *Lamzede* consists of the human enzyme alpha-mannosidase and is produced with recombinant DNA technology. Lamzede® is a therapy for the treatment of serious and progressive disorder called Alpha Mannosidosis, an extremely rare genetic defect that leads to severe and debilitating skeletal abnormalities, deafness, recurrent infections and mental retardation.

Trimbow®, the first Triple combination ICS / LABA / LAMA, indicated for the treatment of Chronic Obstructive Pulmonary Disease (COPD) and administered using a single inhaler, specifically formulated by Chiesi in its Research Centre in Parma ensures that the extra fine particles reach the central airways and lung peripherals.

Investments in Research and development:

JRC EUROPEAN COMMISSION

1st among Italian pharmaceutical companies *

4th among Italian manufacturing Companies *

17th among the European Pharmaceutical companies *

** European Commission - 2016 EU Industrial R&D Investment Scoreboard*

Europaisches Patentamt
European Patent Office
Office européen des brevets

In 2016 **Chiesi** is the 1st Italian pharmaceutical company in Europe for patent deposits

More than **2,900** Worldwide patents in the portfolio Chiesi (12.31.2016)

NUMBER OF EMPLOYEES

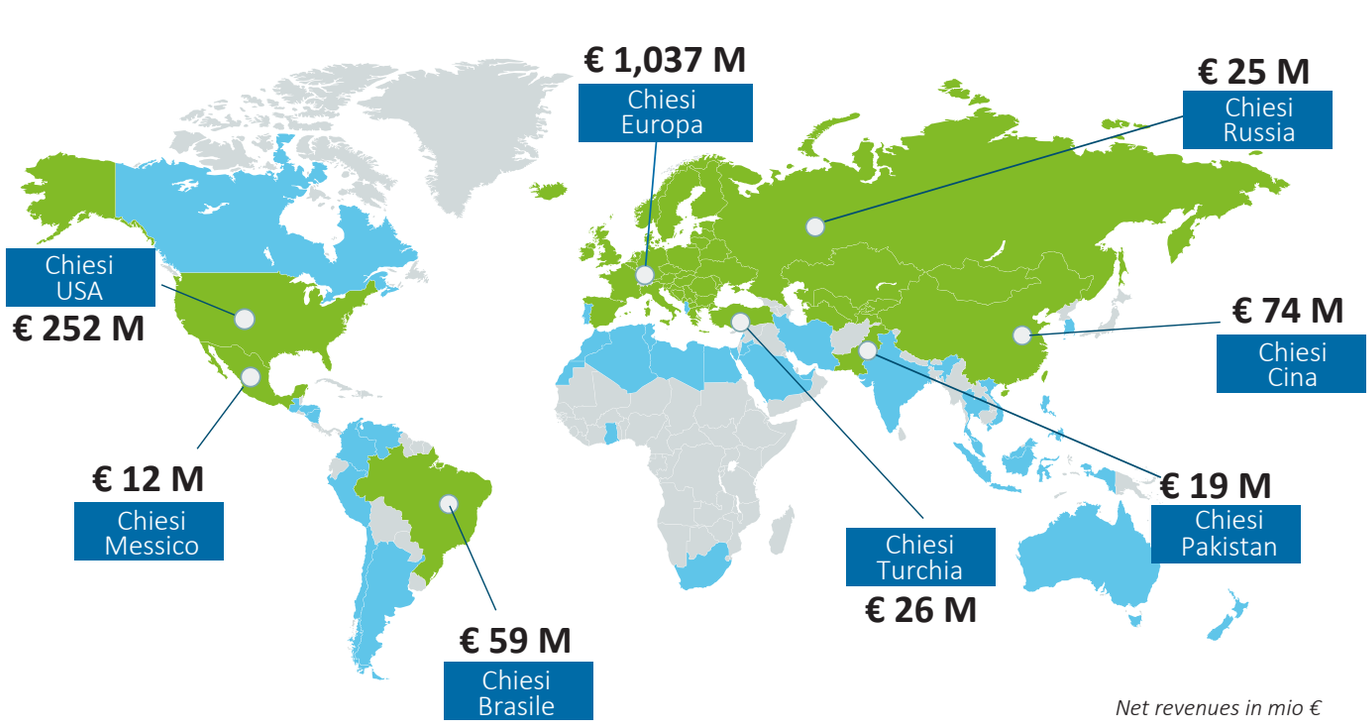
2,058 EUROPE

1,024 EMERGING COUNTRIES

238 US

Italy	543	**Belgium**	45	**Germany**	283	**Russia**	132	**China**	205	**1,495**	
France	249	**Austria & CEE**	208	**UK**	252	**Pakistan**	200	**Brazil**	212	CORPORATE & SUPPORTING	
Spain	242	**Holland**	56			**Mexico**	69	**IMDD**	59		
Greece	64	**Poland**	116			**Turkey**	147				

Chiesi Worldwide



Net revenues in mio €

top EMPLOYER EUROPE 2017 CERTIFIED EXCELLENCE IN EMPLOYEE CONDITIONS

top EMPLOYER ITALY 2017 CERTIFIED EXCELLENCE IN EMPLOYEE CONDITIONS

top EMPLOYER BRASIL 2017 CERTIFIED EXCELLENCE IN EMPLOYEE CONDITIONS

top EMPLOYER UNITED STATES OF AMERICA 2017 CERTIFIED EXCELLENCE IN EMPLOYEE CONDITIONS

top EMPLOYER ESPAÑA 2017 CERTIFIED EXCELLENCE IN EMPLOYEE CONDITIONS

top EMPLOYER FRANCE 2017 CERTIFIED EXCELLENCE IN EMPLOYEE CONDITIONS

top EMPLOYER UNITED KINGDOM 2017 CERTIFIED EXCELLENCE IN EMPLOYEE CONDITIONS

top EMPLOYER GERMANY 2017 CERTIFIED EXCELLENCE IN EMPLOYEE CONDITIONS

top EMPLOYER POLSKA 2017 CERTIFIED EXCELLENCE IN EMPLOYEE CONDITIONS

Chairmen's Statement

Alberto Chiesi

President

Paolo Chiesi

Vice President and R&D Director

For over eighty years, the Chiesi Group has been challenging the boundaries of medical research. Founded on an **entrepreneurial spirit that infuses every aspect of our work to this day**, the company has been shaped by an enduring commitment to innovation. That commitment has seen us grow in pursuit of our mission to develop pharmaceutical solutions that improve the quality of human life. From a single laboratory in Parma, we have expanded our capabilities and our presence year on year, **to become one of the top 50 pharmaceutical companies in the world**.

In 2016, we continued our strong trajectory of growth. Building on the success of established products such as Foster, and through expansion into associated therapy areas, Group sales increased by almost 10% at fixed exchange rates on the previous year (= 16.9% with current exchange rates). This was a major achievement in a volatile economic climate, and evidence that our entrepreneurial, collaborative culture and single-minded focus on innovation continue to generate success.

2016: A year of growth

The significant increase in sales in 2016 was underpinned by the success of a number of our individual brands. The continued growth of our flagship product, Foster, in its various formulations generated sales of €583m, a full ten years after its launch (+16.6%). The product continues to go from strength to strength, achieving significant market share in all countries, especially in the EU where it holds market leadership position in a number of countries, including Italy.

+ 300

employees vs 2015

As a company, we also continued to grow, expanding our global team by around 300 people to reach a total headcount of 4,813 worldwide.

Local growth drives regional expansion

All our affiliates reported growth in 2016, net of the losses incurred by licensed-in products. Countries showing a particularly outstanding performance included the UK – despite a challenging economic climate and currency devaluation linked to *Brexit* – the Netherlands, Germany, Austria and the Eastern European Countries, France, Belgium, China, Brazil, Russia, Mexico and Pakistan.

trong performance at market level translated into **expansion across all Regions** – in particular Europe and the Emerging Markets at fixed exchange rates, as well as the USA. This success can be attributed to a growing numbers of doctors prescribing our established drugs, and a

positive perception of our special care products, for example *Envarsus* and *Holoclar*.

Expanding our portfolio

In 2016 we closed the most important commercial agreement in our history, with the acquisition of the worldwide distribution rights of three cardiovascular drugs produced by *The Medicines Company*, a US based firm. The investment was designed to strengthen our presence in the American market and support our goal of becoming leaders in some areas of hospital and special care products in the United States.
The Group acquired also *Atopix*, a British company that develops a new research project for severe asthma. In addition, we formalized an agreement for the distribution in Europe of OTC medicines produced by *Marco Antonetto*.

These investments are intended to strengthen and expand our presence in the main areas of our interest- Respiratory, Neonatology and *Special Care*- and expand our expertise in related and complementary areas.

Maximising product potential

Chiesi made a number of submissions in 2016 for both new and existing products. Among these, a dossier was submitted to the *European Medicines Agency* (EMA) for the approval of *Trimbow* – an important new therapy for the treatment of moderate to severe chronic obstructive pulmonary disease (COPD). Representing a milestone for the company, and for the COPD community, this is the first-time approval has been sought for a triple combination therapy for COPD in the EU.
A second EMA dossier was submitted for the approval of *Lamzede* – an *enzyme replacement therapy* (ERT) for the treatment of the rare and serious hereditary genetic disease, alpha-mannosidosis.
Developments at industrial level saw our production capabilities improved, with the inauguration of the new *Curosurf* production line, and the expansion of the production line for mono-dose vials in Parma and the new production line for powder inhalers in Blois, France.

A challenging year

2016 was not without its challenges, and it is notable that the successful expansion of our business is set against the backdrop of an unpredictable economic climate.
In particular, the devaluation of the pound sterling and other currencies in emerging countries resulted in a Euro turnover around € 40m lower than budget. A sudden increase in the number of *pay-back* policies and a drop in prices in a number of European countries also served to create unexpected barriers. Meanwhile, the difficulty of breaking into the market with new drugs, above all for *Special Care* and Rare Diseases, was compounded by economic instability in some countries.

Looking ahead

The healthcare market is changing rapidly. We anticipate some exciting innovations for the industry in the near future, including a series of new personalized therapy products in the fields of oncology and rare diseases. But the environment is dynamic and challenging, and new products like these may not be readily available in many markets as a result of the intensifying global pressure on healthcare resources. This pressure poses challenges for everyone in our industry, but with a company history characterised by a proven ability to adapt to change, we are confident about the future growth of Chiesi.

In 2017, we expect sales to continue growing by almost 10% in all the countries in which we operate, with Foster and some of our special care products in particular continuing to develop at a steady rate. We expect *Trimbow* to be approved by the EMA before the end of the year, and *Lamzede* at the beginning of 2018. Further investment will be made in developing new treatments for respiratory diseases with different mechanisms of action, and new therapeutic applications of *Curosurf* will be introduced in neonatology.

We are incredibly proud of our team's achievements in 2016, and that as we look ahead, our future is so full of promise. Our mission is to develop innovative pharmaceutical solutions that improve the quality of

human life. Strong results are not only critical to our ability to continue doing so, they are testament to the growing number of patients who are benefitting from our products. That is the reason we do what we do.

We would like to take this opportunity to thank each and every one of our people for their enthusiastic, intelligent and proactive contribution to the growth of the company. Chiesi is a community. We are shaped by our people, and it is through the passionate commitment of our team to our mission as well as their strong collaborative spirit that we have achieved the excellent results we have seen in 2016.

Going forward, new initiatives will be introduced to support our team and further develop our capabilities in all departments across our network. Our recently-drafted "Vision 2025" foresees continued and sustained growth for the company, with advances in Research and Development, industrial, commercial and internationalisation activities. Everyone in the Group has a role to play in making this possible, and we all need to maintain focus on our shared objectives, such as generating assets and services for the company, reaching milestones in wellbeing both at personal and company level, and supporting the social, cultural and economic development of the areas in which we operate.

The road ahead is a challenging one, but it will also take us on an exciting journey. We are honoured to be sharing it with such a talented, passionate and successful team.

Alberto Chiesi

President

Paolo Chiesi

Vice President and R&D Director

Ugo Di Francesco
Chief Executive Officer
Chiesi Group

Chief Executive Officer's Q&A

Ugo Di Francesco

Chiesi Group Chief Executive Officer, Ugo Di Francesco, answers some key questions and shares his views on the company's performance in 2016 and his goals for Chiesi in 2017.

What are your thoughts on Chiesi's performance in 2016?

Our 2016 performance was very positive. In some respects, it was a turbulent year and we faced some important challenges that had a strong effect on us – in particular, the devaluation of some currencies and the drop in value of the pound after the *Brexit* vote. In spite of this, when assessed at Constant Exchange Rates (CER), our growth was still close to 10%, which is a remarkable achievement.

It makes me very happy that we have seen growth and a strong performance across almost all our geographies, but 2016 has certainly been the year of Europe. The region is usually seen as a part of the world with low growth, strong pricing pressures, cost containment measures and market access challenges. However, in 2016 as well as achieving CER growth of almost 10%, we also exceeded our goal of €1 billion sales, which was an emotional moment for us all at Chiesi.

What have been the key product trends for Chiesi?

It has been another amazing year for *Foster*, our most important product. Even though it was launched almost 10 years ago, it still achieved double-digit growth in 2016, which is a tremendous result. Another of our flagship products, *Curosurf*, also performed exceedingly well and broke the €200 million sales barrier.

Were there any structural changes within Chiesi in 2016?

By the end of 2015, we had made a number of significant structural changes, including starting the process of uniting Europe as a single region and the implementation of individual development plans for some of our managers and young talent. So, our focus in 2016 was to consolidate the changes made the year before.

Going forward, our human resources goal is to develop our own people and encourage more internal promotions rather than going outside the company to recruit people.

How do you think the pharmaceutical healthcare environment is changing and how is Chiesi adapting?

The pharmaceutical environment is changing in many ways, and I believe there are a number of drivers at work. Perhaps the most pressing issue we face is the need to demonstrate value, as every economy in the world now faces questions about the sustainability of their healthcare systems.
As a company, it is our responsibility to ensure that all of our stakeholders understand the value that our products bring – not just in terms of their ability to control or cure a disease, but in terms of their place in the healthcare system and the level of innovation they represent.
The healthcare environment is only going to become more complex in the future. As an industry, we need to get better at understanding the entire patient journey from diagnosis, to treatment, to monitoring and then follow up. This is because every single stakeholder involved in the management of a disease should be considered a customer. Whether it's the physician, the nurse, the patient, the patient association or the payer, each one has their own expectations and their own criteria for assessing the value of a drug. Our duty is to understand all their needs and provide them with solutions that help them better manage a disease at every stage of the journey, as well as demonstrating the value our products bring to every aspect of the healthcare system in which they operate.

What is Chiesi doing to offer customers cost-effective, innovative drugs?

To fulfil the need for medicines that represent value to providers we are increasingly focussing our efforts on innovation. We have more than 50 active projects in our pipeline, which is a huge number for a company of our size. The majority are linked to delivering new chemical entities and real innovation.

How has Chiesi adapted to the need for greater transparency in working with HCPs?

The answer is simple: ethics and transparency have

always been embedded in the core values of our company. Ethical standards are not negotiable at Chiesi.
We are, of course, fully compliant with the new code of ethics implemented at a European level for transparency in all interactions with healthcare providers, but we also have our own internal code of ethics, with which we have always expected our employees to comply.

How will the changing political environment impact on Chiesi in 2017?

The world is heterogeneous, but in 2017 and beyond, more and more countries will face increasing drug pricing pressures, which could have a huge impact on the way pharmaceutical companies operate. This is particularly the case in the US, which is by far the most important country in terms of the size of its industry.

Another emerging trend is that some of the protectionist legislation we are beginning to see implemented in some countries, favouring local production or local companies, may have an impact on us – not only in the coming year but into the future.
Brexit represents another a question mark, in terms of its potential impact on the regulatory process and product approval – something that will become clear when the UK leaves the EU.

What are your goals for Chiesi in 2017?

My first goal is, of course, to deliver on our expectations for results and growth. But more than

that, I'd like to see the evolution of the Chiesi group in line with the strategic direction (explained in '*Our Strategy*' section) we have identified.

We will start monitoring the evolution of *Vision 2025* the coming year (details of which are outlined in our *Chairmen's statement*) – a strategy we developed in 2016 and which has been communicated to all our employees. As our plans progress, I am excited to see how the direction we are taking aligns with the *vision* given to us by our shareholders, and to see Chiesi further develop its products, expertise and capabilities in 2017.

Ugo Di Francesco
Chief Executive Officer
Chiesi Group

Our History

1955

*The laboratory resumes its activities and t**he first scientific collaborator is hired**. Chiesi launches its first penicillin-based ointment. Giacomo Chiesi is considering to acquire more land to build a real factory. The new pharmaceutical factory **is launched in 1955**, has **50 employees** and manufactures an extensive range of successful drugs.*

July 6

1935

***Giacomo Chiesi,** a chemist dreaming of doing research, buys the Laboratorio Farmaceutico Parmense and begins his entrepreneurial adventure in Parma (Italy).*

1940

*The laboratory starts to expand and **sell its products abroad**, exporting drugs to Eritrea and Austria. In 1944, however, part of the company is damaged in a WWII bombing raid, bringing all activities to a stop until the end of the war.*

1966

Giacomo Chiesi hands over the management of the company to his two sons Alberto and Paolo. Chiesi Farmaceutici is a small company already looking at international markets.

1975

*Alberto and Paolo start a **continuous expansion** and internationalisation process: Chiesi Brazil is the first affiliate outside the Italian territory.*

1987

Almost ten years after the Brazilian adventure, the Group's international expansion is very strong, both in the European and non-European countries. Since 1987, Chiesi has opened affiliates in Pakistan, France, Spain, Greece, the United Kingdom, Austria and the Eastern European countries, the United States, Germany, the Maghreb countries, Turkey, Bulgaria, China, Mexico and Scandinavia. The Group's historical products, focussing on the respiratory and cardiovascular therapeutic areas, continue to be well established, and new products for neonatal diseases, musculoskeletal and vascular disorders have also been launched.

1993

Launch of Curosurf
A surfactant for endotracheal administration indicated in the prevention and treatment of neonatal respiratory distress syndrome in premature infants. This syndrome was once the leading cause of neonatal death and it remains a significant contributor to neonatal morbidity.

1979

*The launch of **Clenil** represents a significant turning point: it is a cortisone preparation indicated for asthma, allergic rhinitis and airway inflammation. **Clenil** is a successful drug, especially in a market where effective treatments for such diseases are so few and it leads the way for the Company's commitment to respiratory diseases.*

1989

*Chiesi's interest extends to the anti-inflammatory and pain killer areas: **Brexin**, a fast-acting anti-inflammatory, is now on the market*

1993

The third Chiesi generation
Alessandro, Andrea, Giacomo and Maria Paola - the third Chiesi generation - join the Company at different times and with different roles, between the end of the second and the beginning of the third millennium. Their input opened up new lines of research and development: the Modulite® technology for respiratory products with eco-friendly sprays like Foster®, fixed anti-asthma combination in pressurised metered-dose inhaler with new propellants and the development of the NEXTHaler®, dry powder inhaler, considered the most innovative device in its class

2011

Inauguration of the new Chiesi Research Center in Parma (Italy), *hosting over 500 employees*

2015

EMA approves Holoclar®, the first autologous stem cell based therapy for corneal reconstruction

2016

Trimbow® and Lamzede® dossier submission to EMA

2008

In 2008, Chiesi entered as a pioneer in the world of regenerative medicine by founding Holostem Advanced Therapies Ltd

2013

Acquisition of the Danish biopharmaceutical company Zymenex: Chiesi enters the biotechnology area.

TODAY

Chiesi is an international research-focused Healthcare Group, with over 80 years of experience in the pharmaceutical industry, with affiliates in 26 countries. Chiesi researches, develops and markets innovative drugs in the respiratory therapeutics, specialist medicine and rare disease areas. Its R&D organization is headquartered in Parma (Italy), and integrated with 6 other key R&D groups in France, the USA, the UK, Sweden and Denmark to advance Chiesi's pre-clinical, clinical and registration programmes. Chiesi employs nearly 5,000 people, 671 of which are solely dedicated to R&D and regulatory activities.

Giacomo Chiesi

02 STRATEGIC OVERVIEW

[Our Strategy]

Balancing growth and geography

Our business strategy can be summarised very simply: we aim to continue growing, while maintaining the right balance of locations and therapeutic areas.

Our strategy for our therapeutic areas

Respiratory therapy is our DNA. It is where the company started, and historically, it has been the key driver for Chiesi's growth. But we consider all our therapeutic areas to be equally important, and as we evolve, our strategy is to grow our presence and capabilities in these important areas.

We believe the duty of a market leader is not just to develop drugs, but to deliver a full range of products, services and devices that support patients, physicians and nurses and improve quality of life.

VISION 2025

By **2025** we aspire to be a point of reference for patients affected by chronic respiratory disorders, rare diseases and other health conditions which are difficult to treat, offering them and those who take care of them **innovative solutions** in the management of their needs, even **exploring new frontiers in treatment and care**.

While remaining a family-controlled company, we want to continue to grow ambitiously by focusing on key markets, but also expanding patients' access to care in key emerging countries. We aim to maintain a profitability level adequate to sustain our investments in innovation, development and internationalization efforts.

We believe we can achieve all this only through teamwork, taking care with particular attention of the wellbeing and the excellence of all the people working with us.

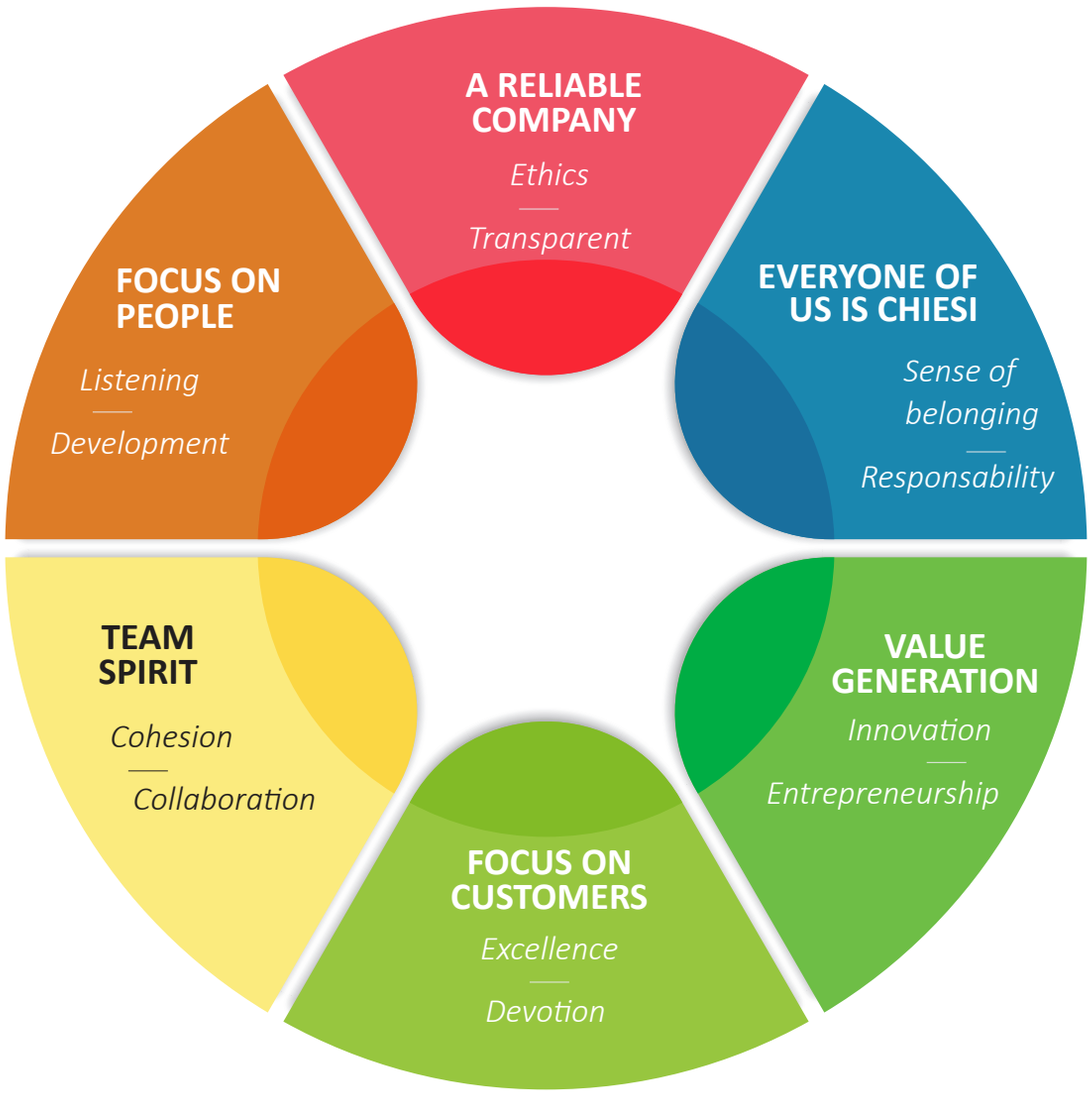
Everyone of us is Chiesi

GEOGRAPHIES	PORTFOLIO	THERAPEUTIC AREA	R&D	FINANCIAL	PEOPLE
Balanced proportion among **Geographies**.	**Focus on key therapeutic areas such as Respiratory, Neonatology and Special care including Rare diseases**		Adopt a **Patient Centric Approach** throughout the Company Emphasise **Innovation**	Have a **sound Financial Performance** and Value Creation	Invest in and improve the **wellbeing and quality of our people**

Our Culture and Values

OUR VALUES IN ACTION

We believe that a spirit of entrepreneurship, self-confidence and collaboration is the foundation for our continued success. Across the world, Chiesi's employees work hard to build a culture in which the values we believe in are put into practice in every aspect of our day to day work.



The way we work is as important as what we do

We want to be recognised as a company that adopts and promotes transparent, ethical behaviour at all levels. This means supporting responsible business practices throughout our organisation. As member of Efpia, **the Group fully support the disclosure of transfers of values from pharmaceutical companies to healthcare professionals and healthcare organisations**, as well as any similar requirement imposed by applicable laws, to ensure that our relationship with external stakeholders is open, transparent, and fully compliant.

We expect our partners to comply with the Chiesi *Code of Ethics*. We are proud of the recognition we receive from the healthcare professionals and organisations we work with for our ethos and responsible approach. In 2016 Chiesi became the first pharmaceutical company in **Brazil** to be named *Programa Pró-Ética* by the Brazilian Ministry of Transparency – an accolade awarded in recognition of our ethical position.

We make an active contribution to the communities we serve. **Chiesi US** launched a corporate social responsibility programme called *Chiesi in the Community* that helped us carry forward legacy support projects, and introduce a new initiative aimed

at improving the student experience and performance at a local elementary school.
In the face of a national financial crisis, **Chiesi Greece** worked alongside non-profit organisations such as *Medecins du Monde Greece*, to provide Chiesi product donations to people unable to meet the costs of treatment. The affiliate also worked closely with universities and professional bodies to support the next generation of clinicians by funding undergraduate and postgraduate scholarships.

Chiesi Poland sought to increase access to innovative hospital equipment via direct donations to hospitals, and supported the Polish Scientific Societies in areas such as respiratory disease, neonatology, cystic fibrosis, transplantation.

In order to increase team spirit among the Chiesi people, and indeed among our employees' own families, **Chiesi Mexico** ran its first ever drawing contest. Children were invited to draw something creative, and winners received entrance to an entertainment park.

Our people are the centre of our company

We believe that people **are our most valuable asset**. Our employees shape the future of the company, and our success is created and sustained by them. We therefore strive continuously to support the development of our staff. We also devote significant focus to fostering a spirit of collaboration and teamwork – based on our foundations as a family company – because we believe that we can achieve much more together than we can as individuals.
Training is a major focus for all our affiliates. In 2016, **Chiesi France** invested 4% of salary costs in coaching, including technical knowledge, management and communications. **France** also set up a new HR process, designed to accelerate the integration of all new Chiesi colleagues via a *Welcome Week*, which includes one full induction day, and a visit to the plant in Blois. **Chiesi Turkey** launched a series of training sessions aimed at shaping the company culture, while **Chiesi Holland** delivered an ongoing training and development programme for the entire salesforce at its bi-annual cycle meetings. **Chiesi Italy** introduced *Creattivamoci*, a training programme offering managers the opportunity to meet and share ideas with highly successful leaders and entrepreneurs from other business sectors.

Chiesi France

Chiesi Mexico implemented unique, tailored training programmes for key groups of employees. For example, first-line managers were assessed and an *Individual Development Plan* was identified for each. As well as receiving leadership training to help improve management skills based on the Chiesi Competencies, they also underwent modules in communication and team development skills, and, where needed, an online English course. High potential employees among second-line managers were identified, and they received communication skills training, how to improve feedback sessions, and emotional intelligence, English language and technical skills development sessions.
To build strong team spirit, establish mutual understanding and support collaboration, many affiliates implemented **new platforms**

designed to support collaboration within and between teams. **Chiesi Turkey** launched *BizBize (Cosy) Gatherings*, bringing together field force and office teams across the country. **Chiesi UK** worked hard to promote team spirit whilst also sharing best practice, bringing all its teams together in organised events with both a business and social aspect. Working to the principle: "*We live like a family and work like a team*", **Chiesi Pakistan** offered coaching sessions and team building activities, such as cricket matches and the communal celebration of religious festivals, designed to develop a well-integrated and committed team of professionals. The team-focused approach at **Chiesi Nordics** had a clear, measurable impact. As part of the Voices employee survey, the level of engagement from colleagues was measured at 100%. **Chiesi China** implemented a new *field force* bonus plan. The plan links team performance to personal performance, highlighting the importance of collaboration, and prioritising success as a team over individual achievements.

Chiesi IMDD

In **Brazil**, the *My New World* programme focused on the inclusion of people with disabilities in the corporate market, and the implementation of Chiesi Day provided an opportunity to communicate all the important information about the company and ensure collective alignment behind the company strategy.

Driving innovation and entrepreneurship

Entrepreneurship and innovation are key pillars of our strategy. We want our people to be proactive in challenging the status quo, and we support them to maximise their own potential for innovation.

Developing high quality entrepreneurial teams is a central focus for leaders at **Chiesi Austria**, supported by a continuous human resources development programme. The success of this approach was confirmed in 2016 by internal market research among employees, and by the market leadership position of our key products within the market. **Chiesi Spain** initiated *WeStart*:- an internal programme in which employees are mentored by expert entrepreneurs, and given time during the working day to develop their own innovative solutions, aimed at bringing greater value to patients.

In 2016, **Chiesi UK** created the new position of *Business Development Director* – an important component of the internal Leadership team. All team members are tasked with and encouraged to work on, suggest and develop new areas of business – even those areas outside our current sphere of experience – to ensure that we continue to grow and to offer value and innovation to our growing customer base.

Chiesi Poland was recognised for delivering highly innovative multichannel marketing, including medical education programmes in transplantation and neonatology, and a digital sales force project aimed at GPs.

Chiesi China launched a number of new initiatives aimed at penetrating the market of lower tier cities, which represent 'Emerging China'. Among them, a programme of small events aimed at training NICU doctors, and a program to support the professional development of young, up-and-coming doctors.

Chiesi UK

Understanding and answering our customers' needs

Knowing our customers is central to the way we work. We are committed **to building relationships so that we can anticipate and answer their needs**. For many of our affiliates, this means investing in research to better understand the experiences of the physicians who use our medicines. For others, it means creating partnerships with professional organisations and delivering comprehensive medical education.

In 2016, **Chiesi France** delivered training designed to develop the acuity of the field force in questioning and understanding healthcare professional needs. Training was also provided to help neonatology physicians gain confidence in intubation techniques, and the *Special Care* team led discussions with experts on how to improve treatment adherence among transplanted patients.

In 2016, **Chiesi Germany** created a new and unique event for Pulmonologists and General Practitioners. The *Pneumology Out of the Box – Into Practice* programme offers scientific lectures and workshops focusing on respiratory diseases. The training received very positive feedback and will now become a regular event.

Chiesi Belgium launched its annual *Chiesi Award* in 2016. Sponsored by the affiliate and presented by the Belgian Respiratory Society, the award recognises local initiatives which have improved the care of respiratory patients.

Chiesi Mexico developed several tools designed to harness innovation to generate value. Focusing on key target physicians, **Mexico** delivered a variety of initiatives, including a *Neonatology Symposium*; a *Nurse Training Program* via which more than 600 nurses accessed neonatology education; mobile phone apps designed to help patients comply with their respiratory treatment; web resources offering insights into the diseases Chiesi's products treat; and a number of campaigns involving physicians and patients, helping in the diagnosis and follow-up of asthma and COPD patients.

Chiesi Holland was recognized as a healthcare partner of the Dutch GP association, after being awarded official Continuing Medical Accreditation for a new Asthma standard. **Chiesi Russia** actively supported a series of educational programmes led by the Russian Respiratory Society, aimed at educating pulmonologists and helping them to

Chiesi Germany

Chiesi Germany

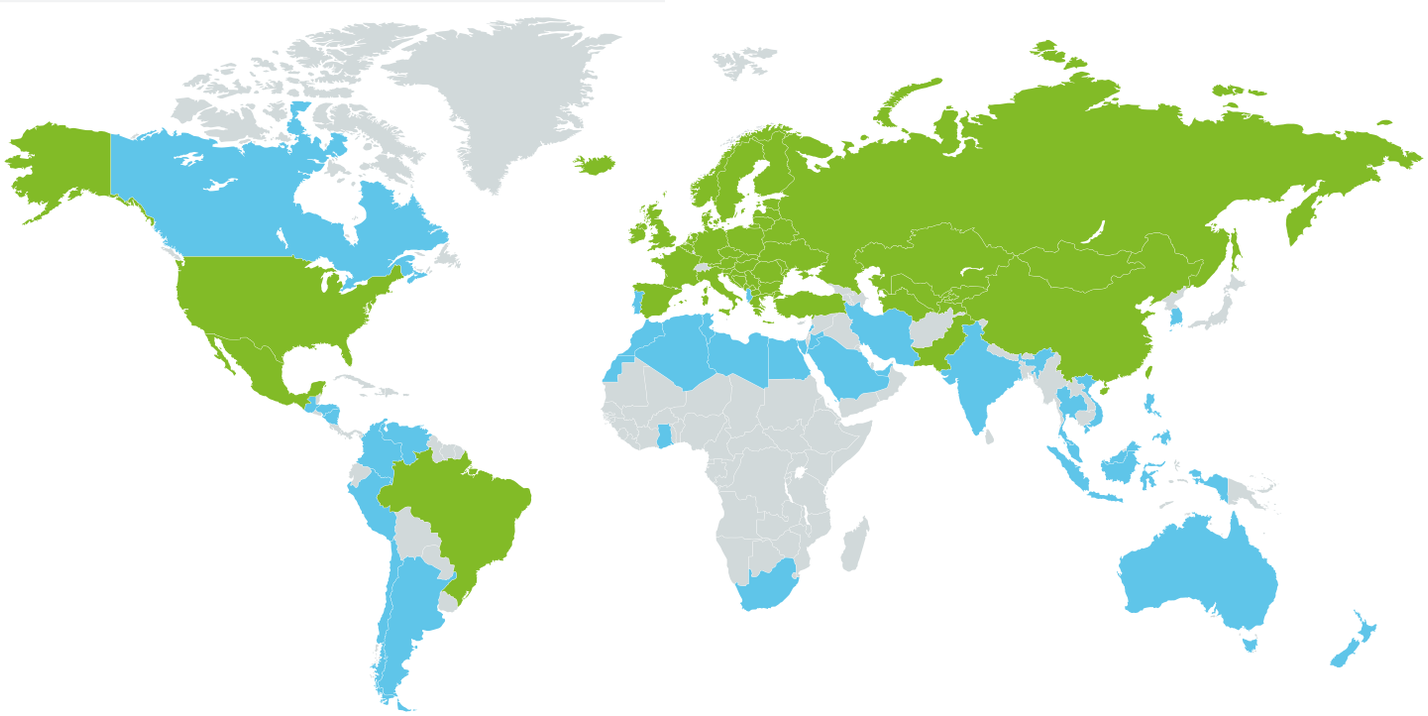
Chiesi Belgium

better treat patients and improve their quality of life. **Chiesi Turkey** strengthened its medical education offering, using a highly collaborative approach, to increase the number of regional meetings with key opinion leaders from 11 in 2014 to 37 in 2016. Two satellite symposiums were also co-ordinated, taking place as part of the two largest national congresses, and reaching more than 30% of pulmonologists in the country. **Chiesi Nordics** focused particularly on working with key *opinion leaders*. Despite being a small team, they successfully rivalled competitors in their communications with physicians, including highly effective external speaker programmes.

Chiesi Spain

Chiesi Spain conducted a detailed exploration of the customer journey, to better understand the experience of primary care physicians, specialists and pharmacists. Based on the results, a value proposition was defined for each group and six projects scoped to answer their needs.

Chiesi China drove knowledge-sharing and education via the *China Heritage* program. This *peer-support* program saw high profile key *opinion leaders* travel to lower tier cities to help local physicians improve their skills and exchange ideas. Reviewing real cases and conducting ward inspections offered an opportunity for the physicians to discuss the problems typically encountered at a local level, and to explore ways in which practices could be improved.



CHIESI WORLDWIDE ● *Local Companies* ● *Local Partners*

Our People

As a business, we continually set ourselves challenging goals. We want our people to share our aspirations for success, and to grow as part of our team. We are always looking for ways to improve the support we offer them, using creative training and development initiatives to help them build the skills they need now, to prepare them for their future roles.

Giorgio Cavalleri
Group People Development Lead

In 2016, for the fourth year in succession, we received the accolade of *Top Employer Europe*. Based on the independent research of the *Top Employers Institute*, this prestigious certification examines the management structures and working conditions of companies with more than 2,500 employees at global level. It is given only to those companies that achieve a *Top Employer* award in at least five European countries – in Chiesi's case, Italy, France, Germany, Poland, the United Kingdom and Spain, as well as the US and Brazil.

The award underlines **our ongoing commitment to supporting and developing our team**. Our people are our most valuable asset, and we believe that our continued success depends on them. We remain focused on equipping all our employees with the skills and knowledge they need to excel in their roles, and on creating a positive working environment in which teamwork and collaboration are our guiding principles.

We are proud that this approach is resonating successfully not only with external audiences, but also among **our most important stakeholder group: our Chiesi team**. *Voices* – a full-company employee engagement survey conducted in 2016 – generated a 91% response rate, and showed that 93% of respondents felt a sense of belonging at Chiesi; that they were aligned with the company's strategy and felt motivated to contribute. The survey also measured aspects of the company culture such as well-being, company image, leadership and communication. Last conducted in 2012, the most recent results showed a strong upward trend, with improvements seen across virtually all categories. They will now form the basis for action planning. Projects designed to build on our success and strengthen our capabilities will be implemented in 2017 and beyond.

Chiesi Germany

Over the course of **2016, our global team expanded by around 300 people** to reach a total headcount of 4,813 by the end of the year. We continue to build our

OVER
4,100
PARTICIPANTS

Voices
Make your voice count

91%

2016
response rate

Chiesi US

human resources (HR) capabilities in line with our growth, ensuring that our employees have access to the support and training they need to flourish. A series of key initiatives were implemented in 2016, designed to consolidate our strategy, build competencies and foster increased collaboration:

1. *The People Development Process* – a new training and support initiative – was rolled out in 2016 following its launch in 2015. The initiative is designed to provide executives from leadership to local management level with the training and mentoring needed to help them excel in their roles. It has been structured around ten core Chiesi competencies identified by shareholders and the Executive Committee. More than 210 managers have been involved to date, receiving individual, tailored development plans that will form the basis of their continued progression.

2. Enrollment for the *Chiesi Academy* also opened in 2016. Organised around two group programmes – *Development for Executives and Leaders* (DEAL), and *Chiesi Corporate Master* (CCM) – the Academy offers participants the chance to learn about and prepare for future challenges, gain visibility within the organisation, expand their network and align around our values and competency model. Delivered in partnership with the *SDA Bocconi School of Management*, the Academy uses highly interactive training techniques to deliver tutorials, classes, assignments and group field projects based on real-life scenarios.

3. The launch of a new HR system in 2016 has supported increased collaboration across the network. Talentia provides a consolidated platform via which both headquarters and local affiliates can now conduct Group HR processes including performance management, appraisals, training and recruitment.

4,813
employees worlwide

Looking ahead

We will continue to focus on wider implementation of these initiatives in 2017. The *Chiesi Academy* CMM programme will kick off with a select group of high performers undertaking the first two modules of a six-module programme. Over two years, they will cover business environment and corporate business strategy, as well as marketing, sales and statistics for marketing decisions. As the Academy programmes continue, it is anticipated that 75 employees including senior managers and young talent will take part.

The roll-out of *Talentia* will also be completed in 2017. This will see the entire affiliate network operating from the same HR system platform, further strengthening the collaborative efforts of our team.

Our Research & Development (R&D) Centers

Building our expertise

The Chiesi research and development (R&D) team has continued to strengthen in size, expertise and technical capabilities throughout 2016. We now have over 670 people employed in R&D and regulatory globally, representing growth of 20% on the previous year.

R&D is led from our main facility – an award-winning,

The continued success of our pipeline relies heavily upon the expertise and commitment of our global R&D team, who work together effectively across multiple sites.

Mark Parry-Billings
Head of Corporate Drug Development

state-of-the-art centre at our Corporate headquarters in Parma, Italy. Our additional six facilities across the world operate in a highly-integrated manner, collaborating and sharing knowledge to contribute to the ongoing success of our pipeline.

In 2016, as part of the acquisition of clinical-stage biotechnology company *Atopix Therapeutics*, we added a new R&D site in Oxford, UK to our organisation. Focused primarily on the development of *Timapiprant*, an orally-administered CRTh2 antagonist currently in Phase 2 trials for severe asthma, the unit further enhances Chiesi's commitment in respiratory medicine, particularly in eosinophilic airways diseases.

Our approach to R&D

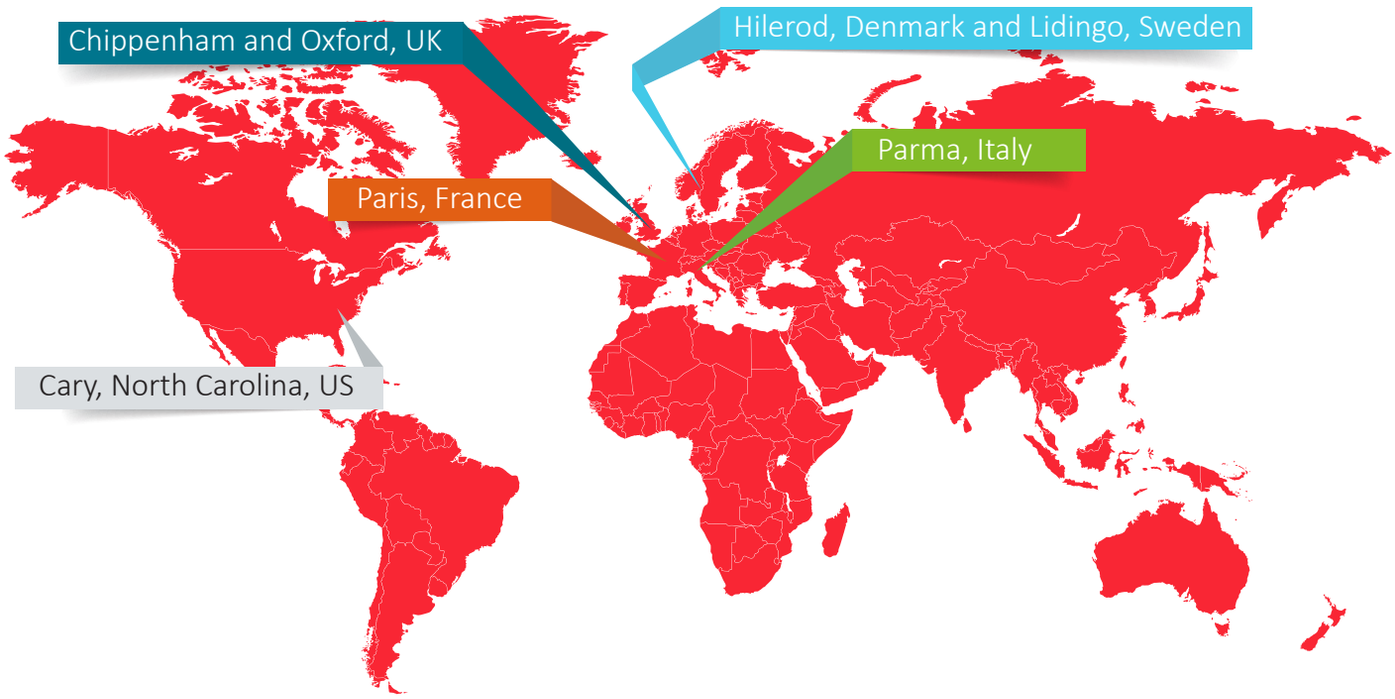
While some of Chiesi's medicinal products have been acquired or resulted from partnerships with other pharmaceutical companies

+ 77.5 %

of our turnover comes from the products discovered and developed by our R&D division.

Our matrix approach to managing projects uses cross-functional global teams to progress R&D assets through the pipeline. Each *project team* includes representatives from the main R&D functional areas as well as our *Global Manufacturing Division* (GMD) and marketing department, ensuring that each product in development, from pre-clinical studies through to post-marketing surveillance, addresses a patient need and is commercially viable.

Parma, Italia



ITALY

430

R&D EMPLOYEES

Discovery
Pre-clinical
CMC
Clinical
Regulatory

Quality
Pharmacovigilance
Intellectual property
Project leadership
Project management

Scientific information
Financial analysis and control

FRANCE

20

R&D EMPLOYEES

Clinical – late-phase clinical studies

UK

18

R&D EMPLOYEES

***Chippenham**: drug delivery technologies, specifically for inhaled drug delivery*

***Oxford**: part of the acquisition of Atopix in 2016, focused on the development of Timapiprant, a phase 2 asset for severe asthma*

DENMARK AND SWEDEN

14

R&D EMPLOYEES

Part of the acquisition of protein therapeutics biotech Zymenex in 2013

US

8

R&D EMPLOYEES

Clinical
Regulatory
Development and registration of US pipeline

More than **670** people in research and registrative activities

Our Manufacturing Plants

Meeting the needs of an evolving market

2016 was an important year for the Global Manufacturing Division. Alongside a number of significant milestones, we saw a sharp increase in sales volume and entered new markets and technology areas.

Antonio Magnelli,
Head of Global Manufacturing Division

Operating on the principles of Lean Manufacturing to ensure efficiency and flexibility, Chiesi's Global Manufacturing Division (GMD) is responsible for the supply of **more than 110 million units of product per year** by our plants in Italy, France and Brazil. To support our aim of achieving excellence in production while meeting the growing demands of international markets, a new organisational structure was put in place in 2016. This network allows for greater integration of expertise and experiences, building more cohesive ways of working by sharing knowledge and ideas across the three plants.

We have also balanced out production across our plants in France and Brazil by transferring *Foster Nexthaler* and *Clenil* MDIs products from one site to the other. This has levelled workloads and maximised our operational flexibility. Seeking to ensure continual improvements to our customer service, GMD also took steps to rationalise our European distribution network, allowing greater control, and supporting our ambitions to deliver excellence.

Our manufacturing achievements in 2016

San Leonardo, Parma, Italy

Our base in San Leonardo is the strategic hub of our worldwide production activities. In 2016 we undertook an ambitious expansion project to increase our vial production capacity and also to accommodate a new *Curosurf* plant which is due for completion in 2017. The scaled-up capability of this facility will allow us to double our previous production output.

The plant has had consistently successful inspections by several regulatory authorities, and in July 2016 it received a positive inspection from the *U.S. Food and Drug Administration*.

San Leonardo Manufacturing Plant

- **490** employees
- **18,632 m²** Total production area
- Registered in over **80 Countries**
- **Certified** ISO 9001– OHSAS 18001– ISO 14001

Production capacity

- **22** million packs in oral solids
- **22** million packs in *Unit-Dose Vials* (UDVs)
- **28** million packs in *Metered-Dose Inhalers* (MDIs)
- **4** million packs in *Dry Powder Inhalers* (DPIs)
- **600,000** vials in sterile suspensions

Blois, France

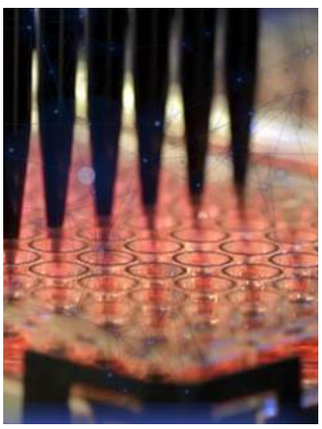
Supporting the activities of the Parma plant, our site at Blois saw the addition of a new production, packaging, storage and control department in 2016, focusing on the *NEXThaler* DPI.

Blois Manufacturing Plant

- **80** employees
- New **8** million packs line for *Dry Powder Inhalers* (DPIs)
- Production of blister packaging for capsules and tablets
- Final assembly stages of the MDIs.
- Supplies Chiesi Group's affiliates
- Distributes directly to domestic market and exports to other markets

Production capacity

- **20** million finished packages each year



Santana de Parnaiba, Brazil

In 2016, a major project began at Santana de Parnaiba, to build a new department catering for an increase in liquid production capacity. The design stage and acquisition of machinery have been completed, and the project is on track to be completed in 2017.
A new microbiological laboratory was also completed, ready to support our network. Spray production will increase by 50%, to accommodate growing demand at the San Leonardo plant.

Santana de Parnaiba Manufacturing Plant

- **100** employees
- Production of solid formulations, liquids and solutions, and pressurised solutions and suspensions for inhalant therapy (MDI)
- Supplies both domestic market and Group's Affiliates
- Exports to licensees and distributors

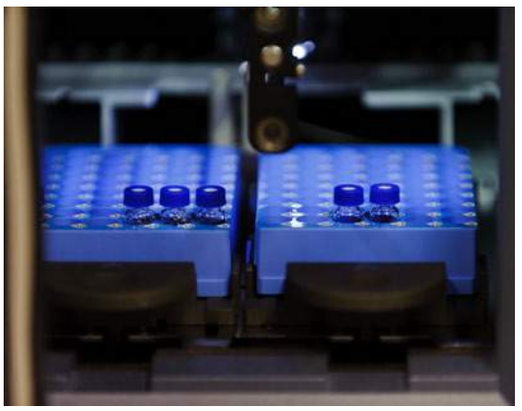
Production capacity

- **16.5** million finished packages per year

Achieving excellence in production

The GMD aims to deliver excellence, every time. *Teamwork, strong communication and integration across all operative levels at our plants is integral to the way we function*. Our objective is to operate as a single cohesive team, united by common goals.

Our team works with passion, dedication and commitment to maintain the highest level of attention to detail. With a common focus across all our sites, every single one of the 110 million packs produced is checked and delivered with meticulous care. This focus on quality is backed up by highly efficient management processes, which are continually reviewed and refined.



Focus for 2017

Looking ahead to 2017, we expect to reach several significant project milestones across our manufacturing network:

- The new *Curosurf* plant in San Leonardo will begin operation, initially making products for European and Brazilian markets
- The production capacity for *NEXThaler* will be increased to deliver over 11 million units
- The new liquid department in Santana will reach completion
- A new dispensing area will be created in the San Leonardo plant

As we continue to grow and strengthen through our ongoing acquisitions, Corporate GMD will strive to maintain consistency through the smooth integration of potential new assets. Staff development will be an important focus in 2017, reflecting our company values, and supporting the communication and collaboration that is critical to the efficiency of our manufacturing network.

The Chiesi Group also aims to increase its production flexibility, working with external manufacturers to increase our capabilities and strengthen future productivity. This is particularly important as we increase our focus in Special Care, and expand our portfolio of products in an area which is associated with highly complex manufacturing requirements.

The production capacity for *NEXThaler* will be increased to deliver over

11

million units

People
Patients | Employees | Communities

Ethics & Compliance

Environment & Safety

Corporate Social Responsibility (CSR)

At the heart of Chiesi's mission and values lies the goal of combining commitment to results with integrity. We are focused on operating in a socially and environmentally responsible manner, and Corporate Social Responsibility (CSR) forms a critical aspect of our business activities.

What does CSR mean to Chiesi?

It is a simple fact that all human activities have an impact on society and the environment. No company operates in isolation, and we believe we have a **responsibility to contribute positively to the civil, environmental and economic development of the communities in which we operate**. This is why CSR is intrinsic to the way we think and act.
Indeed, proactively supporting the sustainable development of the communities to which we belong is not only the right thing to do, but it also plays an important strategic role in our business. Through our CSR projects and our continued involvement in grassroots community initiatives, *we gain a better understanding of the issues affecting society,* and can adapt our business to reflect the changing economic and social landscape. For us, it is not simply a matter of generating profits to reinvest in research and development. It is also about listening to the needs of our communities and integrating them into our business decisions.
CSR at Chiesi effectively concerns all the areas of the company, and we build our activities around three key pillars: *People*, *Environment* and *Ethics*.

PEOPLE
Our patients and their families, our collaborators both now and in the future, and the people in the communities to which Chiesi and its affiliates belong.

ENVIRONMENT
As a Group, we are committed to complying with the strictest international regulations and standards relating to environmental protection and sustainability at all our production sites worldwide.

ETHICS
Integrating ethics and results is pivotal to the Chiesi *mission*, and this has been put into practice by developing codes of conduct and ethical guidelines that support business development and benefit the company's stakeholders.

The desire to integrate ethical values with the company's wealth of skills and knowledge was the primary driver behind our decision to create the *Chiesi Foundation* in 2005. This organisation aims to help communities, which are either geographically remote or difficult to help through the communities in which our Company is already present. As always, patients are the focus, but for the *Chiesi Foundation*, the patients in question are those in the poorest parts of the world – places where our Group has no production site or commercial activities, and in which communities are unlikely to benefit from the social activities we provide. The Foundation – an entirely separate, non-profit legal entity – was therefore set up as a tool to ensure these extremely remote communities with acute needs can be reached, making it one of Chiesi's most effective social responsibility contributions.

Further information on our social commitment and CSR strategies and activities and the Chiesi Foundation programs and projects can be found in the 2016 CSR Report on our group website

www.chiesi.com

Improving neonatal care in Africa: the strategy of Chiesi Foundation

by Cecilia Plicco

In Italy in 2014, neonatal mortality stood at two deaths for every 1,000 babies born alive. In Burundi, the same indicator stood at 29.

World Health Organization, 2017

At Chiesi, we are committed to supporting the communities to which we belong. But we also look beyond our immediate environment. The Chiesi Foundation was born in 2005 to capitalise our legacy of expertise in respiratory and neonatal diseases, and to fight against suffering and inequality. Our work extends across the globe, and, as **CSR & Chiesi Foundation Program Manager Cecilia Plicco** explains, one of the key projects of Chiesi Foundation aims to have an impact on neonatal care in countries with limited resources, such as Africa.

The NEST Project focuses on improving the quality of neonatal care in areas and centres with limited resources, particularly in Africa. Working closely with local hospitals and staff, we aim to establish a model of neonatal care wards that are effective, sustainable and suited to the local context and available resources.

Cecilia Plicco
CSR & Chiesi Foundation Program Manager

What are your experiences of neonatology in Africa?

The first neonatology ward I visited in Africa was in Ngozi – a town located in the north of Burundi, near the border with Rwanda. It was 2014 and the Chiesi Foundation had just set up a joint initiative with the Pro-Africa Foundation to improve neonatal care at the Ngozi state hospital.
At the time of my visit, the neonatology ward comprised an area of about 30 square metres. There were two heating lamps, a broken incubator and cots for the newborn babies. All the infants born at the hospital were treated in the same room, regardless of the type and severity of the disease from which they were suffering.
I was deeply shocked by the conditions in the "ward"; by the newborns that were so fragile, small and underweight, the limited space and the lack of resources available to the staff for their care. And my perceptions were compounded on returning home, when I had the opportunity to visit some neonatal care units in Italian hospitals. It was really only then that I understood just how extreme the inequality is between the technology, equipment and level of care available to newborns in Italy, compared to those in the hospitals working with the Chiesi Foundation in Africa.

What is Chiesi Foundation doing to address this inequality?

Understanding this disparity, and knowing that our heritage in neonatology puts Chiesi in a unique position to help, was what spurred the creation of the NEST Project- Neonatal Essential Survival Technology.
Created by the Chiesi Foundation in 2014, the NEST Project focuses on improving the quality of neonatal care in areas and centres with limited resources, particularly in Africa. Working closely with local hospitals and staff, we aim to establish a model of neonatal care wards that are effective, sustainable and suited to the local context and available resources. Within the frame of the NEST Project, the first pilot interventions are being implemented at the Ngozi Hospital (Burundi), the Saint Camille Hospital in Ouagadougou (Burkina Faso), and the Saint Jean de Dieu Hospital in Tanguietá (Benin).
The NEST Project designs a framework via which we can provide hospitals with medical equipment, develop and communicate the protocols and guidelines for appropriate practices in the care of newborns, including the correct use of basic neonatal drugs, and promote education and training initiatives for local healthcare providers.
The project is gathering pace. A new neonatology ward complete with intensive care, special care and standard

care rooms, breastfeeding and kangaroo mother care areas for the mothers, will be officially open and operative in 2017 at the Saint Camille Hospital. The construction of the new building was entirely funded by the Chiesi Foundation and for the next three years we are planning to work together with the staff to improve the care of newborns by focussing on training, introducing new equipment and developing the ward protocols and guidelines for neonatal care. This represents a milestone of our commitment in the development of the NEST Project and in supporting the right to health of fragile and vulnerable patients in the most disadvantaged areas in the world.

By honouring this commitment, we hope to contribute to rebalance inequities in care, and I am proud that Chiesi's steadfast focus on people – whether colleagues, patients near or far, or citizens in the areas where the company operates – allows us to play a part in making society a better place.

Cecilia Plicco
CSR & Chiesi Foundation Program Manager

nest
Neonatal Essential Survival Technology

02

Performance Review

Financial Results

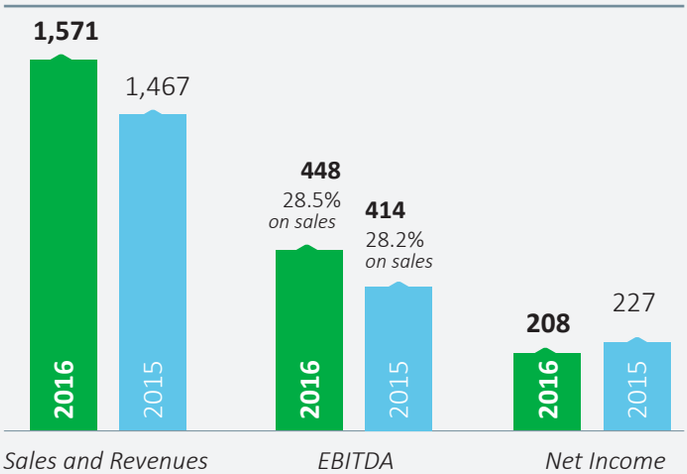
Group Financial Results 2016 (Values in M€)

Chiesi Group closes 2016 on a high with an annual turnover of €**1,571** million, an increase of more than **+7.0%** on the previous year (**+9.6% at constant exchange rates**), and EBITDA equal to €**448** million (a year-on-year increase of over **8.2%**). The robust health of the company is reflected by its investment in innovation and development, with R&D expenditure rising by over **+12.5%** in the 2015-2016 period to reach €**340** m in 2016, 21% of total sales. The Group currently has **51** active research and development projects. The total number of employees now stands at over **4,800**: people as a central focus, passion, entrepreneurial spirit and intercultural dialogue are the values on which the company will continue to base its development in the coming years.

Our company is based on an entrepreneurial spirit that characterises every aspect of our daily activities, as well as a constant commitment to innovation. This commitment has seen us grow pursuing our mission of developing pharmaceutical solutions that improve the quality of human life. From a small laboratory in Parma, we have expanded our capabilities and our presence year after year to become one of the top 50 pharmaceutical companies in the world.

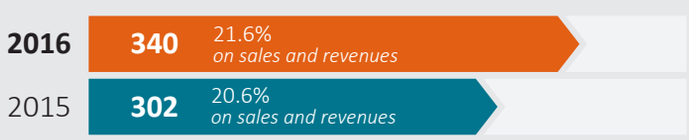
Alberto Chiesi
President of the Chiesi Group

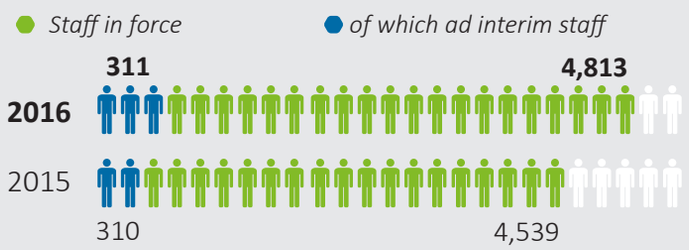
Operating Results *(MILIONS €)*



Other Information

R&D investments





THE PRODUCTS

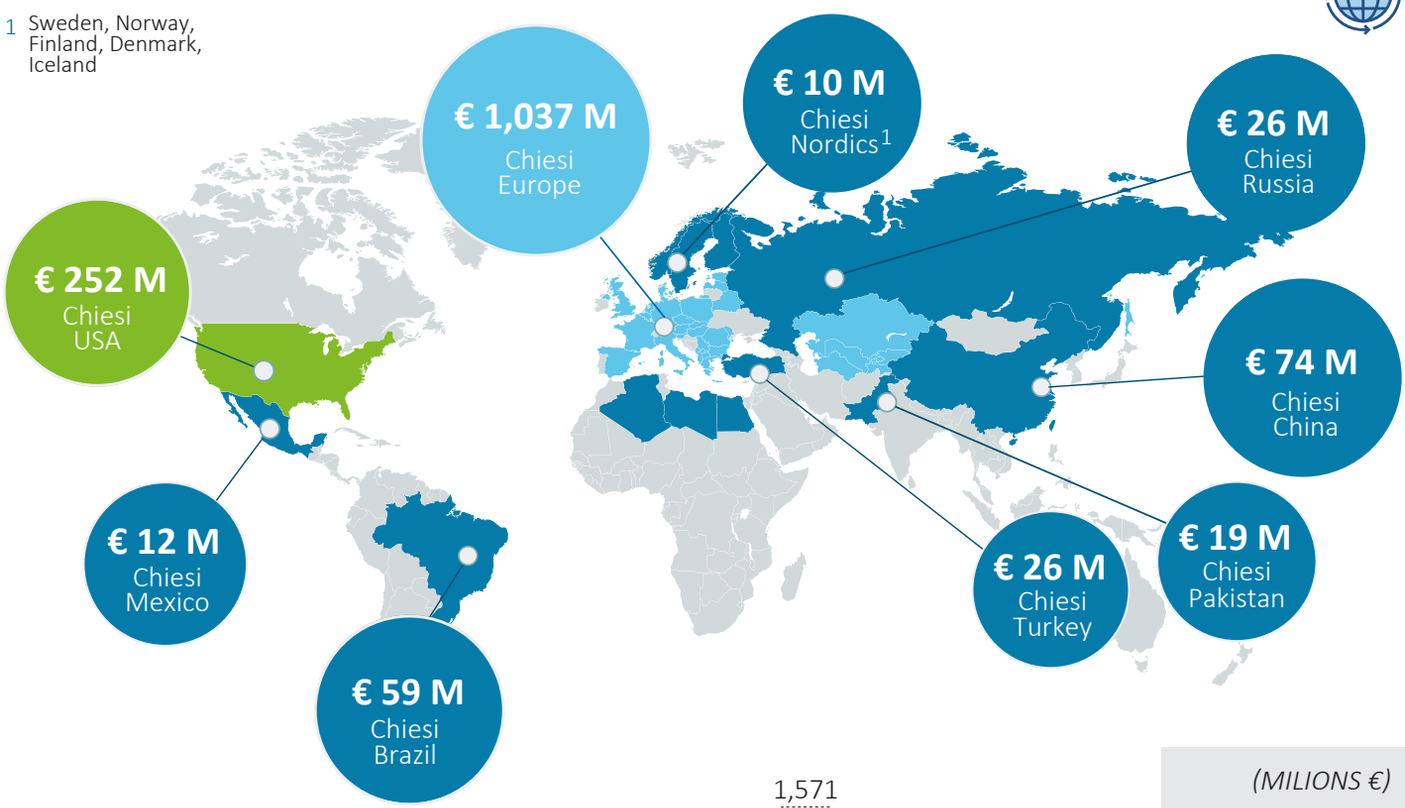
The respiratory drug market is one in which Chiesi is a key global player, and a number of brands in its portfolio are continuing to generate significant growth and revenue: *Foster®* (beclomethasone dipropionate and formoterol fumarate) generated sales for €**583** million, with an increase of **16.6%** on 2015. *Curosurf®* (poractant alfa), has exceeded €**209** million euro, up by **4.3%** on 2015, thus confirming its global leadership as a life-saving medicine. Entirely developed and manufactured in Italy, this drug is indicated for the treatment of respiratory distress syndrome, a rare disorder that impairs lung function in premature infants. *Clenil®* (beclomethasone dipropionate) generated sales of over €**174** million, a slight decrease compared to 2015 due to the negative impact of currency fluctuations.

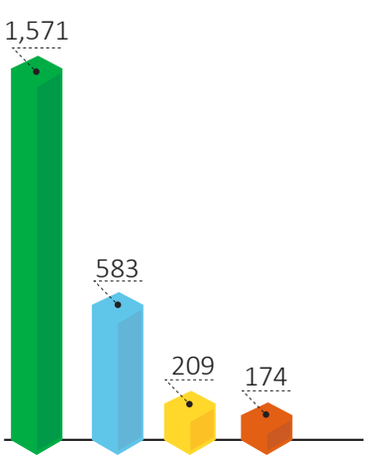
In 2016 we continued our growth trajectory: in the wake of the success of established products such as Foster, and through expansion in our therapeutic areas, the Group's sales increased by almost 10% at constant exchange rates compared to the previous year. This is a major achievement in difficult economic times that makes us think that we are going in the right direction.

Ugo Di Francesco
CEO del Gruppo Chiesi

Chiesi Worldwide

1 Sweden, Norway, Finland, Denmark, Iceland





Global

1,571

Growth on **2015** 7%

(MILIONS €)

- *Sales & Revenues*
- *Foster*
- *Curosurf*
- *Clenil*

Our Affiliates

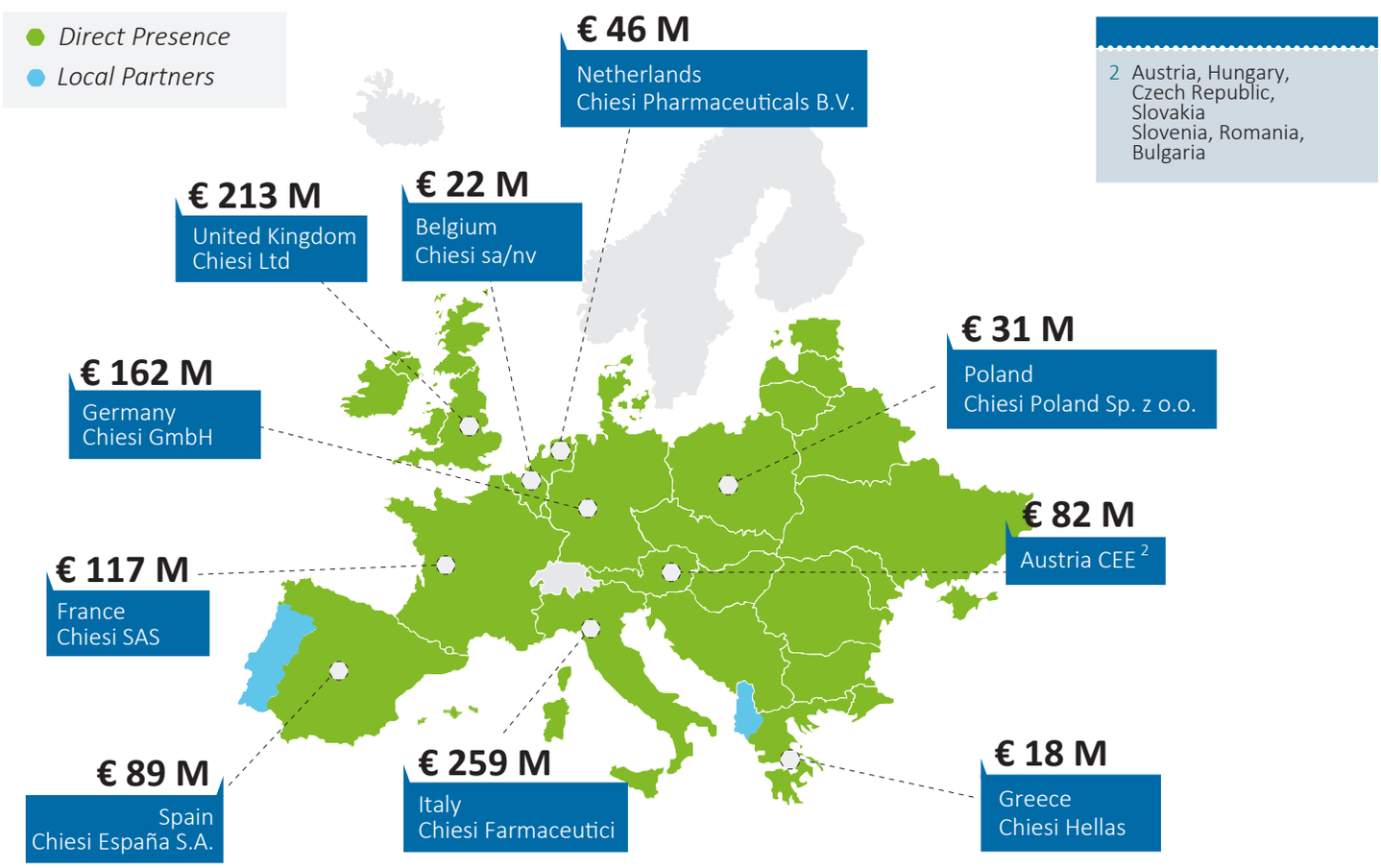
Europe remains a core part of the Chiesi Group's business and continues to play a key role. We are working hard to consolidate Europe in the long-term and reduce our dependency on single markets

Alessandro Chiesi
Head of Region Europe

The European Region

Our Europe Region delivered strong performance in 2016, despite a challenging economic climate and currency devaluation in the UK linked to *Brexit*. Sales reached €1.037 billion, representing overall growth of 4.9% (7.8% at CER), as a result of our focus on core Respiratory and Neonatology products, and an acceleration in growth in the *Special Care* division.

Chiesi France



Respiratory

Our flagship product, *Foster*, reached sales of €542 million across Europe. Equating to growth of 16.6% in terms of value, and over 21% in terms of volume, these remarkable results were due mainly to the consolidation of *Nexthaler* and the launch of our new *High Strength* dosage form.
Foster has now reached market leader position in more than one country – an impressive performance for a product that has been on the market in Europe for over 10 years.
Trimbow, our extrafine fixed triple combination treatment for chronic obstructive pulmonary disease (COPD), was a key focus in 2016. Our efforts in the pre-commercialisation phase have continued, and we look forward to *Trimbow*'s first market launch by the end of 2017.

Neonatology

We have long been committed to developing medicines for the care of premature babies, and *Curosurf* remains the cornerstone of our Neonatology portfolio. In Europe, notwithstanding a decreasing birth-rate, Curosurf kept a slightly increasing trend, thus proving its central role in management of preterm babies also within the current less invasive treatment paradigm.

Special Care

We continued the launch phase of Envarsus. Since its commercialisation in 2015 in Germany, France, Spain, UK, Italy, Poland, The Netherlands and other European countries, the product has now been used in the treatment of more than 4,000 patients across Europe.

In support of this launch and our other new orphan products in the category, we expanded our market access and medical/scientific teams during 2016.

Rare Diseases

Committed to ensuring that patients with rare diseases can access treatment as quickly as possible, we have been working to support patient access for our prelaunch orphan products. As a result of these efforts, the first patients are now being treated with *Holoclar* – our pioneering stem-cell therapy for restoring the eyesight of patients with severe cornea damage. Furthermore, an early access programme in France has ensured that patients affected by Alpha-Mannosidosis can be treated with Lamzede – another orphan drug under registration in Europe, not due to be launched until the first half of 2018.

Unreimbursed products

In 2016, we accelerated on the development of a line of 'out of pocket' products, coupling the development of line extensions of our existing brands with the acquisition of several established ones. A good example is Lipograsil in Spain and a line of products from Antonetto in Italy, which open an opportunity for establishing our presence in some specialized nutritional and female health areas. This is an important development, with potential especially in those markets facing harsher reductions in public healthcare expenditure.

A landmark year for Europe

- The **UK** had an outstanding year, growing by 13.3%, despite the drop in the value of the pound (+28% at Constant Exchange Rate (CER)). The UK is now our second European market in terms of contribution, mainly due to sales of Foster.
- **The Netherlands** were our second fastest developing market (+23%), even whilst undergoing a significant reorganisation during the year.
- **Germany, France, Belgium, Austria-CEE, Poland and Greece** all posted growth of around 10%, ensuring a consistent performance throughout the region.
- **Spain** grew by 5% despite losing distribution of products accounting for almost €5 million sales.
- The only European market that did not experience growth was **Italy**. This was due to a significant price reduction for Foster and other reimbursed products, which had an impact of around €10 million, and to the loss of the remaining sales from *Provisacor* following the end of the distribution agreement in April '16. The Italian affiliate is successfully completing a turnaround that will allow it to fully replace by 2017 the €65 million lost sales linked to the product.
- Our office in Poland became a fully operational affiliate.

Chiesi Europe

2,058
Total Employess

an increase from 2015.

Chiesi UK

Reshaping our European business

Teamwork and entrepreneurship are the cornerstones of our values, and these principles have played an important part in shaping our European business in 2016.

Over the course of the year, the two previously separate regional teams of Northern and Southern Europe were united into a single European organisation, providing a new opportunity to maximise synergies at a regional level, and build a collaborative approach across our European business.

We maintained a focus on improving our own effectiveness, for example by absorbing our Rare Diseases Business Unit into individual affiliate offices. Our total operative costs have now been reduced, giving us the possibility to adequately invest in view of the new launches.

We also increased cooperation between our Corporate division and our affiliate offices, in order to share best practice more effectively across the region. To facilitate this process, an increasing number of employees are moving between Corporate and affiliate offices, providing valuable opportunities for personal growth, integration and the exchange of knowledge and ideas.

A key factor in our success is our people; they are the core of our company and their passionate work is really making a difference to our results.

Alessandro Chiesi
Head of Region Europe

LOOKING AHEAD

Looking ahead to 2017, we expect to see growth in the region of 5%, as a result of the sustained growth of Foster and launches of Trimbow starting at the end of the year.

We plan to maximize our efforts to maintain Foster's market leadership position in Europe, while simultaneously building a new market for Trimbow.

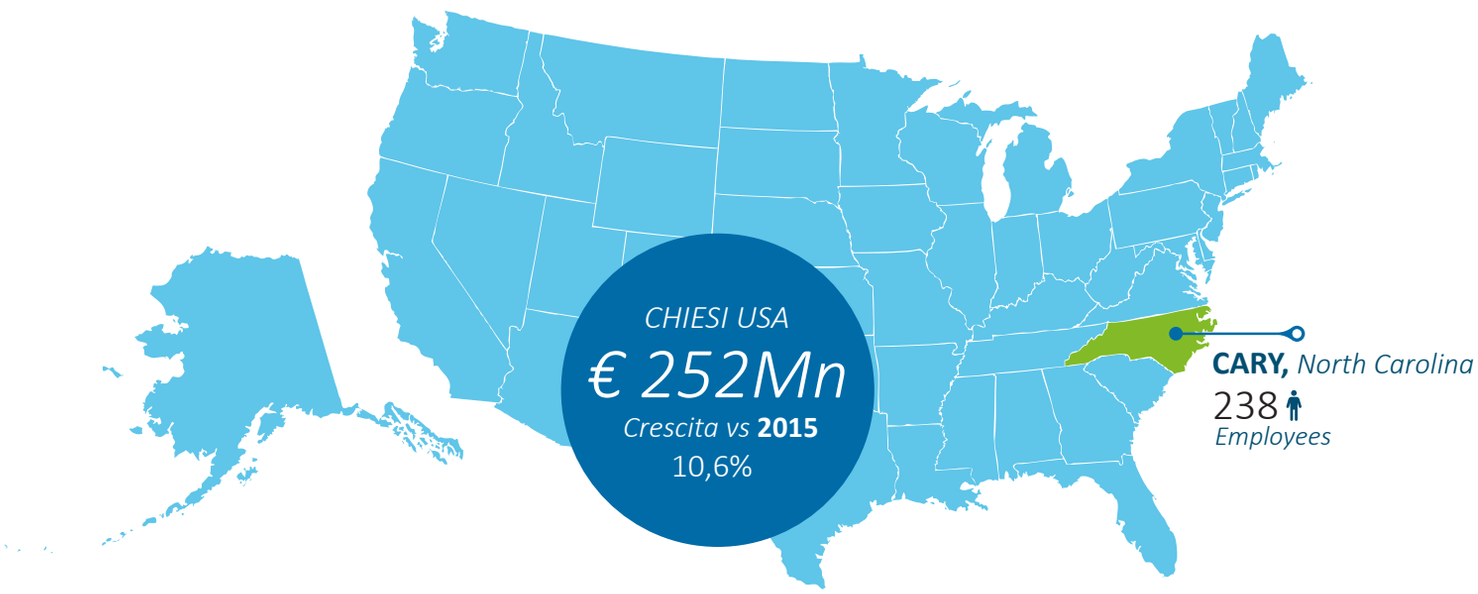
2017 will see the roll-out and subsequent consolidation of our Rare Diseases portfolio including Lamzede, and the acceleration of our Special Care products, particularly Envarsus and Curosurf, the latter thanks to the launch of our new, Less Invasive Surfactant Administration (LISA) scheme. We also expect to begin commercial sales of Holoclar, and several affiliates are currently working on this process.

Transplantation is an area that will require long-term effort and investment. We continue to be committed to building our presence in the area, and to establishing Chiesi as a leader in this field.

The US Region

Expanding our product portfolio in hospital and adjacent specialties is a continuation of our evolution; multiple selling faces with a broader product portfolio really strengthens Chiesi's place in the US and better positions us for further growth in the future

Ken McBean
President and Chief Executive Officer of Chiesi USA



Evolution and expansion

Chiesi USA strengthened its cardiovascular hospital product offering significantly in 2016, through the acquisition of the worldwide rights to three products from *The Medicines Company*. This was the largest business development deal in our group's history, with approximately $262 million paid in cash at closing for *Kengreal* (cangrelor), *Cleviprex* (clevidipine) and the rights to *Argatroban* for Injection, with up to $480 million agreed in sales-based milestones and royalty payment obligations.
The acquisition of these products supports our aim of becoming a recognized leader in hospital and adjacent specialties in the USA. Cardiovascular is a particularly important therapy area in the USA, and the expansion of our portfolio helps us to deliver products that enhance patient care, and meet the needs of providers in this setting. It has also paved the way for the establishment of a new dedicated *Acute Care* sales force, complementing our existing *Special Care* sales force, which is focused on *Curosurf* and several local cystic fibrosis products.

Strong performance in 2016

With sales of $278.4MM US performance exceeded budget by 30%. This was due in part to our new products acquisitions, but also resulted from strong organic growth. With 100% of sales in *Special Care*, Chiesi USA is playing a prominent role in helping the Group to achieve its strategic goal of diversifying into therapy areas beyond respiratory.

Chiesi USA

238
employees

Leading digital innovation

Chiesi USA has particular expertise in the implementation of innovative digital tools to enhance marketing and selling. Examples include a *Customer relationship management* (CRM) system, now used by all field-based employees to collect data, and a number of closed loop marketing programmes. Such programmes include a marketing automation platform that allows the company to carefully orchestrate and segment outbound digital marketing campaigns to HCPs and patients, as well as track customer interactions with various marketing messages and tactics over time (eg, email, banner advertising, website, hosted videos, downloadable content). In addition, the marketing team has worked to refine their content mix to lead HCPs and patients on deliberate online customer journeys intended to accelerate conversion and product interest. Finally, personal interactions between HCPs and the company are now being captured through a blend of digital CRM, tradeshow and speaker platforms; allowing accurate measurement of both interactions and conversions across all branded touch points.

In recognition of its expertise in this area, we have tasked Chiesi USA with leading the Group's digital marketing strategy programmes and sharing *best practice* across affiliates.

In early 2017, we added to Chiesi USA's already strong R&D resources by recruiting six new staff, specifically to progress our respiratory *Triple* programme.

Continued growth in 2017

In 2017, Chiesi USA will continue to pursue high quality, synergistic business development opportunities, including late stage development or marketed product deals. Our focus will remain on hospital and *Acute Care* products, in addition to *Special Care* and orphan diseases.

We will help lead the Group's *Total Care* in Neonatology programme, and focus on acquiring products and service offerings that will expand our presence in the neonatal intensive care unit. This may include the acquisition of medical devices and diagnostics in addition to our existing neonatology drugs. With the Chiesi Group's position as a world leader in this field, we are looking at how we can also achieve market dominance in the US.

The Emerging Countries Region

Our region is not without its challenges – we cover countries that are culturally and economically very diverse – but we are extremely proud of the energy and entrepreneurial spirit shown by our team, and of the extraordinary growth they have achieved.

Cosimo Pulli
Head of Region Emerging Countries and IMDD

Significant growth

The Emerging Countries achieved remarkable growth of **14.8%** at Constant Exchange Rate in 2016. Sales in the region were supported primarily by *Special Care*, and specifically by the key pillars of our neonatology franchise, *Curosurf* and *Peyona*, and boosted by our respiratory drugs, *Clenil* and *Foster*. All the affiliates in the region, with the exception of Turkey, posted a solid double-digit growth, but it was in **China** that we saw an incredible **growth rat**, due in part to the adoption of the "Second Child Policy" promoted by the central government and the *rollout* of an ambitious *field force* expansion project. This growth was delivered by our Neonatology Franchise, together with our respiratory products, promoted through a joint venture with our local partner, Eddingpharm.

	Net revenues *In mio €*	**Number of employees**
Russia	25	132
Pakistan	19	200
Mexico	12	69
Turkey	26	147
China	74	205
Brazil	59	212
IMDD	71	59
EMERGING COUNTRIES	**286**	**1,024**

One of the key achievements in the region was our entrance into the **Canadian** market, where we sold our first pack of *Curosurf* through an agreement with the specialty pharmaceutical company, *Metapharm*. We also set up a direct affiliate in **Iran** – a country in which we expect to increase our business significantly.

In **Russia** – one of the market with the highest potential alongside China – we split our field force into two distinct networks. The *Special Care/Neonatology and Respiratory/Primary Care* lines are expected to enhance sales of our products in these fields.

Products, our people and customers

Our strategy for this large and varied set of markets is to focus on **products**, **our people** and **customers**.

We aim to exploit the potential of all our **products** fully, irrespective of their maturity, and make them available in every part of the world in which we have a presence. We therefore continue to launch our legacy products such as *Foster* and *Clenil* in emerging markets, and we are seeing solid growth in their sales across the region.

Although many of our emerging market affiliates are relatively new, they have nonetheless experienced rapid growth in sales. We are therefore committed to ensuring that we have appropriate organisational structures in place in all our affiliates to keep up with the pace of change.

Our **people** are at the centre of everything we do. Yet our region links a vast and varied array of cultures, and most of the countries it encompasses are situated a long way from our Headquarters in Italy. We therefore strive continually to enhance cohesion and integration across the region, and were rewarded in 2016 with the very high level of satisfaction and engagement reported amongst our people in the companywide 'Voices' survey.

We also invest significant effort and resources in supporting our **customers** – both patients and *healthcare professionals* (HCPs). For example, in Special Care, we take time to provide training and development opportunities to HCPs to help them to master the techniques required by the use of some of our products, through *Continuous Medical Education* programmes in all our countries.

Overcoming barriers to access

Demand for healthcare continues to increase in many emerging markets, keeping pace with rapid local economy development. But in highly populated countries resources can be limited, and access to drugs is frequently a major issue. Delays in the registration process and subsequent price cuts are often significant challenges, but we are meeting them head on and continuing to make significant inroads in the region with all of our products.

Chiesi IMDD

Digital innovation driven by geography

The vast size of some of our countries has necessitated the development of innovative digital tools that enable us to reach HCPs in remote locations. For example, in Russia we have introduced webinars and digital marketing to reach our customers, and overcome the geographical challenges posed by a territory that encompasses eleven different time zones.
In Mexico, we have launched a digital app to train patients in how to use their inhalation devices. These can also be used by doctors to monitor their patients' use of products to aid compliance.
In Turkey, we had an extensive use of different technologies. In the respiratory area, we promoted some educational activities, targeting HCPs and patients through Youtube, a webcast and apps. In Special Care, we focused mainly on disease awareness campaigns delivered through social media.

Looking ahead in rapidly evolving markets

2017 will be an important year in the Emerging Countries, and we expect to see continued high growth of over 13%.
The launch of *Foster NEXThaler* in seven new countries will be a top priority, and we will also ensure market access for the *Foster* line extensions and other products for which we have submitted local registrations this year.

In addition to seeing significant growth in our neonatology products, we also have great expectations for our respiratory products in China. We anticipate that *Foster* will be reimbursed, and sales of *Foster* and *Clenil A* are expected to be strong. We will also prepare for the launch of Trimbow across the region, which will be available first in the Nordics, followed by Mexico and Brazil.

Therapeutic Areas

RESPIRATORY/PRIMARY CARE

In Chiesi, we are committed to improving the quality of life of people with respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD). We have also developed a range of medicines for use in Primary Care across a number of therapy areas including rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and cardiovascular disease.

PRODUCTS	INDICATIONS
Foster® Spray (beclometasone dipropionate plus formoterol fumarate)	Fixed combination Modulite®-based spray formulation (pMDI) of an anti-inflammatory and bronchodilator, indicated for the treatment of asthma as both maintenance therapy (1 or 2 puffs twice-daily) and MART (Maintenance and Reliever Therapy) Approved for the treatment of COPD in 2014
Foster® NEXThaler® (beclometasone dipropionate plus formoterol fumarate)	Dry powder formulation (DPI) for inhalation, dispensed in extra-fine particles by the NEXThaler® device Approved for the treatment of COPD in 2015
Atimos® (formoterol fumarate)	Modulite®-based spray formulation (pMDI) indicated for the prevention and treatment (1-2 puffs twice-daily) of bronchospasm in patients with obstructive pulmonary disease, including bronchial asthma and COPD, as well as allergen or cold-induced bronchospasm, in both adults and children over the age of six
Clenil® (beclomethasone dipropionate)	Range of beclomethasone-containing products, in a variety of formulations indicated for a range of inflammation-driven respiratory diseases, including asthma, allergic rhinitis and bronchostenosis conditions Includes Clenil Spray (pMDI, Modulite®), Clenil A (sterile suspension for nebulisation) and Rinoclenil (nasal spray, suspension)
Brexin (piroxicam β-cyclodextrin)	Non-steroidal anti-inflammatory indicated for the symptomatic treatment of painful and inflammatory conditions in patients with rheumatoid arthritis, ankylosing spondylitis and osteoarthritis
Iperten (Manidipine chlorohydrate)	Long-lasting calcium-channel blocker indicated for the treatment of mild-to-moderate hypertensive patients
Vivace (manidipine and delapril)	Fixed combination of two antihypertensive agents- a calcium-channel blocker and an ACE-inhibitor- indicated for the treatment of hypertensive patients not adequately controlled with manidipine or delapril monotherapy

NEONATOLOGY

For decades Chiesi has been committed to neonatology, working alongside the medical community to improve the care of preterm babies. Thanks for this important relationship, we have become a global partner for neonatologists, bringing our life-saving drugs to more than 80 countries worldwide.

PRODUCTS	INDICATIONS
Curosurf® (poractant alpha)	Animal-derived surfactant, for endotracheal administration in preterm infants, indicated for the treatment of respiratory distress syndrome (RDS), or for the prophylaxis in neonates at high risk of developing RDS or with evidence of surfactant deficiency
Peyona® (caffeine citrate)	Solution indicated for the treatment of primary apnoea in preterm neonates, administered either by slow intravenous infusion or orally

RARE DISEASES

Patients with rare diseases face a number of challenges, including difficulty in receiving an accurate diagnosis and accessing effective treatment.

PRODUCTS	INDICATIONS
Holoclar (Ex vivo expanded autologous human corneal epithelial cells containing stem cells)	The only approved product for the treatment of patients with moderate to severe limbal stem cell deficiency (LSCD) due to physical or chemical burns
Lamzede	Velmanase alfa, recombinant form of human alpha-mannosidase, is a biotechnological product and an enzyme replacement therapy used in the treatment of alpha-mannosidosis (extremely rare genetic disorder that leads to severe and debilitating skeletal abnormalities, deafness, recurrent infections and mental retardation) Marketing Authorisation Application currently under review by the European Medicines Agency

SPECIAL CARE

Chiesi has a strong commitment to the care of patients that have potentially life-threatening diseases, which are primarily treated by specialists in the hospital setting. An important focus for us is offering the medical community new therapeutic options for the treatment of serious genetic diseases such as cystic fibrosis.

PRODUCTS	INDICATIONS
Clipper (beclomethasone dipropionate)	Oral corticosteroid, indicated for the treatment of mild or moderate ulcerative colitis in the active phase, as add-on therapy to 5-ASA-containing drugs in patients who are non-responders to 5-ASA therapy in the active phase
Bramitob (tobramycin)	Tobramycin formulation in a sterile inhalation solution, indicated for the treatment of chronic pulmonary infections caused by Pseudomonas aeruginosa in patients with cystic fibrosis
Hyaneb (sodium chloride and hyaluronate)	Hypertonic inhalation solution for the removal of mucous secretions, indicated for cystic fibrosis sufferers and those with bronchiectasis
Envarsus (tacrolimus monohydrate)	An immunosuppressor indicated for the prevention and treatment of acute rejection in adult kidney or liver allograft recipients

***Curosurf**: Destiny or Chance?*

by Sandra Fernando

Sandra Fernando

The story of the birth of Curosurf is based on a series of chance encounters and blossoming friendships.
Whilst the first recognition of *Respiratory Distress Syndrome* (RDS) or Hyaline Membrane Disease as it was previously known was in 1903, our surfactant story with *Curosurf* began in 1980 with two exceptional scientists - **Bengt Robertson and Tore Curstedt**.

"By chance, both Bengt and I were working at the Karolinska Institutet in Stockholm – he in one hospital and I at another, only 3km apart from each other. One day he called my hospital and said that he would like to speak with a lady about phospholipid analysis. One of my colleagues said "She doesn't work here anymore, but you can speak to Curstedt instead – he is very interested in phospholipids and has been working on them for many years." So they put the call through to me." *Tore Curstedt*

This was the beginning of a lifelong friendship and extraordinarily successful research collaboration.
In 1980, Bengt wanted to develop a protein free surfactant and through the years of research Tore had conducted with phospholipids and proteins, they soon realised that they needed a different way of producing surfactant to retain the useful surfactant properties that the babies needed. Together they produced a porcine surfactant that they named after themselves – *the Curstedt – Robertson surfactant* or *Curosurf* for short. This surfactant was unique in that it went through an additional purification step of liquid gel chromatography, leaving only polar lipids, SP-B, and SP-C with a phospholipid concentration of 80mg/ml.

A pivotal moment occurred in June 1983 when they received an urgent call from a neonatologist at a local hospital, where despite all their attempts to resuscitate, they had a failing preterm boy in his 27th gestational week, who was going to die. Although *Curosurf* had been used successfully in pre-clinical studies, it had never before been given to a baby. Curosurf was given on 'vital indication' and within 5 minutes, he changed from being completely blue to pink. Just one hour later, his lungs were working normally and he no longer needed oxygen.

"It was one of the most magical moments of my life!" . *Tore Curstedt*

They knew at that moment that if the drug was so good, they needed to start clinical trials. One of Bengt Robertson's greatest skills was the ability to identify and get on board potential collaborators. He travelled throughout Europe and visited neonatologists in their intensive care units to discuss *Curosurf*. One of the first collaborators was Professor **Henry Halliday** from Belfast.

"During my first visit to Stockholm to meet Bengt and Tore, they had a call from the neonatal unit at the local hospital – St. Göran, where two very premature twins had been admitted. They had severe respiratory distress syndrome. They were born about 14 weeks early and my only experience at that time with babies born around 26 weeks gestation with severe RDS was that they had a very high chance of dying. Both of these babies were on mechanical ventilation and 100% oxygen. Bengt and Tore took me to the hospital, made up the surfactant, it was administered to these babies, and they dramatically improved. These babies who had been on the verge of dying suddenly became very pink and active. I'd never seen anything like it at the time – for me it was a wonder drug." *Henry Halliday*

In the beginning, no company was involved. For the first two clinical trials, *Curosurf* was produced in the hospital laboratory. It was very labour intensive and a time consuming process. The dose from one pair of pig lungs was only enough for two to three premature babies. It took one month to create enough surfactant for 100 babies to be treated.

"Once we'd completed the first randomised trial which showed improved survival, we realised that this was a drug which could be marketed and would be useful for premature babies throughout the world." *Henry Halliday*

"For the wider use, Bengt Robertson and I realised that it was impossible to make a product like that

by ourselves – we needed to get a company involved. It would cost us enormous amounts of money to make a pharmaceutical product." *Tore Curstedt*

Pharmaceutical companies were approached but they did not feel it would be worthwhile developing this product because the market would be too small.

By another chance, one of the collaborators of the initial trial – Giulio Bevilacqua who was from Parma, had connections with Chiesi Farmaceutici.

"Giulio Bevilacqua introduced Bengt and Tore to Chiesi and right from the beginning they were very interested in developing the surfactant and they were the ones who took at least some risks to put it into the market." *Henry Halliday*

In 1987 the collaboration with Chiesi Farmaceutici began. Chiesi fully believed in Curosurf and took the responsibility of bringing Curosurf to full clinical development, registration and finally to market. By 1992, Curosurf was first launched in Italy and Brazil.

"It was very good for us to have Chiesi. I think that without Chiesi, it wouldn't have become a product." *Tore Curstedt*

Dr Paolo Chiesi e Dr Henry Halliday

Poractant Alfa
CUROSURF®

The emotional reaction of seeing a baby turn from blue to pink before your eyes was the inspiration for our Curosurf logo.

This year, 2017, marks the 25th Anniversary of the launch of *Curosurf*. It is now available in over 90 countries worldwide and it is the world's leading surfactant. We have continued the spirit of collaboration that Bengt and Tore demonstrated so admirably and have developed close partnerships in the global neonatal community. We continue to support the research of the clinicians and scientists alike and continue to invest in our own neonatal research. A brand new plant dedicated to the production of *Curosurf* was inaugurated in Parma in 2015. This investment of more than 20 million euro ensured the highest quality standards are maintained, using cutting-edge technologies, to double our production capabilities.
Professor **Christian Speer** – one of the initial collaborators and the main author of two of the early fundamental clinical studies believes the success of *Curosurf* was down to a uniquely motivated network of people with the desire to optimise surfactant treatment – a legacy of Bengt Robertson.

"But we are still in a situation where we are thinking of how we can improve the results we have obtained by defining new strategies and by utilising surfactant as a carrier for targeted topical therapies." *Christian Speer*

With this belief in mind, Chiesi will launch *Curosurf LISA* this year. LISA is a *Less Invasive Surfactant Administration* technique, which has been demonstrated to improve outcomes. We have also developed a specifically designed catheter – *LISAcath*, in collaboration with neonatologists, to enable LISA to be used. Our aim with *Curosurf LISA* is to enhance CPAP success and ultimately improve the lives of these babies.

Irrespective of whether it was destiny or chance, for us, *Curosurf* was and will always be a wonder drug. To date, we believe that over 3.7 Million babies have been treated with Curosurf and it is impossible to say how many lives have been saved.

Dr. Christian Speer

Patrick e Dr. Tore Curstedt

Sandra Fernando
Global Brand Leader - Neonatology & Special Care Franchise

04 INNOVATION

Innovation in R&D

What has changed at Chiesi in the last few years is the scope of our innovation and our willingness to explore. We have not only grown in size, we have grown in confidence; we believe we can do it and in fact we can do it.

Andrea Chiesi
Head of R&D Portfolio Management

Innovation in R&D is the life-blood of our organisation. With over 80 years' experience at the cutting edge of development, we have a rich history in generating new ideas, and a proven ability to adapt to the dynamic nature of the pharmaceutical industry.

While our heritage in respiratory diseases and neonatology continues to form the core of our focus, 2016 signaled a continued evolution for Chiesi's innovation, as we entered new therapy areas in which we believe our expertise can save and transform lives.

Our commitment to innovation

€ 340 mln

In 2016, investment in R&D continued to grow in both absolute and relative terms – spend reached €340 million, equating to € 0.93 million per day

Spend represented 21.6% of Group revenues. This is an increase of 1ppt on 2015 and a growth of 5.1% over the last two years

The Chiesi Group invests more in R&D than any other Italian company

Respiratory: enhancing patient adherence and addressing unmet medical needs

Respiratory continues to be our most significant area of focus in R&D, in terms of number of ongoing projects and deployment of our resources.

In 2016, we continued to strengthen the *Foster* franchise with two significant European approvals adding the dose counter to both dosage forms of our pressurized metered dose *inhaler* (pMDI). These represent important inhaler device enhancements to facilitate patient adherence to therapy and a novel life cycle management initiative for the Foster brand.
Significant progress was also made with our e-Inhaler programme – a "new generation" inhaler device enhancement being given significant priority in the pipeline.

The marketing authorisation submission for *Trimbow* pMDI, was a major milestone for the franchise, and saw us became the first company to make a submission for a triple combination therapy for the treatment of chronic obstructive pulmonary disease (COPD). The publication of the results of the Phase 3 TRILOGY study in The Lancet also served to highlight the superior efficacy of *Trimbow pMDI* compared with standard therapy.

Neonatology: innovative delivery of life-saving treatment

Our neonatology business is rooted in the surfactant replacement therapy *Curosurf* and as we look to build on our heritage in the area, our R&D efforts have been focused on developing innovative solutions to help improve patient outcomes.

In 2016, we achieved European approval of LISA (Less Invasive Surfactant Administration). This new method of administration reduces the risk of injury to the newborn versus the current standard means of delivery, and is considered a clinically important step in delivering life-saving Curosurf to premature infants.

In parallel, and to further support the commercial roll-out, a CE mark was successfully obtained for the proprietary Chiesi-developed specialised LISAcath (a fine-bore catheter for LISA).

Chiesi: Leading Scientific Innovation in 2016

16
new patents and received 527 granted patents worldwide

2,900
Total portfolio now includes

Oltre 100
Submitted 100+ *peer-reviewed* publications and international conference presentations

1°
According to the European Patent Office Chiesi is the fifth highest applicant of patents in Italy

Special Care: revolutionising medicine through advanced therapies

Chiesi is playing a pioneering role in the new era of advanced therapies for rare diseases.
A major milestone was reached in October 2016, when the first patient was treated with *Holoclar* – the first stem cell-based product ever to have been approved in Europe.
The ongoing efforts to bring novel biotech therapies to market continues, and two important filings took place in 2016:

- In Europe, *Lamazym*, an enzyme replacement therapy for alpha-mannosidosis, was submitted for approval – the first potential therapy for this extremely rare and debilitating disease.
- In the US, we filed *Retavase* (recombinant reteplase) with the US regulatory agency (FDA) for the management of acute myocardial infarction.

A Cutting Edge Digital Strategy

Digital technology is changing the nature of health service delivery. Facilitating a new level of interaction with patients and HCPs, and offering vital data insights, we are able to understand health outcomes in greater depth than ever before thanks to digital innovations such as online patient support platforms, remote diagnostic tools and *peer-to-peer* networking solutions.

As a company, we understand the unmatched opportunity that new technology offers us to better serve our patients and customers. Leading in digital innovation is therefore a strategic priority for Chiesi, and in 2016 we outlined a roadmap that will guide the digital transformation of our company.

Roll-out for our technological evolution will commence in 2017, led by our newly-formed ***Digital Innovation Steering Committee*** (DISC).

By 2022, we intend to apply new digital steps to our way of working. These steps will accelerate the delivery of better, more user-friendly treatment and care solutions for patients and customers, and help us adapt to future market challenges and competition.

Three strategic pillars have been identified, and these are providing a framework for the implementation of a series of new programmes, including internal initiatives to optimise organisational processes, external projects to strengthen customer engagement, and transformational projects aimed at fundamentally changing our business model.

1

DIGITAL ENABLED COMPANY:

Creating an innovative, digital company, with strong execution capabilities, that attracts talent and appeals to third party partners with strong innovation credentials.

2

EXPERIENCE EXCELLENCE FOR PATIENTS AND HCPS:

Introducing a new, digital-focused, multichannel model for HCPs and patients, and offering support to assist doctors in making data-driven decisions, while improving the therapy management experience

3

DIGITAL PERSONALISED HEALTHCARE SOLUTIONS:

Delivering innovative, tailored healthcare services and solutions, facilitated by collaboration with HCPs and ad hoc partners, combined with Chiesi know-how and assets

[Our Pipeline]

Driving towards new research to change the lives of patients

Building on the success of 2016 and our long history of innovation, Chiesi's pipeline of new medicines continues to focus on our core areas of expertise: Respiratory, Neonatology and *Special Care*. At the same time, we continue to explore opportunities to grow in scope, bringing new, innovative therapeutic options to even more neglected diseases, with the aim of changing patients' lives.

2016

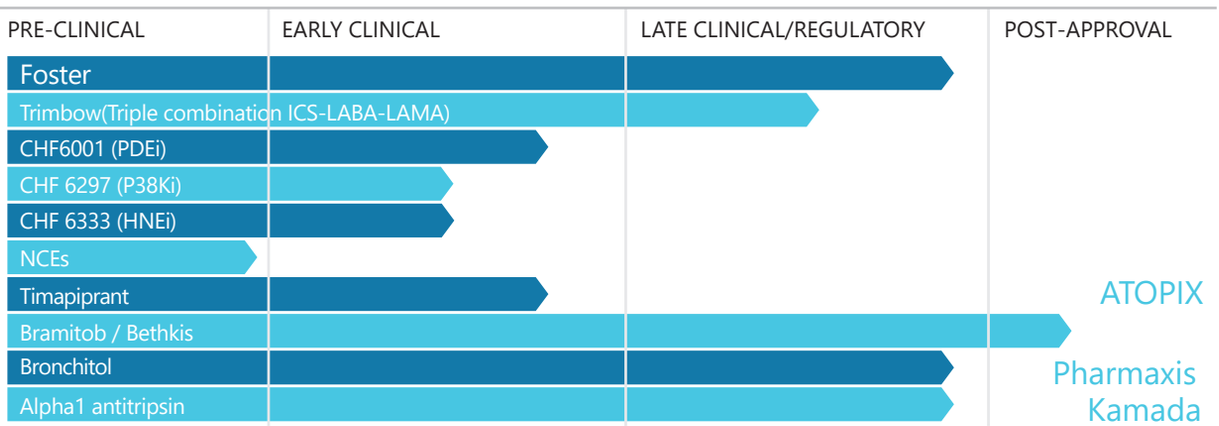
51

projects active in R&D

Our rich and heterogeneous pipeline extends over three main therapeutic areas. The drugs we develop have proved to be very promising for many difficult to treat and incurable diseases: we are committed to achieving this goal

Mark Parry-Billings
Head of Corporate Drug Development

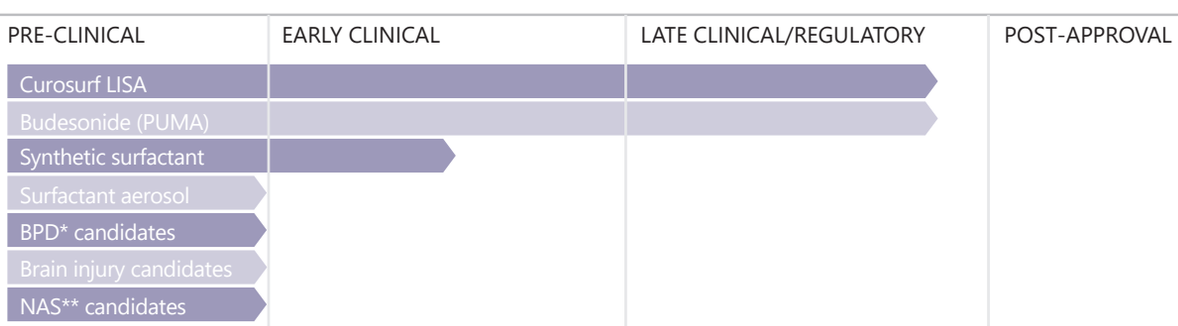
Pipeline overview



Respiratory

In respiratory, our proprietary pipeline of new chemical entities (NCEs) made encouraging progress. We continued to sharpen our focus in this area by leveraging our expertise in asthma and COPD to progress development of other respiratory indications of new chemical entities (NCEs), such as cystic fibrosis (CF), bronchiectasis, *idiopathic pulmonary fibrosis (*IPF) and pulmonary arterial hypertension (PAH). This includes identifying opportunities for collaborations or acquired late-stage assets, such as *Bronchitol* from *Pharmaxis* and *Timapiprant* from *Atopix Therapeutics*.

Pipeline overview



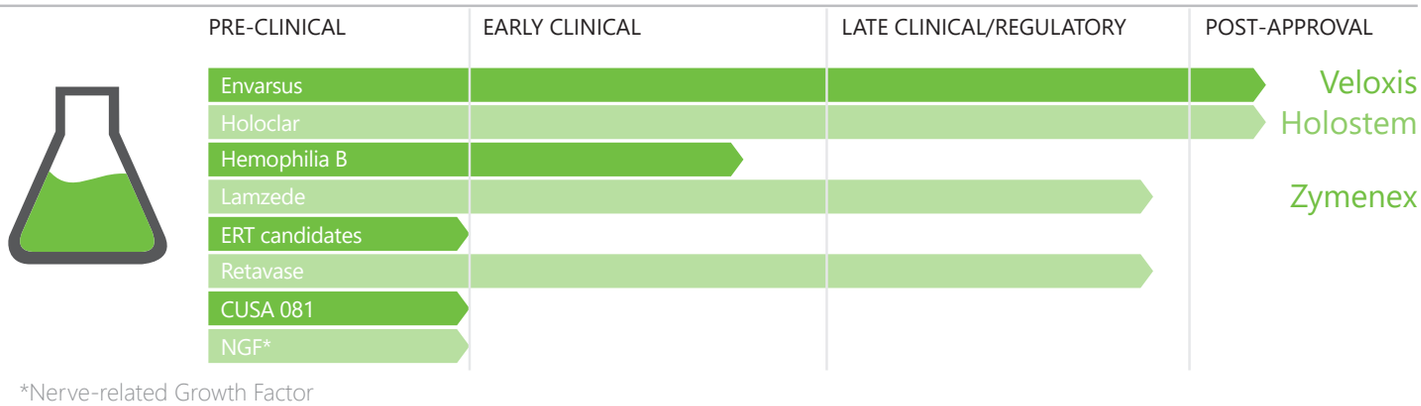
*BPD: Bronchopulmonary dysplasia **NAS: Neonatal abstinence syndrome

Neonatology

A business-critical surfactant project that made significant progress in 2016 was nebulised *Curosurf* – the delivery of surfactant by aerosol rather than intratracheal instillation.

Our commitment to neonatology and the provision of new solutions to high unmet medical needs saw us exploring new neonatal programmes with a focus on neonatal brain injury and neonatal abstinence syndrome (NAS), both of which progressed through pre-clinical phases in the year.

Pipeline overview



*Nerve-related Growth Factor

Special care and rare diseases

In *Special Care*, our exciting pipeline continues to make significant strides in the development of protein, gene and stem cell therapies. Collaboration with other leaders in innovation is allowing us to expand our Special Care portfolio and continue to bring *first-in-class* therapies to market. These include:

- The acquisition of *Zymenex* provided a protein therapeutic platform which has delivered *Lamazym* and is now focusing attention on the pre-clinical pipeline of product candidates in the same class;
- Collaboration with *Holostem* provides a stem cell therapy platform which has delivered *Holoclar* to the market and which now represents an advanced platform to leverage a pipeline of new products.

***Rare diseases**: a daily challenge*

by Leonardo Calzetti

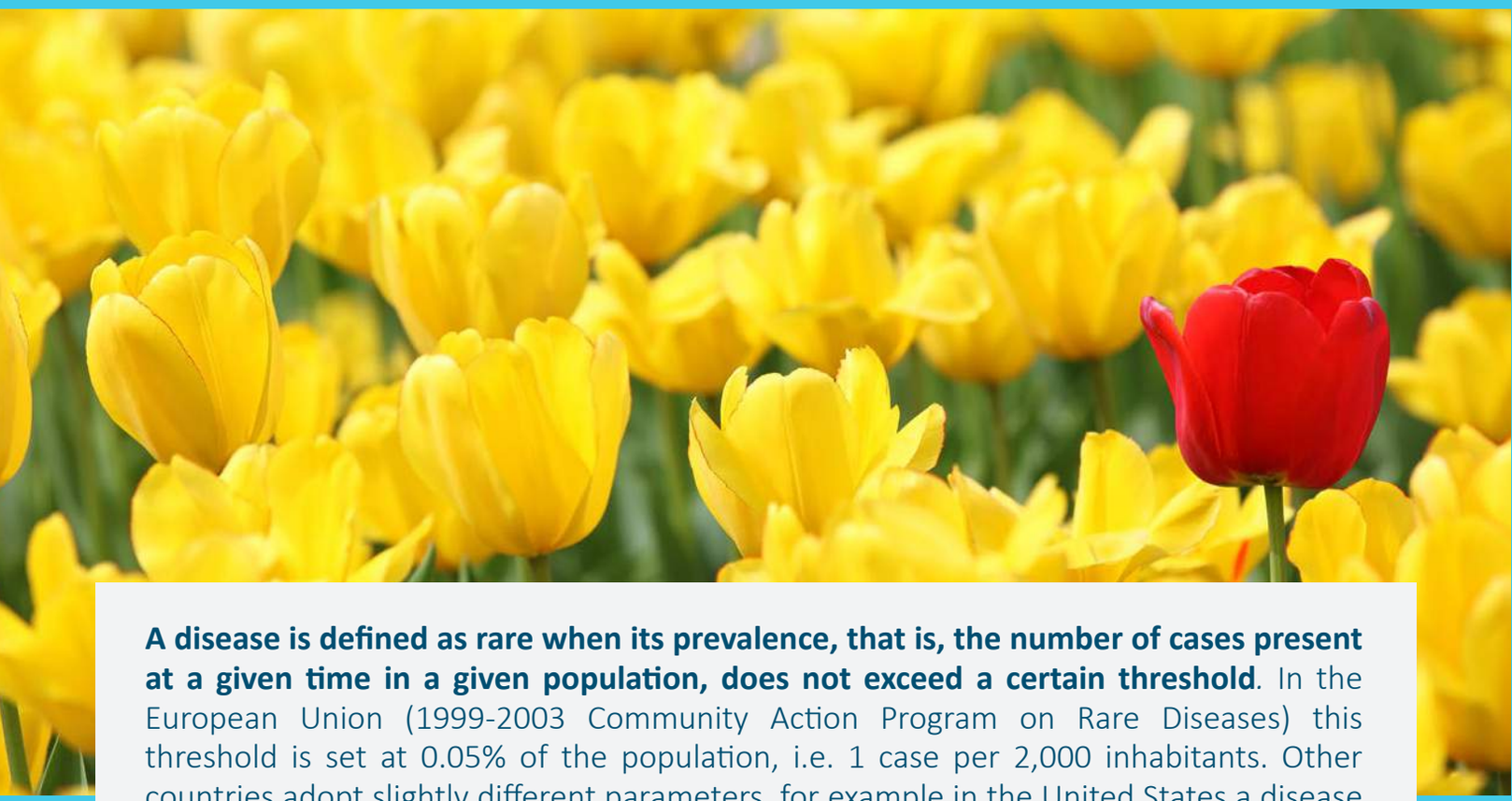
Leonardo Calzetti

My first encounter with rare diseases dates back to 1998. That year I took part in a conference on thalassemia and immediately realised that I was becoming involved with a whole new world, an unexplored territory, where I would come into daily contact with patients and their various conditions, something which was to have a significant impact on how my work was perceived.
Almost twenty years have passed since then, yet I continue go through the same kind of experience. I recently attended a conference on lysosomal diseases where I met a great number of patients, often confined to a wheelchair, accompanied by their families. They were all in search of hope and wanting to understand what the world of research was doing to find solutions that could offer at least some relief for the burden their disease had placed on their shoulders.
Since I first began dealing with these issues, much has been done: research has made progress in understanding the causes and mechanisms of various diseases, the industry has developed several effective therapies and governments, mostly in the more developed countries, have begun to provide assistance for some of the economic and social aspects relating to rare diseases.
Yet all of this is still not enough: it is estimated that there are to date around 300 million people worldwide suffering from one of around 7,000 rare diseases so far identified. Treatment is currently only available for a few hundred of these diseases.

From a medical point of view, rare diseases are characterised by a wide range of symptoms and clinical manifestations, which not only vary from one disease to another but also within the same disease, affecting patients' physical and mental abilities. This enormous diversity further complicates the task of identifying effective solutions.

However, although rare diseases differ greatly from one another, they do have several traits in common:

- Many of them are severe, chronic, degenerative and frequently result in a significantly reduced life expectancy;
- The disease begins during childhood in 50% of the cases;
- The genetic origin has been identified in 80% of rare diseases;
- Most cases are incurable and there is often no available treatment beyond palliative options;
- The complexity of the disease and serious physical and mental disabilities involved mean that patient management is onerous and has a dramatic impact on the patient's quality of life and that of their whole family: a loss of autonomy is frequently the norm;
- Living with a rare disease has serious implications for the patient's daily life and that of their families, who experience problems with isolation and social stigma, difficulties at school and at work;
- Aside from the heavy costs of managing the disease, the families of these patients also experience difficulty when coping with the demands of the disease on top of their work commitments, which then results in financial problems;
- In most cases, obtaining a diagnosis is a fight which goes on far too long and may last an average of more than 7 years;
- Information available to patients is extremely limited both concerning their disease and regarding potential therapeutic programmes;
- Scientific knowledge about the disease and its mechanisms is also limited and research into new treatments or the stipulation of appropriate therapeutic strategies are much more difficult;
- When an innovative treatment has been developed, its availability is limited and geographically inconsistent due to extremely diverse mechanisms concerning approval, price and reimbursement in different countries.



A disease is defined as rare when its prevalence, that is, the number of cases present at a given time in a given population, does not exceed a certain threshold. In the European Union (1999-2003 Community Action Program on Rare Diseases) this threshold is set at 0.05% of the population, i.e. 1 case per 2,000 inhabitants. Other countries adopt slightly different parameters, for example in the United States a disease is considered rare when it does not exceed the 0.08% threshold.

Understandably, working in the sphere of rare diseases is a difficult yet stimulating challenge: every small achievement made represents an important conquest and a source of hope for patients who would otherwise have no real answers.
Chiesi took on this challenge some time ago, making its own contribution in different therapeutic areas, which are characterised by extremely limited numbers of patients.

I am particularly proud of the progress our company is making in the development of velmanase-alfa (Lamzede), an enzyme replacement therapy for the treatment of alfa-mannosidosis, an ultra-rare hereditary metabolic disease belonging to the lysosomal accumulation disease group. The Lamzede registration dossier was submitted to the EMA in September 2016 and its authorisation is expected from the authorities by the end of 2017.
Lamzede will be the first and only treatment available for this small group of patients (the disease affects 1 case in every 500,000 births) suffering from a devastating disease, characterised by immune deficiency (which manifests itself in recurring infections), facial and skeletal abnormalities, reduced mobility, impaired hearing and cognitive impairment.

These neonates often appear normal at birth, but their health worsens progressively.
Early deafness puts the possibility of developing social skills at risk and requires early educational support. Muscular wasting is progressive and many sufferers become wheelchair bound. None of them really have the chance to be autonomous.
The prognosis is poor and most of these patients do not live beyond fifty.
A clear understanding of this situation pushes me to come to work every day with the conviction that we can make a difference for these patients. We can offer them the hope of a new life, albeit not perfect, yet better than the one fate has chosen for them.

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Head of Global Business Unit Rare Diseases

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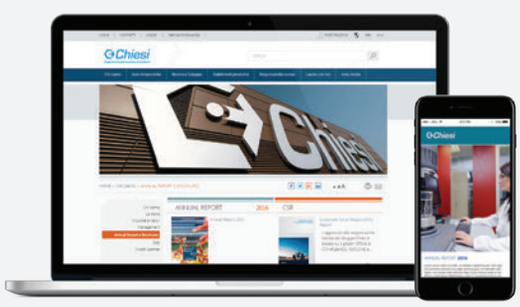
Diesis	*Rinoclenil*
Donegal	*Ventmax*
Flamexin	*Vivace*
Fluibron	



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