Annual Report **2013**

octapharma

For the safe and optimal use of human proteins

Content

The Strategic Pillars

The narrative of the 2013 annual report is structured around the strategic pillars introduced in 2012. For each pillar, there is a chapter highlighting global activities contributing to this pillar. Each pillar chapter is represented by a ring of a particular colour. The pillars should be seen not as a representation of how the company is today, but as a vision of what the company aspires to be tomorrow. As a human company, the story of Octapharma is best told through the perspectives of employees working towards the strategic aims of the company. Each chapter includes only a selection of the global activities contributing to the relevant pillar. In the following report, you will see some of the ways in which the Octapharma global family is working towards making the strategic vision a reality and bringing our pillars to life.

Foreword by Wolfgang Marguerre

The year 2013 has been a good year for Octapharma. Speaking as chairman of this ambitious organisation, this year has met my expectations. We achieved the highest revenue in the company's history, with sales close to 1.2 billion Euro. This performance has been driven by the consolidation of our star product, octagam®, which had a remarkable record-breaking year with the highest ever sales. Across our entire portfolio we report a 26% growth in sales. This increase in revenue will permit us to be even bolder in our investments over 2014, providing the security and confidence to embark on further programs throughout the corporation.

We have reached significant milestones in our quest to enter the recombinant market with our human cell-line based FVIII product with license submissions to EMA, Australia and Canada, and further submissions planned worldwide including USA, Russia, and Brazil. Product approval is expected in Europe during 2014.

Our operating income for 2013 is impacted by major inventory adjustments, resulting from revaluations concerning previous years; it is, however, still 10 % above 2012.

Our history, as illustrated in last year's 30th anniversary report, is built on our plasma expertise. Entering the recombinant market is a major milestone for Octapharma. With our Human-cl rhFVIII we are addressing the key issue faced by patients treated with currently available recombinant therapies, the development of FVIII inhibitors. Promising early results from our "NuProtect" study give us confidence in our vision that a recombinant FVIII from a human cell line offers major advantages compared to products from a non-human cell line. Many years of dedication and hard work have brought us to this stage.

We all take responsibility to ensure that the company is in a strong position to support the needs of patients around the world. The financial performance in 2013 allows us to direct substantial revenue into R&D addressing as yet unmet patient needs. The largest financial investment into a clinical study in the company's history, and an area of clinical research which is very close to my heart, is the octagam®5% MS (Multiple Sclerosis) Study. We hope to be able to provide successful treatment to patients with relapsing MS by demonstrating that it is possible to identify predicted responders to treatment with octagam®5%. If this study is a success our aim is to go to the market with the first personalised treatment for a significant portion of remitting MS patients. Although an investment on this scale comes with an element of risk, this quest is worthy because it could potentially prove to offer life-changing therapies for patients suffering from MS.

In relation to the planned increase in plasma production across all 45 US plasma centres, we are investing around 30 million Euro to build a state-of-the-art facility in Charlotte, North Carolina. This will include a plasma testing laboratory and a plasma storage facility, as well as Octapharma Plasma Inc.'s new headquarters.

We continue to invest in our production facilities with a focus on projects to increase plasma fractionation capacity to help us reach our increased production goals for 2017. Investments in our European production facilities include filling lines in Springe, Stockholm and Lingolsheim. Beyond our 2017 sales goals of 2 billion Euro, we are putting in place a program for 2019 which will address how we should develop and invest to ensure that we can support continuous growth.

Our intention is to register the complete product portfolio in all markets - offering patients around the world access to our therapies, extending our footprint to all geographies.

An important area of expansion is the USA which represents approximately 50 % of the global plasma market. The US market will be a main area of growth in 2014 and our long-term aim is to license the complete Octapharma product portfolio. We have continued to increase our product range with the launch of octaplas® in 2013 and have submitted for approval octagam® 10 %, octaplex® and octanate® (with an indication for ITI).

Our vision of global market access also means expanding into emerging markets; examples include the opening of an office in South East Asia and the expansion of our operations in China.

I would like to acknowledge that none of these achievements could have been possible without the dedication and commitment of talented employees across the organisation. Octapharma now employs in excess of 5,500 people globally. To recognise the importance of our people, our new Global HR function is creating global systems and infrastructures to support employees in forging their own career paths with training and development as well as making them aware of the global opportunities available within Octapharma. We are putting these systems in place to further strengthen our greatest resource, the employees.

We must never allow ourselves to become complacent, or to think that we have achieved "enough". In 2012, we identified the strategic direction of the organisation and the fundamental elements of success required for that journey. The strategic pillars are not intended to be a pretty picture of what the company is today, but of what the company strives to become tomorrow. We all have our eyes on the future and while last year's report looked at our legacy celebrating our 30 year history, this year's report shows our future. Framed around the strategic pillars, each chapter shows global activities aimed towards achieving and exceeding our ambitious goals.

Wolfgang Marguerre
Chairman of the Octapharma Group

The Management Board of the Octapharma Group

Wolfgang Marguerre

Chairman Octapharma Group

Frederic Marguerre

Shareholders' Representative
President, Octapharma Plasma Inc. USA

Tobias Marguerre

Managing Director Octapharma Nordic AB

Paulo Castro

President of the
Global Management Committee

Roger Mächler

Chief Financial Officer

Flemming Nielsen

President Octapharma USA, Inc.

Gerold Rempeters

Corporate Production Officer

Ulrich Thibaut

Research and Development

Josef Weinberger

Corporate Quality and Compliance Officer

At a Glance

Founded
in 1983

Mission
"For the safe and optimal use of human proteins"

Employees
5,514

Net Sales
1.154 billion Euro

Headquarters
Octapharma AG, Lachen, Switzerland

Production and Supply
Octapharma Pharmazeutika Produktionsges.mbH, Vienna, Austria
Octapharma SA, Lingolsheim, France
Octapharma AB, Stockholm, Sweden
Octapharma S.A. de C.V., Mexico City, Mexico
Octapharma Produktionsgesellschaft Deutschland mbH, Springe, Germany
Octapharma Plasma Inc., Charlotte, USA
Deutsche Gesellschaft für Humanplasma mbH, Langenfeld, Germany
Octapharma GmbH, Dessau, Germany

Research and Development
Octapharma Pharmazeutika Produktionsges.mbH, Vienna, Austria
Virus and Prion Safety, Innovationszentrum, Frankfurt, Germany
Molecular Biochemistry, Berlin, Germany
Octapharma Biopharmaceuticals GmbH, Heidelberg, Germany
Octapharma AB, Stockholm, Sweden
Octapharma AG, Lachen, Switzerland

Corporate Medical, Regulatory
Octapharma Pharmazeutika Produktionsges.mbH, Vienna, Austria
Octapharma GmbH, Langenfeld, Germany

International Corporate Marketing
Octapharma AG, Lachen, Switzerland

Subsidiaries and Representative Offices
45

Markets
Europe, Asia, Russia, Middle East, USA, South America, Canada, Mexico, Africa, Australia, New Zealand

Brands
(registered trademarks) albuminativ®, albunorm®, atenativ®, aunativ®, gammanorm®, nanofix®, nanotiv®, octafix®, octagam®, octagam 10%®, octanate®, octanine®F, octanyne®, octaplas®, octaplasLG® , octaplex®, octavi SD Optimum®, pronative®, rhesonativ®, uniplas®, wilate®

Innovations
One of the world's first factor VIII concentrates (KABI 1965 – through acquisition)

First albumin-free genetically engineered factor VIII (development started by KABI in the 1980s – through acquisition)

First company to commercially implement solvent detergent (SD) technology for virus inactivation (1986)

First SD virus-inactivated, standardised plasma for transfusion (1991)

First liquid, ready-to-use intravenous immunoglobulin with a two year shelf-life at room temperature (1994)

First virus-inactivated universally applicable transfusion plasma (2004)

First double virus-inactivated von Willebrand factor concentrate product (2005)

Start of clinical trials using the first recombinant FVIII from a human cell line (2010)

Strategic Vision
The foundation of Octapharma's identity is our patient-oriented corporate culture. We aim to increase our product portfolio to access the global market; to enter the recombinant business successfully; to increase plasma availability and throughput; to nurture a healthy organization with proud and talented employees and to continue to have open and transparent communication. This strategic vision aims to lead to profitable organic growth.

Patient-oriented corporate culture

The foundation of Octapharma's identity is our patient-oriented corporate culture. Alongside the development and production of life enhancing and lifesaving therapies, we continue to invest in programs that are increasingly patient focused. This chapter shines a spotlight on a sample of the numerous and wide-ranging global initiatives.

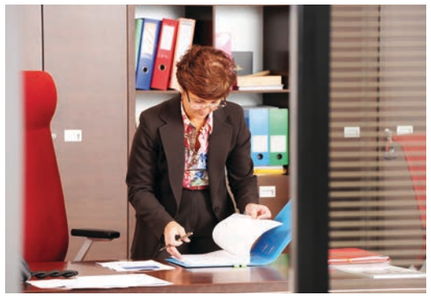
Octapharma France

Marie-Christine Borrelly, General Manager

"The idea for the comics was born out of a challenge faced by many teenage boys with haemophilia: at a certain age they feel they want to escape from their condition and so become reluctant to continue with treatment. We wanted to engage teenagers to show them the importance of continuing their treatment. The hero of our comic is a boy named Alexandre. By reading his story young people can understand their condition better and appreciate that with treatment they can enjoy a normal life. This has been a really creative and successful campaign.

Every quarter we provide the French Association of Haemophilia with the pages of the story, they publish the first page in their quarterly journal which is sent to every affiliation, and the complete story is published on the website. Now teenagers are waiting eagerly for the comic each quarter. Although it was made for teenagers, we have found that adults enjoy it too. We have a lot of ideas for future issues. We plan to show Alexandre going on a trip. It is important for young patients to know that it is still possible for them to have fun, to go on adventures and lead an interesting life, but this is made possible through good treatment and compliance with the treaters' recommendations. It is also important for them that their friends and family have a good understanding of the disease."


Marie-Christine Borrelly



A pull-out abridged version of the comic can be found at the back of this report.

Sylvie Dantin, Medical Manager

"As a medical doctor, I know from experience what it is to treat patients, to infuse and what challenges the patients face. I am responsible for the clinical studies in France including ethical and medical aspects. Octapharma is not simply a producer of product; Octapharma wants to increase knowledge in the pathology. We are dedicated to improving quality of life in patients and are playing a key role in the evolution of treatment. Octapharma is increasingly visible in the haemophilia centres across France and we are doing interesting well-designed studies to improve patient quality of life. Today the main aim in FVIII replacement is to have a product without inhibitors and to have a solution to treat patients with inhibitors. Not only are we involved in important studies for the treatment of inhibitors, but our recombinant product has been designed with the aim of reducing the cases of inhibitors. In France, key opinion leaders are eagerly anticipating the data on the recombinant FVIII previously untreated patient (PUP) study."


Sylvie Dantin


Damien Barrois

Damien Barrois, Medical Affairs & Business Development Haemophilia Manager

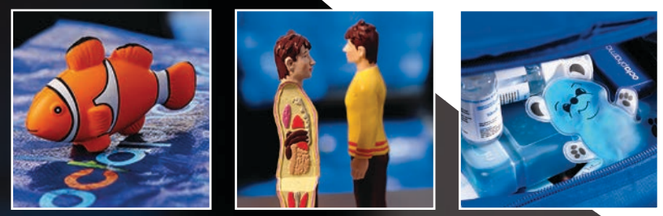
"We are a relatively small team, but every day, somewhere in France a member of our team interacts with physicians or pharmacists involved in the treatment of haemophilia patients. We pride ourselves on our strong scientific background as a company and our strong service support. The French team continuously think of what could be done to help patients more. For example, we have created a booklet addressing the psychological aspects of haemophilia. We also sponsored a book of parent testimonials created by a patients association for parents who have just given birth to babies with haemophilia. They can read the stories of other families and be reassured that a normal life is possible. We are supporting patients to have control of their condition and live as a normal person."


The comic in creation

Sophie Courdioux, Marketing Support & Communication & Event Manager

"Our products treat long-term diseases, so we must focus on the patients and listen to their needs. For example, we provide young patients infusing gammanorm® with tools to help them follow their treatment at home. The gammanorm® fish is a training tool created to help children simulate injection. The nurses teach young patients how to inject; the gammanorm® fish gives the child a chance to practice with the fish before injecting him or herself. We also created the gammanorm® puppet to reassure young patients who might be afraid that the needle goes too deeply and may reach some organs. They can open the body of the doll and see the skin, bones and organs. They can see that the needle stays at a superficial level and so they feel more comfortable and less afraid of the injections."


Sophie Courdioux



Patient education tools including gammanorm® fish and puppet, and travel kit

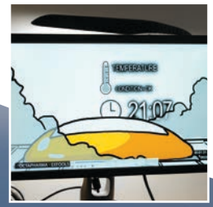
Guillaume Le Ny, Product Manager Immunotherapy and Critical Care


Guillaume Le Ny

"As a pharmacist, I know the importance of having a patient-centred approach. We design and create tools which correspond to the needs of the patient. I meet with key opinion leaders and discuss with them the demands of the patients.

I was watching a film and saw a sequence which represented blood. It suddenly came to me: as a company with many years of fractionation expertise, we should create a film which shows how we make our products. As a result of this we are developing the storyboard of a movie which will track the journey of an immunoglobulin from a donor's arm to the infusion of a patient. The film shows the production steps, including virus inactivation, through the perspective of the immunoglobulin. When you visit a fractionation plant, for example our plant in Lingolsheim near Strasbourg, you see state-of-the-art equipment, but you cannot see what happens within. With this movie, we are showing the inside story so that pharmacists, physicians and patients can better understand this fascinating process."

Bringing the idea to life: storyboard of the film which will show immunoglobulin's journey from donor to patient



Dan Hart, Senior Lecturer in Haemostasis at Barts and The London School of Medicine. Honorary Consultant Haematologist at The Royal London Hospital Haemophilia Centre

"The immune system has a sophisticated way of recognizing things that are foreign to it; evolution has led to it being able to spot a foreign protein or infection by recognizing what is *self* and what is *not self*. Factor VIII (FVIII) is infused during haemophilia A treatment to replace the deficient factor which usually occurs naturally. The infused factor sometimes triggers an immune response which effectively neutralizes the infused factor. Inhibitors are the most serious complication of FVIII replacement therapy affecting approximately 30% of patients with severe haemophilia A. We still don't know why some boys develop inhibitors and others do not.

In science, we must first understand the mechanism of an observation to be able to then propose a therapeutic intervention. There is something fascinating going on immunologically with inhibitors and we need to better understand the immune process at the time of treatment exposure. The next phase is translating this into patient benefit. To understand the mechanism of inhibitor formation, we are starting to use the techniques that are evolving because of genomic medicine. In the RNA sequencing research project with Octapharma, we are using next generation sequencing to look at what happens in a boy's body when he is exposed to FVIII for the first time. The benefit of haemophilia is that we know exactly the time point when the exposure to his haemophilia medicine happens (i.e the first infusion of FVIII). What we want to do is capture the information about what genes are turned on or off at that moment of the first exposure. If we can capture this information, we may be able to see patterns of gene regulation. Once we understand the mechanism, ultimately we hope to be able to predict who may or may not get inhibitors at a very early time point. Once we can predict, then we can change the management of haemophilia A.

The Centre of The Cell, Blizard Institute, Barts and The London School of Medicine and Dentistry, London

Since DNA was discovered in the early 1950s, there has been rapid technological development. We can now amplify the DNA code from only a small volume of blood, as forensic crime teams do. DNA is the blueprint for all the proteins the body produces. To produce a certain protein the gene sequences (DNA) are copied (transcribed) into messenger Ribonucleic Acid (mRNA). What we want to find out is: when FVIII is given for the first time, how does the balance of gene copies (RNA) change, reflecting which genes are turned on and off by the exposure to the FVIII concentrate? We would hope to then identify which genes are important at that moment of first FVIII exposure that might predict if an inhibitor will or will not form.

In the RNA Sequencing Study, we are capturing RNA from all the cells in the blood and in doing so we will have a snapshot of what genes are being used. A small volume of extra blood, an appropriate amount for small babies, is taken at the same time as other samples, so involves no extra visit to the hospital for the patient. This extra amount will be taken 5 or 6 times until 20 infusions. The blood is taken into a special tube that stabilizes the RNA and is sent to our genome centre where the RNA will be sequenced. What we will have then is a huge and important amount of data. This is where bioinformatics comes in; computational experts analyse the data organizing it into different gene families. It will be a lot of work to get this analysis done, but once we have the raw data we have a mine of information for future work, so this is very much an investment with medium and long-term returns.

Dan Hart

I first became aware of Octapharma in 2009, during my haemostasis fellowship, which came out of interaction with the UK Octapharma team who were well informed on inhibitors and the recent literature. They wanted to look at new ways of understanding inhibitors and why they occur. After discussions, we defined RNA sequencing as a potential area to explore. Octapharma funded a research fellow (Octafellow) who started in 2012 to facilitate mutual project development. The structure of Octapharma is such that it allows for a discussion across multiple boundaries, national and international. They have a genuine enthusiasm to take on something quite novel. This will be the first genome-wide study looking at RNA sequencing in PUPS (previously untreated patients). Octapharma and the research team are keen and excited to see where this novel project takes us and the field of haemophilia."

Great Ormond Street Hospital for Children Haemophilia Care Centre

The Haemophilia Comprehensive Care Centre (CCC) at Great Ormond Street Hospital for Children is the largest children's haemophilia comprehensive care centre in the UK and one of the largest five in Europe. The CCC specialize in complications of haemophilia and other bleeding disorders and the management of inhibitors. Kate Khair is a Consultant Nurse who completed her PhD on children's views of living with haemophilia.

Great Ormond Street Hospital for Children Haemophilia Comprehensive Care Centre London

Kate Khair, Consultant Nurse

"We have 130 children with severe haemophilia and admit around 10 new babies every year. We see much more than the average centre because of the population of London. The evolution of haemophilia care has been dramatic over the past decades; babies diagnosed with haemophilia today have much better treatment options and with the right treatment can go on to have relatively normal healthy lives. Today, we have children who have never experienced a joint bleed. They are out playing games and sport like any other child.

Our children have intensive treatment with alternate daily prophylaxis because we want to protect them all of the time. We are protecting brains as well as joints;


Kate Khair

intracranial bleeding can be fatal. Every patient that we see is a new born baby, or a newly diagnosed infant; it is so important to start them out on the right path. We are starting someone on a lifetime of treatment; we have to educate parents from the very beginning. It is important to give control back to the family, for parents to be able to treat their child at home. Some boys actually don't realize that they are different from boys without haemophilia, that not every boy gets an injection of factor concentrate.

Regular exercise strengthens muscles which protects joints. There is a gym and a swimming pool in the centre and when the children come to the hospital for review they are seen by a physiotherapist. We have boys that are very sporty and they know that they have to have treatment to allow them to continue with sport. Despite the advances in haemophilia treatment over the past decades, the most serious complication today remains the development of inhibitors. Inhibitors usually develop around the first 10 to 20 injections. One third of the children have no previous family history of haemophilia treatment, and for those that have their family members had not developed inhibitors. Inhibitors are another complication which can be very unsettling, these families need additional support.

In the UK, we recognize the importance of identifying inhibitors early and have national guidelines recommending screening for inhibitors every third exposure day. We have boys that have all the risk factors, and yet don't develop an inhibitor and those who have none of the risks that do. This is something that we don't yet fully understand. That is why the scientific research to better understand immunity is so important. If a child develops an inhibitor they have to go on a much higher dose treatment for up to three years and we sometimes add in immune suppression. Our therapy is intensive, it's tough and if there are bleeds along the way, these children do not respond so well to factor replacement. It's hard work for their families as well as us; they need more support than someone without an inhibitor.

At Great Ormond Street Hospital we are involved in the studies for Octapharma's Human-cl rhFVIII product. Results are looking good. Theoretically it is safer to have a human-derived product than an animal product, because we don't yet know what 50 years of exposure to recombinant proteins derived from animals does. To have something more like the factor VIII in our own bodies should be a great improvement."

Immunotherapy

Octapharma's immunoglobulin sales reached an all-time high for the second year in a row in 2013. Octapharma obtained a worldwide market share of approximately 11%. Physicians and patients all over the world appreciate not only our products octagam®, gammanorm® and rhesonativ®, but the presence of Octapharma as a responsible supplier of immunoglobulin products. Our sales of the polyvalent intravenous (IVIG; octagam® 5% and 10%) and subcutaneous (SCIG; gammanorm® 16.5%) immunoglobulin preparations were more than 60% higher in 2013 compared to 2012. In 2013, we also achieved two very important milestones in the company's history: one million standard annual treatment doses from our immunotherapy portfolio, as well as the launch of octagam® 10% in Canada under a long-term contract with Canadian Blood Services. In 2014, we aim to launch octagam® 10% in the USA, which will further strengthen Octapharma's position as a significant provider of immunoglobulin therapy options in this important region and worldwide.

It is this continued success that allows for further investments into our future immunotherapy product portfolio. With tremendous interest in both octagam® and gammanorm®, as well as our anti-D product rhesonativ®, the constant strive to provide enough products was a major challenge to both production and supply chain management this year. Thus, major investments were undertaken in 2013 to meet these increased requirements.

Octapharma's fundamental principal of improving patient care worldwide ensures we are ever vigilant of the need to develop our portfolio to meet the growing global demand for immunoglobulins. Octapharma's investments in the immunotherapy field targets both new indications for existing products, as well as new immunoglobulin concentrates for future commercialization.

New product development

Octapharma is developing a new 10% IVIG to accompany our current octagam® product range. Three regulatory clinical trials were completed in 2013. Fifty-one patients were enrolled into a primary immune deficiency (PID) study, of which 21 also participated in an infusion speed study, and 40 subjects were included in an immune thrombocytopenia purpura (ITP) trial. These safety and efficacy studies are now in the final reporting phase and we intend to file for marketing authorization in the European Union, USA, Canada and several other countries around the world in 2014. In order to meet the increasing demand for SCIG, far beyond what the gammanorm® production line

can deliver, we have taken the decision to develop a second 16.5% SCIG based on the octagam® manufacturing process. We intend to enroll over 50 patients, children included, from Europe and the USA in a clinical trial in PID. This new product is expected to be ready for launch in 2016. We are very excited about the development of this new SCIG product, and look forward to making it available to support patient care in one of our main focus areas, North America.

Our IVIG octagam® has been a very important product for Octapharma's development during the last 19 years and its strongest attributes are very good tolerability and impeccable efficacy. In terms of clinical performance, gammanorm® is an excellent counterpart for subcutaneous administration at home, allowing for more freedom in regular therapy and thereby quality of life. We believe that the new generation immunoglobulin products will not only be able to replicate this record, but will also be of great importance in the future supply of treatment to patients in need of immunotherapy around the world.

Research into new indications

Over recent years, the worldwide use of immunoglobulins in neurological indications such as chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN) has grown significantly and surpassed the traditional indications such as primary and secondary immune deficiencies (PID and SID). In addition, the wish to improve quality of life for patients has generated a need to provide SCIG for home infusion in these settings. Based on the interest in SCIG for the treatment of patients with CIDP and MMN, Octapharma has taken the decision to invest in a clinical study program run by 'The Danish CIDP & MMN Study Group'. Altogether 118 patients on active drug will be included in three different clinical trials and we expect the results to be available in 2015.

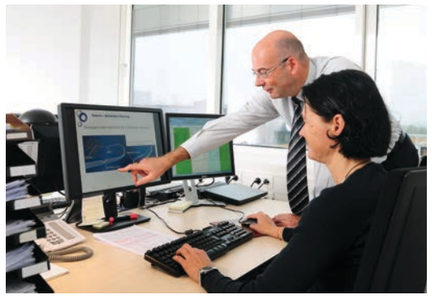
Octapharma's commitment to improving patient care in neurological conditions is exemplified by the largest clinical trial investment in the company's history, the GAM-27 Study in relapsing multiple sclerosis (MS). Many patients with MS cannot be treated with today's first and second-line drugs, due to pregnancy or severe side effects. In addition, there are many people with MS who would like to find an alternative treatment to these medicines in order to improve their quality of life. We believe that octagam® 5% with its very good tolerability would be an excellent alternative to current options. The study is the first step towards providing a licensed individualized therapy for patients with this severe neurological condition.

Relapsing Multiple Sclerosis GAM-27 Study

Multiple sclerosis (MS) is a heterogeneous, life-long inflammatory neurodegenerative disease of the central nervous system presenting with a wide clinical, pathological and genetic spectrum. Affecting approximately 2.5 million people worldwide the first symptoms in most cases start before the age of 30. No curative therapy for MS currently exists, and the life expectancy of sufferers is reduced by about 5-10 years compared to the general population. Thus, MS is a disease that people live with for 40-45 years and can cause, among many other symptoms, muscle weakness, chronic pain, sensory loss, poor balance, slurred speech, fatigue, bladder, bowel and sexual dysfunction, depression, visual problems and, later in the disease, cognitive dysfunction and paralysis.

Treatment of MS with intravenous immunoglobulins (IVIG) has been reported for 30 years and is currently recommended as second or third-line therapy in treatment guidelines (e.g. the European Federation of Neurological Sciences), for patients in whom first-line treatments are contraindicated, ineffective, not well tolerated or simply not acceptable for other reasons. However, not all patients benefit from therapy which suggests that there is a sub-population of patients who are responsive to IVIG therapy due to the heterogeneous pathology and the variable genetic background of the disease. To date, it has not been possible to predict which patients are likely to respond to IVIG treatment.


Stefan Wietek



Stefan Wietek, Head of Corporate Medical & Scientific Affairs, Octapharma

"In our phase II/III trial GAM-27 for the targeted treatment of early relapsing MS, we will recruit 216 patients at approximately 35 European sites across several countries. This randomized, two year active-controlled study aims to confirm preliminary results of our predecessor trial GAM-25 which suggest it may be possible to identify potential responders to treatment with octagam® 5%.

The centrepiece in GAM-25 was laboratory tests that only require a simple blood sample from the patient. The derived Heidelberg Assay Panel (HAP) score is based on functional genomic and protein expression tests conducted centrally by Prof. Meuer and Dr Giese of the Institute of Immunology at the University of Heidelberg, Germany."

Stefan Meuer, Professor of Immunology at the Department of Immunology at the Ruprecht Karls University of Heidelberg

"The potential for this HAP test to accurately identify the 20-30% of patients with relapsing multiple sclerosis who should benefit from octagam® 5% treatment could provide a significant step towards personalized therapies for this patient group."

Clinical responders are patients who do not relapse or worsen in disability or show disease activity (lesions) in magnetic resonance imaging (MRI): their condition does not deteriorate over a 2-year treatment period. We hope to be able to successfully classify patients into predicted responders and predicted non-responders.

As with most studies, there is no guarantee of success. However, this could benefit a significant subgroup of patients with relapsing MS who experience disabling side effects with current first-line treatments or in whom first-line treatment is not effective.


Stefan Meuer

Increase plasma availability and throughput

Octapharma converts source plasma into plasma protein products through fractionation and processing. To fulfil increasing global demand and to exceed its ambitious goals, the company is increasing plasma availability by sourcing higher volumes of plasma and increasing the capacity of production plants to convert more source plasma into product. This chapter explores some of the ways in which Octapharma is increasing plasma availability and throughput.

Increasing plasma availability Octapharma Plasma, Inc. USA

Octapharma Plasma, Inc. (OPI) provides 75% of the overall plasma supply of the Octapharma Group. The overarching goal of OPI is to meet Octapharma AG's requirements by providing the highest quality source plasma at the most efficient cost. Quality, production and cost are key drivers in all activities at OPI. Since OPI was established five years ago, staff development and continuous improvement programs have been major contributors to the overall performance and success.

OPI operates 45 plasma collection centres throughout the United States and is in the process of identifying locations for an additional 12 new centres over the next two years. To fulfil Octapharma's strategic goal of increased plasma availability, OPI's growth over the five year strategic plan is projected to be 15%, year-over-year.

Plasma collection centre activities

Monica Byd

Monica Byrd, Senior Director of Regulatory Affairs and Quality Assurance

"With the increase in production across all centres we must ensure that we establish robust quality systems that are flexible enough to support increases in production. As we forecast what our production needs are going to be, we are constantly re-evaluating our quality system. We are always reviewing our metrics since information is critical to identifying opportunities for improvement or proactively identifying any potential system or process issues.

During 2013, we had 14 inspections from our European regulators. In October, we established the Regulatory and Quality organization for which I am responsible (this was previously two separate areas). One of our key tasks is to build inspection readiness into all centres every day of the year. We promote a culture that instils the belief in all employees that quality is everyone's responsibility, not just the staff with the word "Quality" in their title. We all work hard to collect a quality product and ensure donor satisfaction and safety. Periodically, we hold events where a plasma product recipient gets the chance to meet a donor. It reminds us all how important our work is and how vital it is to adhere to the quality systems in place to ensure that only the best product is shipped from our centres to the European production sites."

New state-of-the-art facility

To fulfil the planned increase in plasma production over the coming years, Octapharma has invested $39.2 million to build a state-of-the-art facility in Charlotte, North Carolina. The new facility will centralize some key activities of the plasma donation centres, allowing OPI to be more responsive to the needs of Octapharma. The 27,432 m² building will also be home to OPI's new corporate headquarters.

Jessica Alps, Project Manager

"As Project Manager, I am responsible for managing all aspects of the Project to ensure that OPI remains within budget and timelines. The key success factor of my role is to ask the right questions, to the right people, at the right time. I must know the resources to call on both internally and externally, and effectively communicate any information to relevant parties. Inherent in this success factor is having an excellent team. The Project team has proven to be reliable, capable, and integral to project planning and execution.

We initially considered developing an existing building but we eventually found our green field site. Having the ability to design the facility from the ground up has been invaluable and enabled OPI to meet its specific requirements. Working with the architect, the executive level wanted to create a building with that Octapharma feel to it: an open environment with lots of glass. To aid in the design of the facility, the Project team was provided the opportunity to visit several of Octapharma's European facilities.

I am honoured to be part of an exceptional team dedicated to building a state-of-the-art facility for the future success of the company. The new facility is a foundation that will allow OPI continued success in supplying quality plasma, ultimately providing benefit to patients."

Jessica Alps

New donor centre
Salt Lake City, Utah

In May 2013, OPI relocated its donor centre in Salt Lake City, Utah. This newly relocated centre is a flagship for OPI and has in place many of the key features that will be rolled out in other centres. The key concept behind this facility is the focus on flow; the entire centre has been designed to optimize donor flow. Not only is there a bigger capacity (the new centre has 54 beds, the old centre had only 26), but specially designed features enhance productivity, for example a self-queuing service for donors reduces waiting time.


Allison Voeller

Allison Voeller, Quality Assurance Supervisor

"My role is to ensure that we are compliant with the regulatory requirements of authorities in terms of quality, purity and donor safety.

The layout of the new centre is fantastic. It all contributes to optimized flow and increased efficiencies. The visibility is amazing; you can see and hear everything. We now have a much bigger space to accommodate new donors. It was actually an adjustment to get used to how big the centre is!

In Salt Lake City, the Church of Jesus Christ of Latter-day Saints is very dominant and this has always been a good giving community. When we moved we had lines of people waiting to come in. Last week we had more than 1,000 donors, in the old centre 700 a week was a success. The high volume of new donors brings challenges because we need to ensure they can donate. We use our robust screening process to ensure that they meet our stringent requirements.

The layout has been very well designed. For example, for each donor we need to print a label so we can ensure traceability of plasma. In the old centre the label printer was between reception and the donor floor so you would print out the label and the screener would grab the label and put it in a pending box for the phlebotomist to call it out on the floor. In the new centre the labelling machine is placed in the centre of the donor floor so labels are printed there; the phlebotomist has the label in their hand before the donor walks to the floor. It may seem like a small detail, but these details save time and make us more efficient.

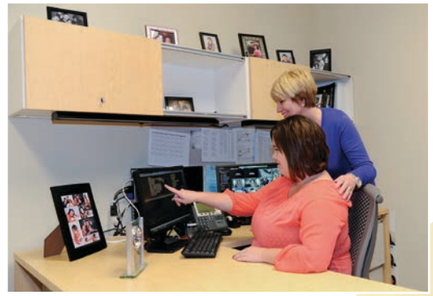
In June 2013, OPI's annual Center Leadership Meeting (CLM) was held in Salt Lake City, the first time the meeting has taken place outside of OPI headquarters in Charlotte, North Carolina. The meeting brought together 140 leaders of OPI, from centre directors, quality supervisors, regional directors and OPI corporate. They were given a tour of the new centre and it was so nice to hear colleagues talk about how impressed they were; the sense of ownership and pride from our staff was tremendous. A very close relative of mine had to receive plasma-derived product recently. I have seen personally the importance of our quality processes, of ensuring the documentation is completed properly, that correct procedures are followed from the moment the donor enters the centre until they leave. Our robust processes are in place so we know that the plasma we collect is pure and that the donor is safe."

Carly Laupepa, Donor Centre Director

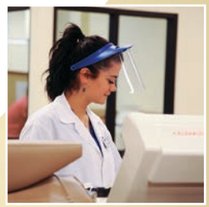
"The new facility in Salt Lake City is a beautiful and highly efficient centre with lots of space and an open concept. The centre has been designed to optimize flow. The layout is such that management and quality overlook the donor floor. The physician substitutes are in the front. This accessibility contributes to making this a safe environment for donors and staff. The layout is more optimal than our old centre and the staff have easy access to what they need so people can do their job more efficiently.


Carly Laupepa

In the first 5 months of being in the new centre we almost doubled our production. With this dramatic increase we must ensure we continue to be quality driven and compliant and maintain good processing times. We are much busier than before so we have to hire new staff to manage the increase in donor numbers. When employing new staff we look for people who are personable, friendly but understand the important balance of treating donors with respect, but at the same time facilitating an efficient donation process.



In my 11 years working in plasma I speak from experience when I say that OPI is a very well organized company that really understands plasma. They focus on donor as well as employee needs. At OPI we pride ourselves on our good customer service and good processing times, this makes donors want to come back because their time is valuable. Donors are impressed when we know their names and understand their lives, they enjoy coming here. Our centre has free wifi, so donors can get online on their phone or bring their laptops to do their homework. There are 10 other donor centres in a 50 mile radius, but our donors come to us because we focus on good customer service and provide a safe and clean environment which is pleasant to be in. My key objective is to ensure that as we grow and increase production we continue to be compliant and maintain high levels of quality."



Increasing plasma throughput Springe, Germany

Octapharma has ambitious goals to increase production capacity over all plants by 2017. Beyond this, Octapharma is launching a 400 million Euro investment program which by 2019 will more than double the corporation's plasma throughput capacity.

Frank Marks, Plant Manager

"In Springe, we have doubled the basic fractionation capacity from 600,000 to 1.2 million litres over 2013. This was achieved by engagement of new staff and increasing auxiliary equipment, for example purchasing new tanks and new chromatographic equipment. To meet the aggressive production targets, Springe plans to increase capacity to 1.7 million litres by end of 2014.

The Heparin Sepharose chromatography step, which was included in the fractionation process of all plants in 2010, requires additional process time and extra space for additional equipment including tanks and columns. This additional space and time limits our fractionation capacity. We have addressed this bottleneck with a 3.5 million Euro investment. During 2014, three separate chromatography lines, each consisting of column, control system and two product tanks, will be put into operation. The buffer supply will be managed centrally through a new buffer preparation and storage area. With these improvements we will be able to run 1.7 million litres of plasma over the columns, thereby exploiting the maximum fractionation capacity of the Springe plant.


Frank Marks

The partial activation of a new production building in Springe is in line with these activities. The building has a ground area of 1,300 m² with six floors: two technical floors; three production floors and the quality control floor. The production floors are double the height of the regular floors, so the building itself is rather high. Over the next two years, the building will be prepared for the new large volume parenterals (LVP) filling line and to house new product lines. These projects are closely related to the increase of fractionation capacity."

Andreas Tschech, Head of Production Unit

"I am responsible for fractionation, purification, pharmaceutical production and operation support, which covers validation and qualification activities. With the increase in the basic fractionation capacity we need to increase the albumin filling capacity. This requires investments in new ultrafiltration equipment, bigger batch pasteurization tanks and a liquid filling machine of high speed to cover the large volumes of albumin produced.

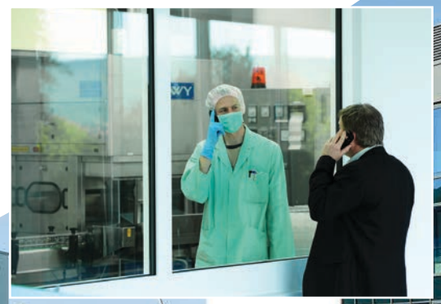
The new LVP liquid filling machine is part of the company-wide filling lines and freeze driers (FLFD) project implementing new state-of-the-art harmonized equipment in the four European production plants. The LVP filling line is where vials are prepared, filled automatically and covered with a stopper and cap. More accurate filling means we will benefit from less loss. We will have a higher sterility assurance level by reducing the risk of contamination in this aseptic process. Once the machines arrive, they will be assembled and then we begin the phase of tests and qualification. The machines will be prepared to fill albumin from up to 6 million litres of plasma by 2016.

Much of our activity over 2013 is related to the Food and Drug Administration (FDA) pre-approval inspection in 2014. This is the first FDA inspection in Springe. We will be delivering intermediates for the production of Octapharma's new immunoglobulin which will be produced in the Lingolsheim plant. We began this project with gap analysis conducted by internal and external personnel leading to an FDA compliance project to ensure that we achieve the quality that is required by the FDA. There is a lot of experience to share across Octapharma production sites; we have a lot of contact with our colleagues in Vienna and Stockholm and are working closely with Lingolsheim to ensure we meet all the requirements of the FDA.

The next challenge will be the recruitment and training of new personnel to meet the increased capacity and larger volumes of plasma that we will be fractionating."


Andreas Tschech

Fraction II manufacturing plant, supervisor of equipment sterilization and central refrigeration plant



Final pasteurization step of albumin: racks with filled vials are dipped and rotated in a heated water bath

Jörg Herrmann,
Head of Quality Control

"The increase in plasma throughput directly impacts quality control (QC) activity because with more fractionation batches and final product, QC must perform more tests. Given the increased activities of QC, it was recognized that the previous facilities, rented from the German Red Cross, would not provide the space needed.

After 20 years working in basement labs with views of parked cars, I am delighted to be working in this light space with such wonderful views. We are all proud of the new labs which represent a significant investment of 3 million Euro. As the qualified person in Springe, I am responsible for the certification of batches: the approval of raw material, intermediates and final product. Our labs run approximately 400 tests per day, applying hundreds of testing methods.

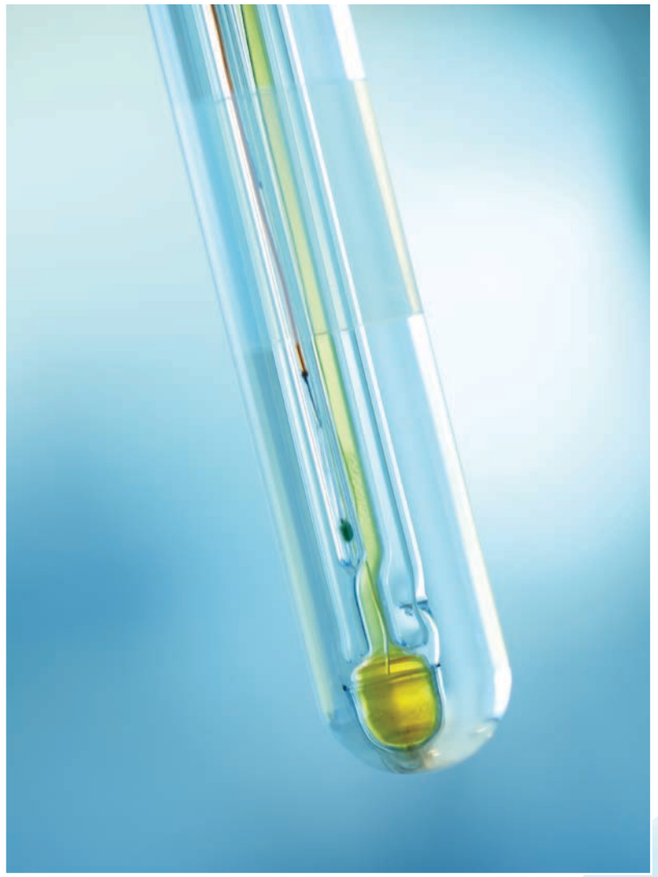

Jörg Herrmann

The new QC lab is located on the 3rd floor of the new building and covers an entire floor of 1,300 m², three times larger than the old rented facilities, consisting of six lab rooms: three biochemical labs, a microbiological lab, including a sterile isolator lab, a separate clean room and two labs for clotting analysis.

We relocated our labs during the two week Christmas shut down period in the last week of 2012 and the first week of 2013. This was the moment when three years of planning would be executed.

To move a qualified lab with qualified equipment is a lot more complicated than moving furniture. This has been a huge project. Our task was to deliver the final in-process samples in the last production week of 2012 then shut down, pack all instruments and move them to the new lab. Once in the new lab we had to unpack everything and begin requalification of all instruments to be ready to deliver the first in-process results at the beginning of week 2 of 2013. I am happy to say the Christmas move went surprisingly smoothly largely due to good planning. The core project team included myself, a trainee (Anika Lehmann) and three experienced lab managers: Ortrun Herms, Group Leader Biological QC; Ulrike Garbe, Group Leader Biochemical QC and Cindy Zacharias, Group Leader QC Validation & Special Tasks. We also had invaluable support from the technical group.

Over 2014, the major projects include the plasma throughput increase; the qualification of the new production rooms and the FDA work for approval of the first intermediate of our new immunoglobulin product."



Quality control activities including chemical, biochemical and microbiological analysis being carried out on various stages of Octapharma products

Global market access
with increased product portfolio

USA

Louis DiCriscio, Vice President, Finance & Operations

"Octapharma USA is undergoing a dramatic shift in activity due to increasing the product portfolio. With the launch of octaplas™ in 2013 and the expected launches of octagam®10%, octanate® and octaplex® over 2014, we will increase the portfolio from three products to seven. With a number of products from the global Octapharma portfolio entering the US market simultaneously, we expect to potentially see a 50+% increase in revenue in 2014 compared to 2013. Octapharma USA has contracts with approximately 30 distributors and group purchasing organizations (GPOs). They all seek consistency of supply. Octapharma is a nimble company and 2013 has been a record year in production. We need to have strong demand forecasting and be able to anticipate when our next release is going to be to ensure inventory is available at all times and in the right places. We work very closely with our supply chain colleagues in Europe. It's an intricate relationship with supply and production so we need regular communication. Information needs to flow rapidly as circumstances can change daily. We develop new reports to monitor and project the inventory in the distribution channel and marry this information with what is coming from production and the supply chain. Staying very close to the distributor is important. We have a national accounts team to manage the day-to-day relationships with the GPOs and distributors. I work closely with them and with the GPOs and distributors, as well as Octapharma USA President, Flemming Nielsen. We are constantly sharing information. It's a real team approach.


Louis DiCriscio

Octapharma understands its own strengths and weaknesses and decides where best to invest resources, either internally or with intelligent external partnerships. There are particular products for which we are exploring the possibility of commercializing with a partner company when it makes good business sense, allowing us to channel investment to areas of core competence.

The growth to date of Octapharma USA has been the result of smart investments and maximizing our current portfolio. The investment now is for new products and this should really set us up for dramatic growth over the coming years."

David Holliday, Vice President of Commercial Development

"Octapharma has always had a very strong history in Europe and we see substantial growth opportunities in the United States where we have a relatively small proportion of our global business compared to most companies in our industry. We know that a high quality product, along with the company heritage, has a strong influence on why healthcare professionals would consider prescribing products for their patients.


David Holliday

Octapharma has an impressive legacy with a strong background in R&D and manufacturing. The "Science" behind Octapharma is extremely important: we have a powerful story to tell.

Today, we are expanding our footprint in the coagulation market, recruiting a dedicated coagulation team responsible for our growing coagulation product portfolio. Wilate®, our first product approved in the US, is a strong foundation from which we are building our portfolio to meet the current and future needs of patients and clinicians. We have recently submitted the BLA for octanate®. The next addition to our portfolio will be Human-cl rhFVIII and we are excited to have the opportunity to bring our first recombinant product to the US market.

Most people with haemophilia can now live a normal life because of the quality products available, but patients are also looking for improved quality of life, for example reduced infusions and lower chance of developing an inhibitor. Our intention is to expand our coagulation portfolio to meet the needs of all patients by contributing to patient care and improving quality of life through high quality products, education and services. It is essential that we think ahead and ask what it is we want to be doing to support patients with bleeding disorders in the future. We want to engage with the future leaders, for example by supporting education and training for healthcare professionals who wish to specialize in coagulation, building long-term, meaningful partnerships. It's an exciting period in Octapharma USA's history as our portfolio and overall presence grow over the coming years in this increasingly important market."

Brenda Cannon, Product Director

"As Product Director, I have marketing responsibility for the immunotherapy and critical care portfolios. Octaplas™ is Octapharma's first critical care product in the US and received FDA approval in January 2013. In the pre-launch phase following approval, we focused on increasing disease state awareness and presented the scientific benefits offered by a pooled, solvent-treated plasma alternative. Our goal has been to collaborate and partner with the national and regional blood centres, as well as hospital blood banks, to ensure that octaplas™ is made widely available to our customers across the US. To support the introduction of octaplas™, we have recently strengthened our medical affairs team to provide supportive scientific exchange with blood bank medical directors, transfusion medicine specialists, as well as liver, transplant and cardiac surgeons.

For the immunotherapy portfolio, our aim is to raise awareness of Octapharma's immunology franchise and to demonstrate our ability to translate a vast body of global experience to benefit patients in the US. We will leverage octagam®'s strong legacy outside of the US, for example its reassuring adverse event profile. Octagam®10% is currently under review by the FDA. Octagam®5% and 10% are different concentrations of the same product, but we have to treat them differently from a commercial standpoint because they will have different clinical indications.

Enhancing our product mix allows us to provide more US patients with potentially lifesaving therapies from a broad plasma portfolio."


Brenda Cannon

Mexico

Ivonne Salinas, Medical Responsible

"Today, Octapharma has one of the most complete blood-derived product portfolios in Mexico. Our plasma expertise, plus the experience of product efficacy and viral safety that has been demonstrated in Mexico throughout 19 years of Octapharma's presence, gives doctor and patient confidence. I perform the medical director activities including medical marketing, regulatory, pharmacovigilance, scientific and training. I develop the commercial strategies and work on marketing campaigns with the marketing manager. Over 2013, we have maintained our leadership of immunglobulin supply in the Mexican market. We have opened up new markets and started relationships with new specialist areas. Key developments in 2013 include the launch of gammanorm® and octaplex®.

In April 2013, Octapharma Mexico officially launched octaplex®. Pre-launch activities included participating in local and regional anaesthesia and intensive care congresses. Physicians have responded positively to octaplex®, it has been of great interest for them to control bleeding in less time than fresh frozen plasma and without the viral risks involved; it leads to many benefits for both patient and physician. Our objective is to enter the market of cardiology and for more physicians to be aware of octaplex® when patients require a rapid reversal of vitamin K antagonists. We participate in discussion panels, lectures, workshops, monthly meetings and congresses of related medical associations.


Ivonne Salinas

Gammanorm® can improve patient quality of life with fewer hospitalizations which reduce hospital costs and nosocomial infection. We presented the administration of gammanorm® in congresses with voluntary patients. The feedback from physicians has been excellent; every day more doctors and patients are using gammanorm® with full confidence. The reduction of hospital costs and improved patient quality of life are evident."

Verónica Aguirre, Quality Control Health Regulation

"My responsibility is to demonstrate that Octapharma products comply with the quality the patient deserves. I am proud to be responsible for securing and maintaining the registrations that allow Octapharma to have one of the most complete blood-derived product portfolios in Mexico. Over 2013, we have redesigned the quality control laboratory. There are nine people in the QC team who conduct quality control, quality assurance and validation activities including performing physicochemical and microbiological analysis of the raw material, in-process product, bulk-phase product and finished product. We moved into the new lab in the first week of June 2013. I was involved in the design of the new arrangement of the areas, reviewing the proposals with architects and assessing potential suppliers of furniture and equipment. We had to determine how we could accomplish the redesign without affecting production. Activities included qualification of design, installation and validation of the equipment. The new laboratory is more optimally distributed, enabling better performance of the activities.


Verónica Aguirre

I am responsible for regulatory compliance so my role is to be aware of changes in regulations and follow-up with the guidelines as well as correspond with the health authority in Mexico. The health regulation in Mexico is becoming increasingly strict and harmonized with the regulation of other countries. Amendments related to GMP in blood derivatives came into force in September 2013, my role is to ensure that we continue to comply with regulations when such amendments are made.

Our next exciting goal over 2014 is to secure the registration of the recombinant factor VIII from a human cell line."




Kazakhstan

Since the representative office was opened in 2008, the development of the market in Kazakhstan has been dramatic. Kazakhstan is the 9th largest country in the world with a territory of 2.7 million square kilometres. Larger than Western Europe, the six person team is responsible for a huge geographical area. When Octapharma entered Kazakhstan in 2008, there were very few plasma companies with a presence. The market has since developed considerably. In a tender driven market, the relationships built over these five years put Octapharma in a strong position.

Svetlana Safarova, Head of Representative Office Octapharma AG in Central Asia

"When I started in 2008 we had only one product available from the Octapharma portfolio: octanate®. Today, almost all products in the Octapharma portfolio are registered in Kazakhstan. In 2014, we plan to have the entire portfolio registered. It is very important to have a broad product portfolio so you can speak to physicians about all products. It's about rationalization of marketing resources."

Svetlana Safarova

Haematology

Haematology is a very developed market in Kazakhstan: all adults and children have access to preventative prophylaxis FVIII replacement: 4.7 international units per capita, which is quite exceptional for a CIS (Commonwealth of Independent States) country. Our largest portfolio is haematology with octanate®, octanine®F and wilate®. Our activities include improving diagnostics to identify new patients and creating social and educational programs for patients as well as promoting prophylactic and home treatment. We orchestrate, usually with the director of the local haemophilia organization, educational events, lectures and discussions attended by patients and physicians.

Improving diagnostics is key; Kazakhstan is a very big country and really good diagnostics is only available in the two main cities, but patients are everywhere. Our task over 2013 was to increase diagnostic quality in the region. With help from our Russian colleagues, we were able to educate with the support of international colleges, including in St Petersburg and Frankfurt, several laboratory technicians and doctors to conduct screening locally.

Our strategy for 2014 is to promote healthy lifestyles, especially for children and teenagers with coagulation disorders. Promoting physical activity helps preserve mobility. The combination of a healthy active lifestyle and prophylactic treatment gives great health benefits.

Wilate® is the only product available directly addressing von Willebrand disease (vWD), the most common inherited bleeding disorder which affects both men and women. We have created a short film about the history of women who suffer from vWD featuring a woman who tells the story of how prophylactic treatment changed her life. This video can be shown to gynaecologists to increase

awareness and it can be shown to patients, for example in the haemophilia school. The haemophilia school involves regular meetings of patients to facilitate better understanding of their condition. Doctors give lectures and hold discussions so patients can be educated on treatment and infusion of factor concentrates.

We have successfully introduced ITI therapy with four patients undergoing ITI treatment with octanate®, this figure will increase to six patients in 2014.

The government is increasing the use of recombinant products, buying 32 million international units of recombinant product and 55 million international units of plasma-derived product. With the increasing use of recombinant, there is a huge potential in Kazakhstan for Octapharma's upcoming recombinant FVIII product.

Immunotherapy

We began immunotherapy campaigns in 2010. At that time IVIG use in neurology was close to zero. In only two years, octagam® sales grew more than 12-fold by 2012. In 2013, the most important objective for us was to win the government tender for IVIG. We were successful and won the tender for 70kg of octagam® for 2014. We have developed the market from scratch mostly in neurology and primary immune deficiency (PID). We work with key opinion leaders in hospitals and set up education programs for diagnosis of neurological conditions. In 2013, we conducted road trips with a specialist in diagnostics to identify new patients. We work with the PID patient association in Kazakhstan and expect the number of patients diagnosed with PID to increase; in the east especially we expect a higher number with genetic diseases due to the improvements in diagnostics. We work with the Scientific Center of Paediatric Surgery in Astana which provides innovative treatment of PID by very skilled staff and the National Research Centre of Maternal and Child Care in Astana. These centres help with PID diagnostics and treatment.

We are main sponsor of a big neurological congress in Kazakhstan. The Chief Neurologist of Kazakhstan presented the result of the social program for the treatment of patients with myasthenia gravis. She demonstrated data of how many patients were diagnosed and the result of treatment with different medical criteria, including IVIG treatment. We invited international speakers to present on the treatment of CIDP (Chronic inflammatory demyelinating polyneuropathy) and octagam® studies.

In neurological disease there is a benefit to switching to home treatment. If the hospital is located 300 km from a patient's home and they have to go to hospital once a month, switching to home treatment is beneficial. In 2014, we have a pilot project to switch four patients (two neurological and two PID) to gammanorm®.

Critical Care

Our critical care portfolio is at the early stages of development, the first product from the portfolio, albumin, was launched in Kazakhstan only in 2012. In 2013, we launched octaplex®. At the moment there is no governmental budget for prothrombin complex concentrate (PCC). We are developing the PCC market in Kazakhstan. We hope to get octaplex® included in the Ministry of Health list. Although there is currently no large governmental purchase of octaplex®, we expect it will be possible in 2015. We have our first orders of octaplas® from the hospitals, once the doctors use the product we expect it will be positively evaluated by the doctors which will bring increased demand.

Enter the recombinant business successfully

Entering the recombinant market represents the beginning of a new era for Octapharma; in stepping into this new territory we are pioneers. Our human-cell line recombinant factor VIII (Human-cl rhFVIII) will be the first recombinant product in Octapharma's portfolio and is likely to be the first native recombinant FVIII of human cell line origin available in Europe.

Olaf Walter,
Senior Vice President International Business Units


Olaf Walter

"Along with the steering group members, I am leading the preparations for the launch of Human-cl rhFVIII which is at late stage development. Colleagues and customers are becoming increasingly enthused the more we prepare for the approval of the Human-cl rhFVIII. We set an ambitious project and now it is likely that we will be the first company with a human recombinant FVIII in the European market. We are at a very exciting phase involving many departments including biopharmaceutical production, clinical R&D, preclinical R&D, QA, regulatory, the business unit haematology and local marketing and sales organizations.

Working in partnership with the corporate brand management department, we have established a global launch team (GLT) for the Human-cl rhFVIII. The GLT provides a platform which allows the exchange of experiences, ideas and vision between the local organizations and the international business unit haematology and corporate branding. The aim is to develop a global product strategy that fits with the local market and customer needs. It provides an opportunity for all participants to bring new ideas, e.g. for early life-cycle management or pre-launch activities and also to gain support from the central functions to ensure a successful product launch globally in late 2014 and early 2015. Our two pivotal ongoing studies, NuProtect and NuPreviq, are addressing so far unmet clinical demands. This is clear from meetings with the investigators and from discussions with potential customers, as well as the notably high recruitment rate of the studies.

The critical success factors for 2014 will be that we continue to have a successful recruitment rate for our studies; that we see confirming data from these studies; and that together we successfully progress through the different review processes with all the major regulatory authorities in the world. Having the review processes in parallel with the late stage development, including the first life-cycle management activities, represents a huge challenge to the team since now we have many important activities happening at the same time.

One of the company's strategic pillars is 'Global market access with increased product portfolio'. Our first recombinant product is filling a gap in our coagulation portfolio. The Human-cl rhFVIII is complementary to our plasma-derived portfolio and we are very happy to be able to offer to our customers a recombinant factor VIII alongside our plasma-derived therapies. Moving into the new world of recombinant, Octapharma is in parallel continuing to invest in our plasma-derived portfolio: plasma R&D, life-cycle management, and marketing. Entering the recombinant business allows us to present an enhanced overall global portfolio combining both plasma-derived and recombinant products.

It has been incredibly rewarding to be part of the global, cross-departmental, cross-functional collaboration in preparation for the launch of Octapharma's first recombinant product. Aligning the activities of many talented people creates momentum and I am proud to work with many highly skilled and excellent colleagues. Together we can achieve more than we may think, as Aristotle said, 'the whole is greater than the sum of its parts.' Today our focus is the launch of our Human-cl rhFVIII. Our collective experience developing and launching this innovative product will provide a solid foundation for future launches in Octapharma's recombinant portfolio."

Haematology international business unit based in Lachen, Switzerland

Sigurd Knaub,
Vice President, Clinical R&D Haematology

"We design the global clinical development plans for all coagulation products and conduct the operational activities from study set up to the final study report, with the support of clinical research organizations. We organize investigator meetings where the physicians get all the information they need to conduct the study, including scientific and logistical information and a reminder of the good clinical practice requirements.

In 2013, our main activities have been to complete the submission package for the European Medicines Agency (EMA) and Food and Drug Administration (FDA) for our human cell line recombinant factor VIII (Human-cl rhFVIII); and to launch the much anticipated previously untreated patient (PUP) study, NuProtect, which investigates the immunogenicity of Human-cl rhFVIII in 100 PUPs with severe haemophilia A (<1% FVIII). The patients taking part in the PUP study are usually very young with some entering the study soon after birth and starting treatment with the first bleeding episode. With this study we hope to prove our hypothesis that due to the absence of antigenic epitopes our product has a lower immunogenic potential than other products on the market, resulting in less inhibitors. Inhibitor rates of 30-40% have been reported with the currently available rFVIII products produced from hamster cell lines. If we can manage to show a reduced inhibitor rate this would be a huge benefit to patients. Key opinion leaders have shown keen interest in the progress of the PUP study as the development of inhibitors is regarded as the most severe complication in haemophilia patients today.


Sigurd Knaub

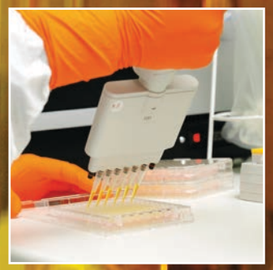
Another study for Human-cl rhFVIII is the personalized prophylaxis study, called NuPreviq. This study's primary objective is to compare the average annual bleed rate (ABR) of individualized tailored prophylaxis treatment with the ABR from a former on-demand study (GENA-01). The goal of prophylaxis treatment is to avoid bleeding by keeping FVIII plasma level above 1%. Data from a previous pharmacokinetic (PK) study indicate Human-cl rhFVIII has quite a long half-life. This study starts for each patient with a PK assessment and based on the individual PK data a prophylactic regimen is recommended with as few as possible infusions per week, making treatment more convenient for the patient."

Maya Tiemeyer,
Scientific Head of Octapharma Biopharmaceuticals, Heidelberg

"In Heidelberg, as the R&D team involved in the development of the process and analytical methods to characterise the product, we are providing the production team in Stockholm with scientific support. For submission related activities presently there is a team of 20 people in Heidelberg supporting the Human-cl rhFVIII project. One of the main working packages is the analytical characterisation package. A more in-depth evaluation of the characteristics of the molecule is needed for submissions. For example, we are looking at supplementary analytics like FVIII activation and inactivation kinetics. Heidelberg is also supporting studies within FVIII purification. We are also very deeply involved in the completion of submissions and responses for the authorities."


Maya Tiemeyer

Developing the next generation therapeutics: from idea to technical scale



Stockholm – recombinant production


Karin Stackerud

Karin Stackerud, Head of Biopharmaceutical Production

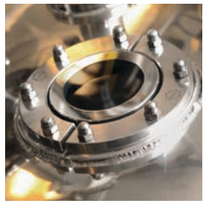
"I began working in the QC laboratory for plasma products in 1993. In 1999, I moved into pharmaceutical production and in 2005 I moved into fractionation and later became manager for plasma purification. I moved into recombinant in 2011 and as Head of Biopharmaceutical Production I am responsible for the entire process of cultivation and purification.

We often talk about cultivation as being complicated, in fact both purification and cultivation is complex, but in Octapharma our background is plasma fractionation so we have more experience and expertise in purification of proteins. The cultivation expertise in the company is concentrated in Heidelberg and Stockholm. In recombinant there are more manual steps compared to plasma production; the process itself is complex and demanding on personnel. As we are expanding here in Stockholm our greatest challenge is recruitment and training. It takes 6–8 months of training before new recruits can be operational. Between June and September 2013 we recruited 13 new employees. There are now 49 people in the team split between purification and cultivation.

Our 2013 activity has been focused on building the submission file for the EU and preparing and performing the US validation for the 100 litre scale. My personal 2013 highlight is when we completed the final production batches for the US validation. Next year I look forward to completing the validation for the 500 litre scale for commercial production.

It's very exciting to approach the major milestone of going into commercial production and earning money for the company rather than spending it. There are many people here who have been involved in the recombinant project from the beginning and have played an important part in where we are today."

Chromatography column for purification, bioreactor for cell cultivation and separator for cell separation



Ulrika Nilsson, Project Manager

"I was responsible within biopharmaceutical development for setting up the clinical supply for Human-cl rhFVIII. We started the development activities for production in 2003 and began clinical production in 2008. A big challenge is to ensure that there is enough product available to be able to supply all ongoing clinical trials. Ensuring clinical supply is critical because if there is no product to send, you might have to exclude patients from the studies.

The logistics of the clinical studies are very complex because there are many investigators (doctors) and many sites involved. Specific labels are needed to be able to trace the product that is sent to each investigator. As more countries joined the studies, the process became more complex because every country and each individual investigator need their own labels. This put a lot of pressure on our packaging facility in Dessau, Germany, and on the Qualified Person (QP) release. Now that we have established the routines for clinical packaging and shipping the clinical supply is smoother.


Ulrika Nilsson

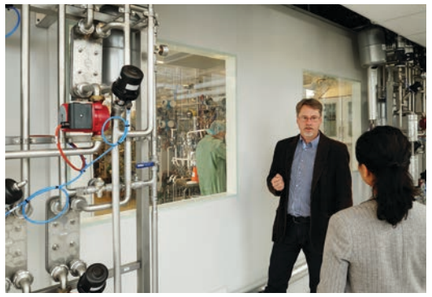
I was also part of the team that developed the freeze dried vial and team leader for selection of water for reconstitution and injection components. When the patient opens the package they find several components in addition to the vial: the injection device; needles for injection; the water in a pre-filled syringe. We selected the injection components and decided on a method for reconstitution together with IBU haematology in order to achieve a final product with a high level of convenience for the patient.

In the beginning of 2013, I took on my new role as Project Manager within operation support. The big project now is the new state-of-the-art SVP (small volume parenterals) filling line. All freeze-dried products within the Stockholm plant, as well as the recombinant product, will be transferred to the SVP line. I am responsible for the transfer of the production processes from the existing filling lines to SVP; the process validations are planned for 2014."

Tomas Åslund,
Product Manager and Responsible Scientist

"I am Project Leader for the process validation of the Bio 100 submission to the US authorities. As Responsible Scientist, I am responsible for the scientific aspects of the batch protocols. I joined Octapharma in 2005 in what was then Biopharmaceuticals R&D. This function has now been transferred to Heidelberg, Germany. When I joined, I was responsible for the pilot plant. In fact, on my very first day I went to Germany for a factory acceptance test for the first bioreactors which are now used for production. Between 2005 and 2009, my role was to scale-up the process to the 100 litre scale and produce recombinant factor VIII (rhFVIII) for clinical trials.


Tomas Åslund



In plasma, you get the factor VIII from plasma donors and then purify it. In recombinant, we actually produce the FVIII itself. We do this by using a human cell line. The gene for the production of FVIII is inserted in a human kidney cell. We begin with a small vial called a 'working cell bank' which is stored in liquid nitrogen. You start by thawing the small vial then continuously grow the cells in bigger flasks, until you have enough cells to start the 20 litre bioreactor. The process takes five weeks to reach the billions of cells needed. Once you have the cells in the 20 litre bioreactor you grow the cells for three days, then transfer to the 100 litre bioreactor where the production of the rhFVIII takes place. After 12 days, the production is finalized and the cell culture is transferred from the bioreactor. The first purification step is a chromatography step in which the solution is pumped through a glass tube with small gel beads in it. The beads have on their surface chemically active molecules that the rhFVIII stick to. While the rhFVIII is captured on the beads, the impurities are washed away and finally the rhFVIII is released from the beads by changing the chemical composition of the fluid which is being pumped through. The purification process contains five chromatography steps with different chemically active beads in each step. The most important step is where we use an affinity molecule which is very specific to rhFVIII. This gives a very high purity product. With recombinant FVIII the risk for viruses is very low. Nevertheless we have two virus inactivation steps: solvent detergent (S/D) and a step with a very narrow filter (nanofiltration).

Over 2013, all of my time has been dedicated to the process validation for the US submission. To validate a process you must demonstrate the capability of the process to produce product within the set limits for all quality parameters. We run about 25% of a full year's production to prove that we can run the production to fulfil all the demands of the process in terms of purity and reproducibility. We also show that FVIII can be produced even under challenging conditions during the process validation. A lot of analytical resources are needed so the challenge is to get all these samples analysed alongside the analysis being carried out for the current commercial products.

When you compare to a much larger pharmaceutical company, Octapharma has achieved a tremendous amount with a relatively small team. With a previous company, I worked for 10 years in development and production of a product that didn't reach the market. After all the efforts of everyone involved it will be very satisfying when our first recombinant product is launched."



Bioreactors for cell cultivation and Bio 100 line 2

Martin Linhult,
Section Manager of Bio 100 line

"I joined Octapharma in 2004 as a process engineer for the pilot plant in research and development. I became the link between R&D and clinical production for trials. We ran the first technical batch in 2005. As Section Manager for Bio 100 line I am responsible for the clinical production for the studies. My group is responsible for both cultivation and purification of the cells. We thaw the cells and then expand the amount of cells so we can transfer them to the bioreactor. During cultivation you supply the cells with nutrients so they will have enough sugar, oxygen, salts etc. In the beginning of the cultivation you work with flasks then transfer them to the bioreactor. After harvesting we begin the purification. Many of the team in purification gained their experience in plasma as the techniques are similar between plasma and recombinant. The cultivation in GMP is something new for Octapharma.

I have been highly involved in the validation of the Bio 100 line, working on protocols and validation reports mainly for European regulations as well as some work for the US. We have submitted to Europe and are anticipating authorization from European authorities during 2014.

It takes a long time to reach this stage. I am proud of what we have achieved so far. The big challenges have been technical issues, which we solved with the support of engineering and R&D. The next challenges are to build up the full production line. This has been very challenging but ultimately gratifying work.

I will eventually be responsible for producing material for market. This is what I am most looking forward to because it will be very satisfying to give something back to Octapharma when the first product is sold."


Martin Linhult

Open and transparent communication

The corporate brand management department was established in January 2013 with the aim of enhancing and optimizing communication across the organization. When this department was founded, Wolfgang Marguerre said, "We have reached the point in the company's growth that demands a dedicated department to define key messages: in branding, in online communications, in congresses and in marketing materials".

The strategic pillar "Open and transparent communication" requires channels both within Octapharma, and between the organization and the outside world. This chapter highlights examples of communication 'best practice' from across the organization.

Bringing the pillar to life

Octapharma's Board recently defined the five year strategic vision for the company. Whilst several of the key elements of this vision were self-explanatory i.e. 'enter the recombinant business successfully', the two pillars which focused on employee engagement 'proud and talented employees in a healthy organization' and 'open and transparent communication', were less well defined. Over the course of 2013, several workshops were conducted to identify the activities and actions necessary to bring these two pillars to life. Whilst these workshops uncovered areas for further development, it is recognized that there is more to be gained by extending this work across the whole organization during 2014.

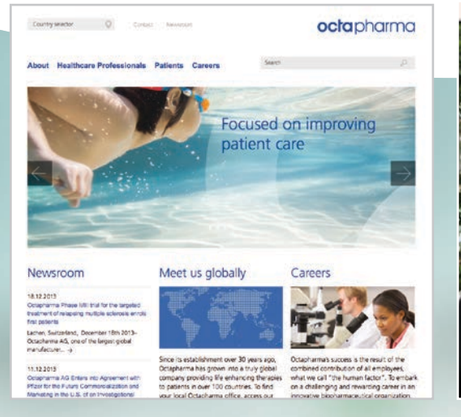
Within this chapter we specifically focus on the strategic pillar 'open and transparent communication'. The significant success and growth experienced by Octapharma over recent years presents its own challenges for openness and transparency in communication. The communication channels that previously satisfied the needs of the organization require further enhancement for the long-term. Those practices of open and transparent communication that currently exist locally must be integrated into our global culture and we continually strive to identify new processes and resources that support the evolving communication needs of all Octapharma stakeholders.

Website

Octapharma has gone through a dramatic regeneration and reinvigoration over the past few years and is raising the standard in all areas of the business. With ambitious growth objectives over the next five years, we recognized this as the perfect opportunity to examine our online presence and enhance our global corporate website to reflect the Octapharma of today and tomorrow. Octapharma's corporate website is a key platform in the strategic value of 'open and transparent communication'. The website must accurately reflect to stakeholders, both internal and external, our core vision and values. The content must be an informative resource for the user, whilst meeting the stringent regulatory requirements of the pharmaceutical industry.

Octanet

Octapharma's original intranet was launched in 2004 and since that time the company has grown four-fold. Today, Octapharma is a truly global company with over 5,500 employees spread around the globe. It was recognized that our intranet platform, Octanet, needed to be re-imagined to better serve the needs of today's organization. The core objective for the update was to improve internal communication. Much has changed since 2004, especially when it comes to how we all engage with technology. Today people are far more internet and technology savvy and have much higher expectations. The new Octanet was launched in June 2013, creating a space where colleagues from around the world can share information and ideas. The new front page has been specifically designed to look and feel like an online newspaper and in this way we are nurturing a sense of a shared global Octapharma community. The site requires continual development to ensure it is an optimal communication platform for our growing organization.



Per Eriksson, Head of Marketing Communication, Stockholm

"Over the past few years we in the Stockholm management team have focused on a communicative perspective on all decisions. The global introduction of the open and transparent communication pillar has been a welcome confirmation that we are on the right track. Effective internal communication creates a team feeling where everyone is involved and takes responsibility for contributing to our common goals. Openness prevents misunderstandings and conflicts, allowing us to face challenges and solve problems in an optimal way. In our policy for internal communications a good guiding principle is being proactive, answering questions before they are asked. Our main channel for information is our well established local intranet where you can find everything you need as a Stockholm employee, from policies and forms to news and updates.


Per Eriksson

Our next exciting step is to set up a system with digital signage over the whole site to reach everyone regardless of access to computers. Initially 25 screens will be placed in strategic locations meaning we can reach many more colleagues with a mix of central and departmental information and messages. Of course not all communication is done via a screen! We also have a well established meeting structure to channel our communication out to the organization through our managers. This is achieved through quarterly information meetings for managers and a well-structured meeting chain to quickly channel information from the bi-weekly plant management meetings all the way to our departments through the unit management teams. Through strong communication we have become good at working in teams and facing any challenges together because we often have a good understanding of what needs to be done and why."

Ulrich Thibaut,
Board Member, Research & Development

"Open and transparent communication is a two-way process that requires mutual trust and respect. In the R&D world, the empowerment of cross-functional project teams is a living example of this; information must flow effectively from project teams to the management and vice versa. It is important that as managers we make ourselves available. People have to trust they will not be punished for coming to the management with an issue. This is especially true in R&D where we often work in unknown territory. You cannot predict the outcome of a study and if something goes wrong this provides a learning opportunity, but only if we allow people to come up to say that there is a signal we did not expect or even did not like, or a mistake has been made. Such mistakes can have costly impacts but the cost of not raising the alarm is greater. The framework in R&D management is that we have open and transparent communication in both directions. I try to teach the R&D leadership team to ask open questions: 'What did happen?', 'Why did this happen?', 'What can we do to avoid it happening again?' We also have to communicate the experience to other parts of the organization so they too can learn from it and to ensure it does not stay in the realm of R&D. A learning organization should behave like an organism; the different organs operate and work together, and if one hand is bruised or burnt, the other hand heals it, it does not punish it.

I allow people to set the agenda for leadership team meetings, I ask them a couple of weeks in advance if they want to put anything on the agenda. In the protected environment of the meeting room we can have candid and sometimes controversial discussions. People need to feel free to discuss issues openly, and management should


Ulrich Thibaut

listen carefully. R&D interacts with many functions throughout the organization, including regulatory, marketing and production. Open and transparent communication means the necessary information flows through the correct channels. Open and transparent communication does not mean that everyone needs to know everything at the same point in time. Some things need to be mature to be communicated. It comes down to creating an environment of trust and mutual respect."

Barbara Rangetiner,
Director of International Drug Regulatory Affairs/General Manager OPG

"There are three streams of open and transparent communication which are essential in regulatory affairs. Firstly, it is very important we communicate within our department the latest news, developments and guidelines from the authorities. Secondly, we have to communicate these developments to other departments throughout the company. Finally, we have to communicate openly and transparently to the authorities, maintaining the same standards in all communications.

Our biggest tool for communication is our regulatory database in which we enter all important information on our products. The database was launched in 2007, before that the information was on big excel lists and we had to compile reports for the relevant parties on a case-by-case basis, so it was time-consuming and not feasible in the long-term with Octapharma's rate of growth.

When developing this platform it was important for us to make this information available to everyone in the company. A person fills in a form entering which product/procedures he or she is interested in and whenever there are changes, the database will send automatic updates on the topic. The database can be used by anyone who is interested, but is also a daily working tool for those people who need the information as part of daily life in production, material management, logistics etc. They can access the database and use the customized searches; for example material management


Barbara Rangetiner

have all the regulatory information they need for a product for a particular market. Although the database today is used primarily as an internal platform, the regulatory database is a validated tool and we use it to communicate with the authorities, for example we can export information and upload this directly from the database to the relevant authority or use searches for compliance checks during audits (e.g. pharmacovigilance)."

Proud and talented employees in a healthy organization

Octapharma believes that in a healthy organization, everyone knows where we are going and how we will get there. Studies indicate that companies that invest in goal setting and alignment across the organization outperform their peers at every level. When clear goals are set and communicated, every employee understands the company strategy and targets and knows what he or she needs to do to support their achievement.

Global Performance Management Process

Beverley Cox,
Vice President, Global Human Resources

"In 2013, the new Global Human Resources department reviewed how Octapharma performance is managed and recommended the implementation of a global performance management process. Performance management is a business process that should be consistent across the organization. It is a cyclical process of managing all aspects of the company's performance all year round: it is not just a yearly employee performance review.

In 2014, HR's vision is that all employees will understand the company's goals and through performance management meetings with their managers, will know how they can individually contribute to the achievement of those goals. The annual review is the culmination of this cycle of setting goals, providing feedback and measuring achievements. These in-year and annual discussions allow employees and managers to review performance against goals and identify areas for improvement as well as training and development opportunities.

At Octapharma, we have a strong record of promoting from within which is made possible in part by our philosophy of providing training and development opportunities at both the corporate and subsidiary level. Octapharma has a number of corporate development programs as well as excellent local training initiatives across the organization. In this chapter we highlight examples of these programs."

Corporate Trainee Program

In 2013, Octapharma launched its first Corporate Trainee Program. While the company has a strong history of promotion from within and a variety of training and development opportunities for current employees, the Corporate Trainee Program has been designed to attract highly talented and motivated individuals to the Octapharma family. The program is just one way in which Octapharma is strengthening the pool of people who can support the strategic growth objectives of the business.

In October 2013, the 13 individuals who made it through the rigorous selection process started their journey with Octapharma. Five of the individuals are on the Finance and Marketing track, the main focus of which is in-depth training in finance, sales & marketing, human resources and IT. Eight are on the Production and Engineering track which offers in-depth training and hands-on experience in all aspects of protein-based pharmaceutical production. The trainees will spend 18 months learning alongside colleagues throughout various Octapharma production sites. Determined by where their skill sets are most needed, on successful completion of the program the trainees can be placed anywhere in the Octapharma Group.

Corporate Talent Pool Program

Talent Pool is a corporate management development program designed for current Octapharma employees with at least 2 years experience. The Talent Pool participants are nominated by their manager having demonstrated leadership abilities and the capability of taking on additional management responsibilities. The program consists of 7 modules on the critical business topics of leadership, communication, cultural diversity, sales and marketing, finance, innovation and creativity.

The Talent Pool Program is an excellent example of Octapharma proactively identifying talented individuals already employed by the company who are key contributors at an early stage of their career progression. The program allows these individuals to develop their skills, better positioning them to become future leaders. In September 2013, twenty-five individuals graduated from the 14 month program which started in June 2012.

As well as excellent corporate level programs there are many local training and development initiatives. Examples of local initiatives at two subsidiaries are highlighted on the next page.

New corporate trainees in Vienna begin their 18 month traineeship

Springe, Germany
Octapharma Management Training Program

Annett John, HR Manager

"The Springe facility has gone through considerable growth and recruitment since Octapharma purchased the site in 2008. In 2012, Stephanie Kauert and I began the process of establishing a management training program tailor-made for Springe. We developed the Octapharma Management Training (OMT) program working with an external training partner to bring in additional expertise. The objectives of the OMT are: the application of leadership knowledge and tools; teaching a common learning process for developing a management team and creating a platform for the exchange of experiences. The focus of the training is on social competencies as well as professional expertise, including employment law and business knowledge.

To shape the training to the requirements of Springe, we had to identify the most important topics on which to focus. We did this by asking what are the competences expected of a manager in order to achieve their targets. Topics included: communication, taking responsibility, clarity of thought, conflict capability, team-building, decision-making and employee development.

The first topic to be covered is the Predictive Index (PI). It was a vision of Wolfgang Marguerre to introduce PI across the organization. During a job interview as well as being asked about skills and qualifications, you are also asked about your personality and work style. PI interviews ensure that the needs of the role are matched by the candidate. The two day training on this topic was a big success. Introducing PI has already improved the interview process considerably. In September 2012, we conducted training about critical communication. In January 2013, we organized training on implementing annual appraisals.

Each level of management will go through the training program. The intention is to run at least one workshop a year which will cover a specific current management topic. The topic will be determined by speaking to the managers to identify common issues or areas of interest. In these ways we are creating a culture of training and development in Springe."

Octapharma Plasma Inc.
Management/Leadership Development Program

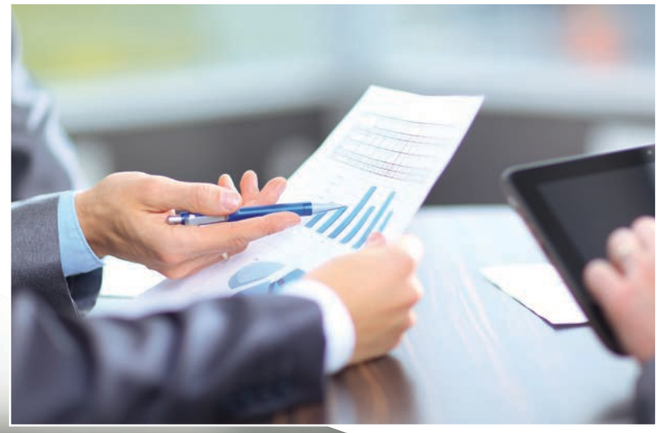
Mike Williams, Senior Director Employee Training & Development

"Octapharma Plasma Inc (OPI) has 45 centres across the United States. The corporate training function is led by myself and consists of four training managers. OPI`s management development program (MDP) was launched in 2009. At this time OPI had only nine centres and was in the process of a series of acquisitions which brought three or four different cultures. It was important for us to develop our own culture. The aim of the MDP was to build one identity for our management level.

The centres are the ones who deal with the donors, who create the customer experience and the quality of product. The quality of people in each centre therefore is extremely critical. We talked to the management teams across all centres to identify gaps in training. The first phase of MDP involves 1–3 months of technical training in the centre operations area. The second phase is 4.5 months of management-focused projects where the participants are asked to think critically about different processes. The topics are financial, operational and HR related, i.e. systems, reports and inventory management. In the final phase the trainees come to corporate headquarters for management skills training. This gives the trainees a better understanding of what happens once the data leaves their centre and how strategic decisions are made based on the data. The management training program gives perspective; it allows the trainees to see and understand the bigger picture.

There are three levels of management training: 'Taking the Step up to Supervisor'; 'Management Training Program' and 'Regional Director Program'. In 2012, we launched the Supervisor Program which is a self-paced program consisting of nine modules including communication, coaching skills, conflict resolution and employment law. During 2012, 53 supervisors completed the program, 40 of whom have since been promoted to Assistant Manager, one promoted to Field Training Manager and one to Centre Director. Over 2013, we launched the Regional Director/ Field Quality Management training, a two phased training program involving knowledge/ competency and leadership skills training.

Since its conception in 2009 the MDP has evolved based on participant and management feedback. Not only has the content of the program changed but the demographic has changed; now this training is largely for internal candidates in the process of promotion. Today, almost 100% of management positions are filled through internal promotions. The management trainee program will be invaluable in fulfilling the management roles which will be created during the significant growth planned for OPI over the coming years."



Annual Accounts

The Octapharma Group significantly exceeded 1 billion Euro net sales in the year 2013. The main driver once again was the increasingly strong performance of octagam® 5% and 10%. The significant increase in net sales and moderate investments into fixed assets led to a net cash position of 149 million Euro. This strong position facilitates the significant investments that the Octapharma Group has committed to with the launch of the capacity extension and efficiency improvement program, "Program 2019".

Net sales for 2013 are reported at 1.154 billion Euro, which represents an increase of 238 million Euro or 26% compared to the 2012 figure. This very satisfying result in net sales can be attributed to the increasing volumes sold in the Immunotherapy area, together with the development of sales in the Haematology and Critical Care areas.

Gross profit in 2013 was 312 million Euro, 27 million Euro higher than in 2012 and includes a non-2013 related depreciation of inventories. The reported gross margin is 27% and although on the surface is 4% lower compared to 2012, in actuality the adjusted gross margin, without the major inventory adjustments, was 32% and therefore represents a satisfactory increase of gross margin of 1%.

Operating expenses were 162 million Euro, 14 million Euro higher than in 2012. In relation to sales, operating expenses are below 15%, once more reaching an acceptable percentage of sales.

Earnings Before Interest and Tax (EBIT) are reported at 150 million Euro, 207 million Euro without the major inventory adjustments. This reflects a 10% increase compared to 2012 (51% without the inventory adjustments).

The Octapharma Group reports a net cash position of 149 million Euro at the end of 2013.

Net inventory decreased by 96 million Euro in 2013. A further, normal, decrease of work-in-progress inventory is expected during 2014.

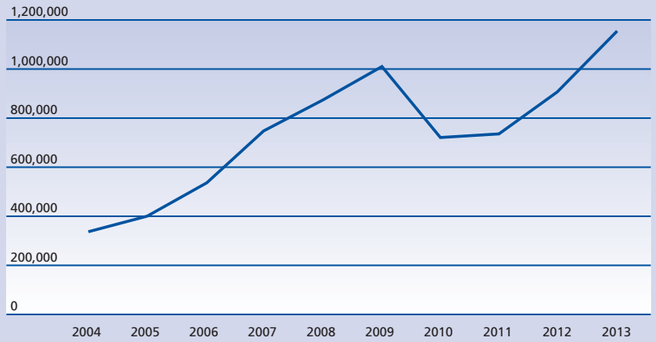
The investment in fixed assets was 65 million Euro in 2013. The development plan of our six modern production plants has been initiated. The so-called "Program 2019" will result in significantly increased investments into fixed assets in the forthcoming 5-7 years.

The equity ratio remains unchanged compared to 2012 at 82%.

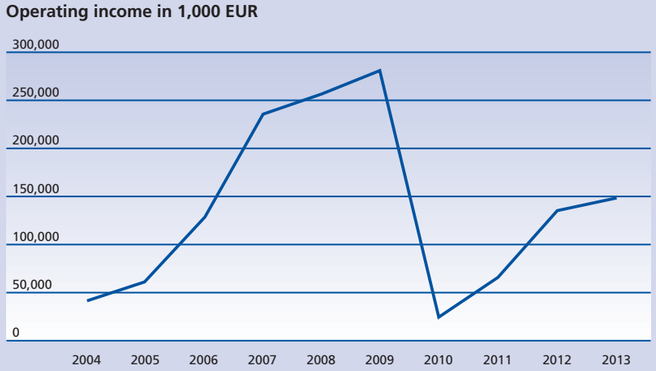
The very solid cash position and further planned improvements in profitability in 2014 are the key elements to finance our Program 2019 key objectives of capacity extension and efficiency improvement.

Key Figures of the Octapharma Group

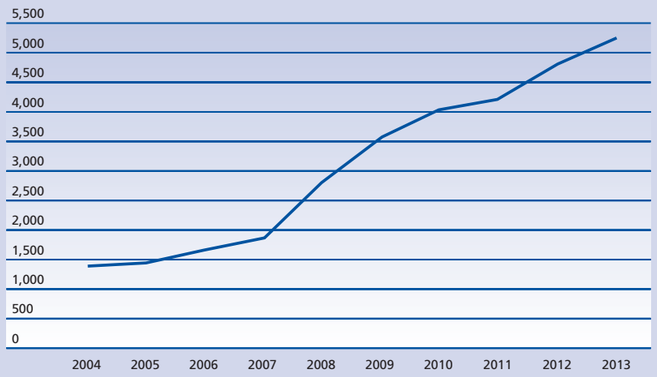
Net sales in 1,000 EUR



Operating income in 1,000 EUR



Average headcount



(monetary figures are in 1,000 EUR)	**2013**	2012	2011	2010	2009
Operating income	**149,924**	136,778	63,758	24,140	278,320
Net profit of the year	**124,398**	135,755	72,082	45,807	253,533
Year-end headcount	**5,514**	4,939	4,514	4,238	3,977
Return on average equity	**10%**	12%	7%	5%	29%
Profit from operations per employee	**28**	28	15	6	78
Current ratio	**594%**	591%	463%	533%	517%
Days of sales in receivables	**113**	115	145	106	93
Average days to sell the inventory	**274**	379	396	282	173
Cash flow from operations	**205,558**	131,559	-43,501	-62,003	169,433
Expenditures to ensure future prosperity	**111,236**	97,637	91,660	151,114	175,346
• Research and development	**45,780**	36,741	43,491	40,347	38,502
• Capital expenditures and investments in activities	**65,456**	60,896	48,169	110,767	136,844

Financial Statements of the Octapharma Group

The following summary financial statements are derived from the consolidated financial statements of Octapharma Nordic AB, Stockholm and comprise the summary income statement for the period from January 1 to December 31, 2013, the summary balance sheet and the summary cash flow statement for the year then ended, aggregating non-material financial statement captions.
Prior year numbers have been restated due to the adoption of IAS 19 (amended 2011).

Consolidated Income Statement of the Octapharma Group

January – December

(all figures in 1,000 EUR)	**2013**	2012 as restated
Gross sales	**1,257,978**	970,117
Sales deductions	-103,901	-54,465
Net sales	**1,154,077**	915,652
Cost of sales	-841,665	-630,557
Gross profit	**312,412**	285,095
Research and development	-45,780	-36,741
Selling and marketing	-74,078	-67,643
Regulatory affairs/quality audit	-9,016	-8,111
General and administration	-42,040	-36,719
Other income	9,243	2,107
Other expense	-817	-1,210
Total operating expenses	**-162,488**	-148,317
Operating income	**149,924**	136,778
Non-operating income and expenses	-5,381	2,542
Profit before taxes	**144,543**	139,320
Income tax	-20,145	-3,565
Net profit of the year	**124,398**	135,755

Consolidated Statement of Financial Position of the Octapharma Group

at 31 December

(all figures in 1,000 EUR)	**2013**	2012 as restated
Assets		
Cash and cash equivalents	148,603	32,060
Trade receivables	390,285	305,869
Other receivables	11,764	11,929
Inventories	539,899	636,328
Other current assets	25,834	24,641
Total current assets	**1,116,385**	1,010,827
Financial investments	6,528	8,850
Deferred tax assets	63,328	63,614
Loans to related parties	810	821
Property, plant and equipment	347,787	344,384
Other non-current assets	0	130
Total non-current assets	**418,453**	417,799
Total assets	**1,534,838**	1,428,626

(all figures in 1,000 EUR)	**2013**	2012 as restated
Liabilities and equity		
Trade payables and other payables	71,453	70,056
Payables to related parties	93	107
Income tax payable	25,123	13,074
Accruals and current provisions	91,288	87,925
Total current liabilities	**187,957**	171,162
Deferred income	1,881	2,258
Provisions	52,780	48,859
Deferred tax liabilities	26,184	28,722
Total non-current liabilities	**80,845**	79,839
Total liabilities	**268,802**	251,001
Share capital	100	100
Retained earnings	1,271,697	1,172,039
Currency translation adjustments	-5,761	5,486
Total equity attributable to owners of the Company	**1,266,036**	1,177,625
Total liabilities and equity	**1,534,838**	1,428,626

Consolidated Statement of Cash Flow of the Octapharma Group

January – December

(all figures in 1,000 EUR)	**2013**	2012 as restated
Net profit for the year	**124,398**	135,755
Depreciation on tangible and intangible assets	56,182	55,994
Change in fair value of non-current assets	-5,465	-12,822
Share of (profit) loss of associates	0	-5,869
(Profit) loss on sale of property, plant and equipment	-174	86
Changes in long-term liabilities and provisions	4,028	-447
Unrealised foreign exchange (gain) loss	4,639	-1,150
Cash flow before changes in working capital	**183,608**	171,547
(Increase) decrease of working capital	21,950	-39,988
Net cash from operating activities	**205,558**	131,559
Acquisition of property, plant and equipment	-65,456	-60,896
Proceeds from associates, current and non-current financial investments	1,933	1,512
Proceeds from sales of property, plant and equipment	787	886
Net cash used in investing activities	**-62,736**	-58,498
Financing activities	-25,000	-67,471
Net cash used for financing activities	**-25,000**	-67,471
Net change in cash and cash equivalents	**117,822**	5,590
Cash and cash equivalents beginning of period	32,060	26,521
Effect of exchange fluctuation on cash held	-1,279	-51
Cash and cash equivalents end of period	**148,603**	32,060

KPMG

KPMG AG
Audit
Badenerstrasse 172
CH-8004 Zurich

P.O. Box 1872
CH-8026 Zurich

Telephone +41 58 249 31 31
Fax +41 58 249 44 06
Internet www.kpmg.ch

REPORT OF THE INDEPENDENT AUDITOR ON THE SUMMARY FINANCIAL STATEMENTS

Octapharma Nordic AB, Stockholm

The accompanying summary financial statements on pages 66 to 70, which comprise the summary balance sheet as at 31 December 2013, the summary income statement and summary cash flow statement for the year then ended, are derived from the audited financial statements of Octapharma Nordic AB, Stockholm, for the year ended 31 December 2013. We expressed an unmodified audit opinion on those financial statements in our report dated 28 February 2014. Those financial statements, and the summary financial statements, do not reflect the effects of events that occurred subsequent to the date of our report on those financial statements.

The summary financial statements do not contain all the disclosures required by International Financial Reporting Standards (IFRS). Reading the summary financial statements, therefore, is not a substitute for reading the audited financial statements of Octapharma Nordic AB.

Management's Responsibility for the Summary Financial Statements

Management is responsible for the preparation of a summary of the audited financial statements on the basis described on page 66 of this report.

Auditor's Responsibility

Our responsibility is to express an opinion on the summary financial statements based on our procedures, which were conducted in accordance with International Standard on Auditing (ISA) 810, "Engagements to Report on Summary Financial Statements."

Opinion

In our opinion, the summary financial statements derived from the audited financial statements of Octapharma Nordic AB for the year ended 31 December 2013 are consistent, in all material respects, with those financial statements, on the basis described on page 66 of this report.

KPMG AG

Orlando Lanfranchi

Markus Ackermann

Zurich, 28 February 2014

Contact Details

Headquarters
Octapharma AG
Frederic Marguerre
Ulrich Thibaut
Roger Mächler
Seidenstrasse 2
8853 Lachen
Switzerland
Tel. +41 55 4512121
Fax +41 55 4512110
frederic.marguerre@octapharma.ch
ulrich.thibaut@octapharma.com
roger.maechler@octapharma.ch

Australia
Octapharma Australia Pty. Ltd.
Frederic Marguerre
Matt Riordan
Jones Bay Wharf
42/26-32 Pirrama Road
Pyrmont NSW 2009
Australia
Tel. +61 2 85725800
Fax +61 2 85725890
frederic.marguerre@octapharma.ch
matt.riordan@octapharma.ch

Austria
Octapharma Pharmazeutika
Produktionsgesellschaft m.b.H.
Tobias Marguerre
Barbara Rangetiner
Oberlaaer Straße 235
1100 Vienna
Austria
Tel. +43 1 610320
Fax +43 1 610329300
tobias.marguerre@octapharma.se
barbara.rangetiner@octapharma.com

Octapharma
Handelsgesellschaft m.b.H.
Norbert Müller
Oberlaaer Straße 235
1100 Vienna
Austria
Tel. +43 1 610321220
Fax +43 1 610329103
norbert.muller@octapharma.de

Azerbaijan
Representative office
of Octapharma AG
Namik Pashayev
96 Nizami str., The Landmark I
AZ1010 Baku
Azerbaijan
Tel. (+994) 12 498 8172
Fax (+994) 12 493 5931
namik.pashayev@octapharma.com

Belarus
Octapharma AG
in the Republic of Belarus
Nadezhda Lagoiko
Office 207,
Exhibition Centre „Aquabel"
Crossing of Logoisk Highway
and Minsk Ring Road,
223053, Minsk region
Republic of Belarus
Tel. +375 17 237 95 02
Fax. +375 17 237 94 98
nadezhda.lagoiko@octapharma.se

Belgium
Octapharma Benelux S.A./N.V.
Eva Priem
Researchdreef 65
1070 Brussels
Belgium
Tel. +32 2 3730890
Fax +32 2 3744835
eva.priem@octapharma.com

Brazil
Octapharma Brasil Ltda.
Samuel Mauricio
Av. Ayrton Senna 1850, loja 118
22775-003 Barra da Tijuca
Rio de Janeiro
Brazil
Tel. +55 21 2421 1681
Fax +55 21 2421 1691
samuel.mauricio@octapharma.com

Canada
Octapharma Canada Inc.
Frederic Marguerre
Sri Adapa
308-214 King St W
Toronto ON
M5H 3S6
Canada
Tel. +1 416 531 9951
Fax +1 416 531 8891
frederic.marguerre@octapharma.ch
sri.adapa@octapharma.ca

China
Octapharma Beijing
Representative Office
Matt Riordan
Chen Xuyu
Suite 815, Zhongkun Plaza
59 GaoLiangQiaoXieJie
HaiDianQu, Beijing 100044
China
Tel. +86 10 62169126
Fax +86 10 62193528
matt.riordan@octapharma.ch
chen.xuyu@octapharma.com

Czech Republic
Octapharma CZ s.r.o.
Petr Razima
Delnická 12
170 00 Prague 7
Czech Republic
Tel. +420 266 793 510
Fax +420 266 793 511
petr.razima@octapharma.com

Denmark
Octapharma Nordic AB
David Andersson
Elersvägen 40
SE-11275 Stockholm
Sweden
Tel. +46 8 56643000
Fax +46 8 56643010
david.andersson@octapharma.com

Finland
Octapharma Nordic AB
Janne Nissilä
Rajatorpantie 41 C
01640 Vantaa
Finland
Tel. +358 9 85202710
Fax +358 9 85202713
janne.nissila@octapharma.fi

France
Octapharma S.A.S.
Frédéric Cambecèdes
Fanny Chauvel
70-72 rue du Maréchal Foch
67381 Lingolsheim
France
Tel. +33 3 88788989
Fax +33 3 88788978
frederic.cambecedes@octapharma.fr
fanny.chauvel@octapharma.fr

Octapharma France S.A.S.
Marie-Christine Borrelly
62 bis Avenue André Morizet
92100 Boulogne Billancourt
France
Tel. +33 1 41318000
Fax +33 1 41318001
marie-christine.borrelly@
octapharma.com

Germany
Octapharma GmbH
Frederic Marguerre
Norbert Müller
Hubert Franzaring
Elisabeth-Selbert-Straße 11
40764 Langenfeld
Germany
Tel. +49 2173 9170
Fax +49 2173 917111
frederic.marguerre@octapharma.ch
norbert.mueller@octapharma.de
hubert.franzaring@octapharma.de

Octapharma Dessau GmbH
Sybille Werner
Otto-Reuter-Straße 3
06847 Dessau-Rosslau
Germany
Tel. +49 340 55080
Fax +49 340 5508111
sybille.werner@octapharma.de

Deutsche Gesellschaft
für Humanplasma mbH
Frederic Marguerre
Hubert Franzaring
Sybille Werner
Elisabeth-Selbert-Strasse 11
40764 Langenfeld
Germany
Tel. +49 2173 9170
Fax +49 2173 917111
frederic.marguerre@octapharma.ch
hubert.franzaring@octapharma.de
sybille.werner@octapharma.de

Octapharma Produktionsgesellschaft
Deutschland mbH
Gerold Rempeters
Wolfgang-Marguerre-Allee 1
31832 Springe
Germany
Tel. +49 5041 77918170
Fax +49 5041 77918126
gerold.rempeters@octapharma.com

Octapharma
Biopharmaceuticals GmbH
Carola Schröder
Im Neuenheimer Feld 590
69120 Heidelberg
Germany
Tel. +49 6221 1852 520
Fax +49 6221 1852 510
info-heidelberg@octapharma.com

Greece
Octapharma Hellas SA
George Kalbitzer
60, Posidonos Ave.
166 75 Glyfada Attiki
Greece
Tel. +30 210 8986500
Fax +30 210 8986044
octapharma.hellas@octapharma.gr

Italy
Octapharma Italy Spa
Abramo Brandi
Via Cisanello 145
56124 Pisa
Italy
Tel. +39 050 549001
Fax +39 050 5490030
abramo.brandi@octapharma.com
info.italy@octapharma.com

Kazakhstan
Representative office
of Octapharma AG
Svetlana Safarova
Dostyk Str. 180, office 42
050051 Almaty
Kazakhstan
Tel. +7 7273201541
Fax +7 7273201541
svetlana.safarova@octapharma.com

Latin America
Eric Ballestraz
Seidenstrasse 2
8853 Lachen
Switzerland
Tel. +41 55 4512121
Fax +41 55 4512110
eric.ballestraz@octapharma.ch

Mexico
Octapharma S.A. de C.V.
Angel Sosa
Calzada México Tacuba No. 1419
Col. Argentina Poniente
C.P. 11230 México, D.F.
México
Tel. +52 55 53995644
Fax +52 55 55270527
angel.sosa@octapharma.com.mx

Norway
Octapharma AS
John Erik Oern
Industrivegen 23
NO-2069 Jessheim
Norway
Tel. +47 63988860
Fax +47 63988865
john.erik.oern@octapharma.no

Poland
Octapharma Poland Sp. z o.o.
Jaroslaw Czarnota
39A Domaniewska Street
02-672 Warszawa
Poland
Tel. +48 22 2082734
Fax +48 22 2082767
jaroslaw.czarnota@octapharma.se

Portugal
Octapharma Produtos
Farmacêuticos, Lda.
Paulo Castro
Abramo Brandi
Rua da Graça, 14
1170-169 Lisboa
Portugal
Tel. +351 21 8160820
Fax +351 21 8160830
paulo.castro@octapharma.pt
abramo.brandi@octapharma.com

Octapharma Gestão
Estratégica e Operacional, Lda.
Paulo Castro
Quinta do Lamas Lote 5
Cave, Zona Industrial da Paiã
1675 – 076 Ponthina
Portugal
Tel. +351 21 8107000
Fax +351 21 8107010
paulo.castro@octapharma.pt

Russia
Octapharma Russia LLC
Olga Koniuhova
Northern Tower, 19th Floor
10 Testovskaya Street
Moscow 123317
Russian Federation
Tel. +7 495 6621815
Fax +7 495 6621891
olga.koniuhova@octapharma.com

Saudi Arabia
Representative office
of Octapharma AG
Maher Abu Alrob
Al-Thalia Street
PO Box 301712
Riyadh 11372
Kingdom of Saudi Arabia
Tel. +966 920000406
Fax +966 1 2176404
maher.abualrob@octapharma.com

Slovakia
Octapharma AG, o.z.z.o.
Miroslav Gresik
Zochova 6/8
811 03 Bratislava
Slovakia
Tel. +421 2 54646701
Fax +421 2 54418321
miroslav.gresik@octapharma.com

South Africa
Octapharma South Africa (Pty) Ltd
Matt Riordan
Sean Hancock
Building # 3
Design Quarter District
Cnr William Nicol and
Leslie Avenue East
2191 Fourways
Tel. +27 11 465 4269
Fax +27 11 465 4301
matt.riordan@octapharma.ch
sean.hancock@octapharma.com

Spain
Octapharma S.A.
Diego Garcia
Parque Empresarial de San
Fernando
Edif. Berlin - planta Baja
Av. Castilla 2
28830 San Fernando de Henares,
Madrid
Spain
Tel. +34 91 6487298
Fax +34 91 6764263
diego.garcia@octapharma.es

Sweden
Octapharma AB
Tobias Marguerre
Alex Scheepers
Elersvägen 40
SE-11275 Stockholm
Sweden
Tel. +46 8 56643000
Fax +46 8 56643010
tobias.marguerre@octapharma.se
alex.scheepers@octapharma.se

Octapharma Nordic AB
Tobias Marguerre
Elersvägen 40
SE-11275 Stockholm
Sweden
Tel. +46 8 56643000
Fax +46 8 56643010
tobias.marguerre@octapharma.se

United Kingdom
Octapharma Limited
Sue Griffin
The Zenith Building
26 Spring Gardens
Manchester, M2 1AB
United Kingdom
Tel. +44 161 8373770
Fax +44 161 8373799
sue.griffin@octapharma.co.uk

USA
Octapharma USA, Inc.
Flemming Nielsen
121 River Street, Suite 1201
Hoboken, New Jersey 07030
USA
Tel. +1 201 6041130
Fax +1 201 6041131
flemming.nielsen@
octapharma.com

Octapharma Plasma, Inc.
Frederic Marguerre
Judy Smith
3525 Whitehall Park Drive,
Suite 500
Charlotte, North Carolina 28273
USA
Tel. +1 704 6544600
Fax +1 704 6544700
frederic.marguerre@octapharma.ch
judy.smith@
octapharmaplasma.com

Ukraine
Octapharma AG
Victoria Bondarenko
4A Verchniy Val av., office 27/1
04071 Kiev
Ukraine
Tel. +38 050 3330016
victoria.bondarenko@
octapharma.com

octapharma

Octapharma AG · Seidenstrasse 2 · 8853 Lachen · Switzerland
Tel. +41 55 4512121 · Fax +41 5 5 4512110 · www.octapharma.com
Editor: Claudie Qumsieh · Content: Frederic Marguerre, Octapharma AG

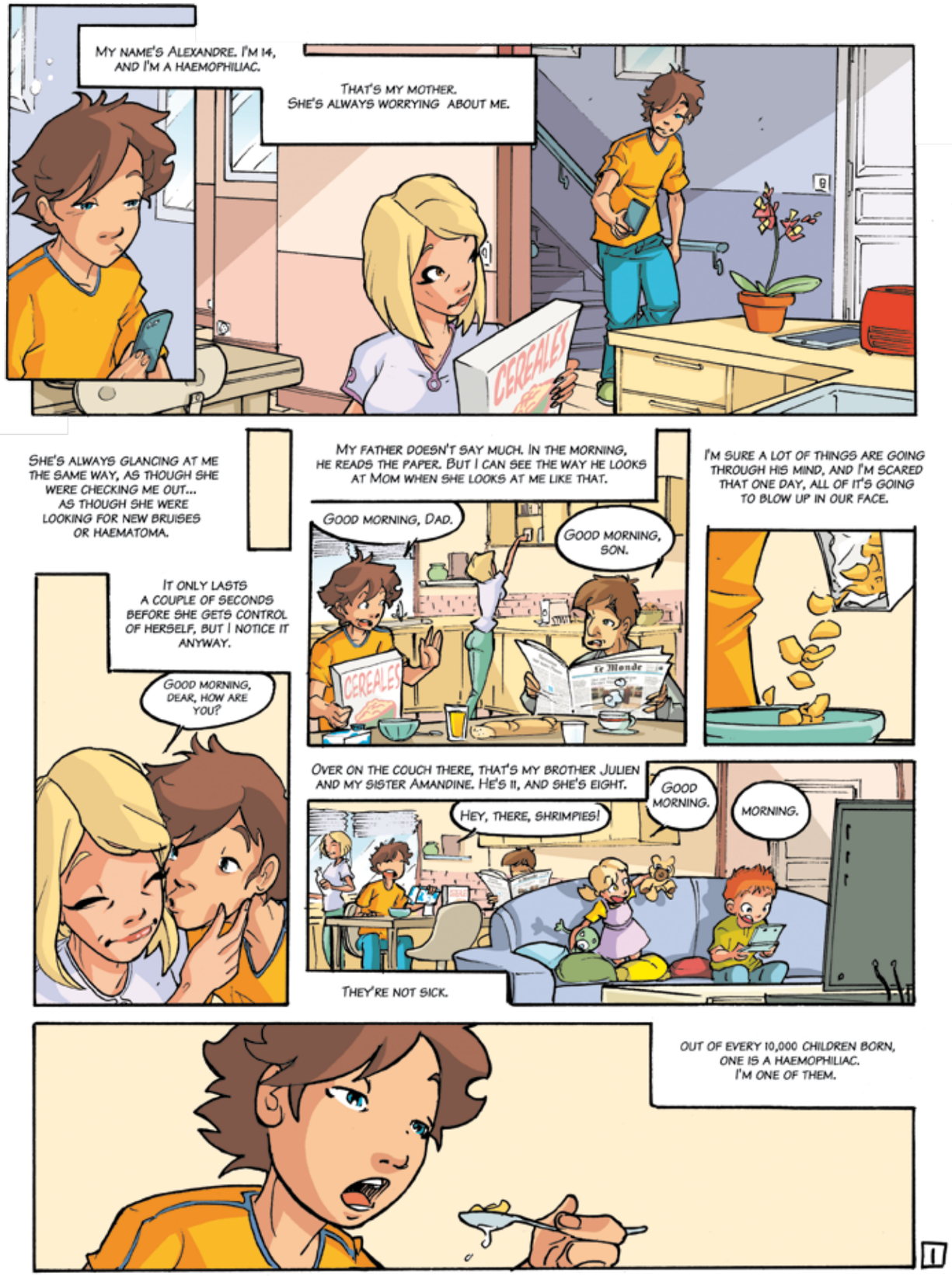
Of every 10,000 children born, one is a haemophiliac. I am one and this is my story.

octapharma

For the safe and optimal use of human proteins

Octapharma France developed the idea for the comics out of a desire to engage teenagers and to help them better understand haemophilia. Collaborating with a paediatric haemophilia expert, Octapharma France defines the story lines for the comics covering important topics like genetics, prophylaxis and self infusion. The comics are published regularly on the website of the French Association of Haemophilia. The aim is to tell an authentic story with messages relevant to young people. With the help of a talented illustrator, Alexandre's story is brought to life.

octapharma



My parents knew that something was wrong when I was five months old.

I had bruises all over my upper body. I've heard them tell the story hundreds of times.

The women who took care of me at the nursery were in a panic. My parents were frightened to death. I know my mother thought I had a fatal blood disease.

My parents took me to a paediatrician, but he looked at them doubtfully. My Mom told me that he thought they were abusing me.

So they took me to a hospital. They did a blood test. The diagnosis came back: Haemophilia.

My parents didn't even know what haemophilia was.

They thought it was an incurable illness, like leukemia, and I was going to bleed to death if I even got a scratch. They thought they had to protect me, constantly keep an eye on me. That I'd never be able to go to school, or live a normal life.

The doctor had to repeat over and over that it was treatable, and that progress was constantly being made, before my mom stopped crying.

She said that she didn't stop crying that day until she saw me smile.

They don't tell me that story anymore. They're not afraid of haemophilia now. They're over it.

These are my best friends, Hugo and Mélanie. At first, they asked me all sorts of questions about haemophilia. They didn't know anything about it.

Mélanie thought I'd die if I fell off my bike. But a haemophiliac doesn't bleed faster than anybody else; it just takes him longer to stop bleeding.

When someone bleeds, little cells called platelets jump into action. Special proteins that circulate in our bloodstream make a kind of glue that thickens the blood and seals the wound. That's called coagulation.

These proteins are called Factor 8 and Factor 9. If your body doesn't make them, or doesn't make enough of them, your blood can't coagulate when you get hurt.

I've got severe type A haemophilia. That means that there's hardly any Factor 8 in my blood, so it can't coagulate. That's all.

That made Hugo laugh. He said that I was doing a good job of taking care of my haemophilia, because he couldn't tell I was sick.

He said I was lucky, because I didn't have to invent excuses to tell my parents so I wouldn't have to go to sports.

WHAT'RE YOU DOING THIS WEEKEND? DO YOU WANNA GO TO THE CARNIVAL?

YEAH!

JULIEN'S GOT A SOCCER GAME.

DO YOU HAVE TO GO?

YEAH, WE COULDN'T CARE LESS ABOUT YOUR BROTHER'S FOOTBALL GAME.

OH, I DON'T KNOW. I THINK IT'S A BIG GAME FOR HIM. AND I MISSED THE LAST TWO. MY MOM SAYS I SHOULD GO WITH HER AND DAD THIS TIME, IT MEANS A LOT TO MY LITTLE BROTHER FOR ME TO BE THERE.

YEAH, THAT'LL JUST REMIND YOU THAT YOU'D LOVE TO BE ABLE TO PLAY SOCCER.

LISTEN, IT'S NO BIG DEAL THAT I CAN'T PLAY SOCCER.

YOU ALWAYS SAY THAT, BUT I DON'T THINK YOU REALLY MEAN IT..

AND HE NEVER GOES TO SEE YOU ROW. ISN'T THAT IMPORTANT FOR YOU?

YEAH, WELL, THERE'S A SOCCER GAME EVERY WEEKEND.

HE NEVER BOTHERS TO MAKE EXCUSES. HE'S ENVIOUS OF YOU. SO, ARE YOU COMING, OR NOT?

ENVIOUS OF A HAEMOPHILIAC? DON'T MAKE ME LAUGH! I CAN GO IF YOU DON'T LEAVE BEFORE FOUR.

OKAY, MEET YOU AT FOUR-THIRTY. WE'LL COME BY TO PICK YOU UP!

AND YOUR BROTHER HAD BETTER GO TO YOUR NEXT ROWING MATCH!

...AND I TELL YOU, HE'S ENVIOUS!

AMANDINE, WHAT'RE YOU DOING? I'VE TOLD YOU BEFORE, DON'T PLAY WITH THAT!

BUT I NEED IT! LOOK, MY BABY'S BLEEDING!

WE'VE ALREADY BEEN OVER THIS. YOUR BABY IS NOT BLEEDING!

YES, HE IS! HE'S A HAEMOPHILIAC! YOU CAN HELP ME GIVE HIM HIS SHOT. HE'LL DIE IF YOU DON'T, I KNOW HE WILL!

OK, OK, WE'LL GIVE HIM HIS SHOT. BUT HE WON'T DIE BECAUSE HE'S A HAEMOPHILIAC, YOU KNOW.

REALLY?

ZIP

YES. YOU KNOW IT'S TRUE IF I TELL YOU SO.

YOU SOUND LIKE A DOCTOR.

THERE WE GO, ALL BETTER!

DO YOU THINK THAT SOMEDAY I COULD BECOME A HAEMOPHILIAC, TOO...

...LIKE MY BABY?

THAT'S NOT HOW IT WORKS.

I'M SCARED, YOU KNOW. AND MOM SAYS I'M TOO LITTLE TO UNDERSTAND.

WELL, I THINK YOU'RE BIG ENOUGH TO UNDERSTAND.

IT'S KINDA COMPLICATED, SO PAY ATTENTION, ALL RIGHT?

OK !

INSIDE OUR BODIES WE HAVE CHROMOSOMES, AND THEY'RE WHAT MAKE US EITHER GIRLS OR BOYS. CHROMOSOMES ARE MADE UP OF DIFFERENT PARTS, CALLED GENES. AND THE GENE FOR HAEMOPHILIA IS IN THE X CHROMOSOME.

GIRLS HAVE TWO X CHROMOSOMES, AND BOYS HAVE AN X CHROMOSOME AND A Y CHROMOSOME.

OKAY.

DID YOU KNOW THAT GRANDPA ROGER HAS THE SAME DISEASE AS I DO? THAT HE'S A HAEMOPHILIAC, TOO?

YES.

SO, HERE ARE GRANDPA ROGER'S TWO CHROMOSOMES, X AND Y, SEE?

Papi Roger X Y

AND HERE'S GRANDMA. SO, WHAT CHROMOSOMES DOES SHE HAVE?

Roger Y — Mamie X X

XX !

GOOD! YOU'VE GOT IT.

GRANDPA'S A HAEMOPHILIAC. THAT MEANS HIS HAEMOPHILIA GENE DOESN'T WORK RIGHT. IT CAN'T MAKE THE FACTOR THAT KEEPS YOU FROM BLEEDING FOR TOO LONG. DO YOU UNDERSTAND?

THE FACTOR?

Papi Roger X Y — Mamie X X

YES, THAT'S THE ELEMENT IN BLOOD THAT KEEPS YOU FROM BLEEDING FOR A LONG TIME. YOU DON'T HAVE IT IF YOU'RE A HAEMOPHILIAC.

GRANDPA AND GRANDMA HAD A BABY.

Papi Roger X Y — Mamie X X — Maman

YEAH I KNOW. THEY HAD MOM.

THAT'S RIGHT. EACH PARENT GIVES ONE CHROMOSOME TO EACH CHILD THEY HAVE. MOM'S A GIRL, RIGHT?

DUH! OF COURSE!

SO, THAT MEANS THAT GRANDPA GAVE MOM AN X CHROMOSOME AND GRANDMA DID, TOO?

Papi Roger X Y — Mamie X X — Maman X X

THAT'S RIGHT. BUT THE HAEMOPHILIA GENE IN GRANDPA'S X CHROMOSOMES DON'T WORK, INCLUDING THE ONE HE GAVE MOM.

SO, MOM'S A HAEMOPHILIAC, TOO?

NO, BECAUSE HER OTHER X CHROMOSOME DOES WORK THE WAY IT SHOULD.

AND SHE CAN MAKE THE FACTOR.

RIGHT!

I THINK YOU'VE GOT IT. SO, NOW YOU GO ON.

HERE!

PERFECT! YOU' RE REALLY SMART!

Mamie X X — Maman X X — PAPA XY — ALEXANDRE XY — JULIEN XY — AMANDINE XX

SO, YOU SEE, DAD GAVE ME HIS Y CHROMOSOME, AND THAT'S WHY I'M A BOY. AND MOM GAVE ME ONE OF HER X CHROMOSOMES.

AND SHE GAVE YOU THE ONE WHICH DOESN'T WORK RIGHT, AND THAT'S WHY YOU'RE A HAEMOPHILIAC?

YES, THAT'S WHY. YOU SEE, BOYS HAVE ONLY ONE X, SO IF IT DOESN'T WORK RIGHT, THEY'RE HAEMOPHILIACS.

BUT WHY DIDN'T MOM GIVE YOU THE OTHER X, THE ONE THAT WORKS RIGHT?

IT'S NOT THE MOTHER WHO DECIDES WHICH CHROMOSOME SHE GIVES TO HER CHILDREN. IT'S JUST SHEER CHANCE.

SO THAT'S WHY YOU'RE A HAEMOPHILIAC AND JULIEN ISN'T?

YES, LOOK.

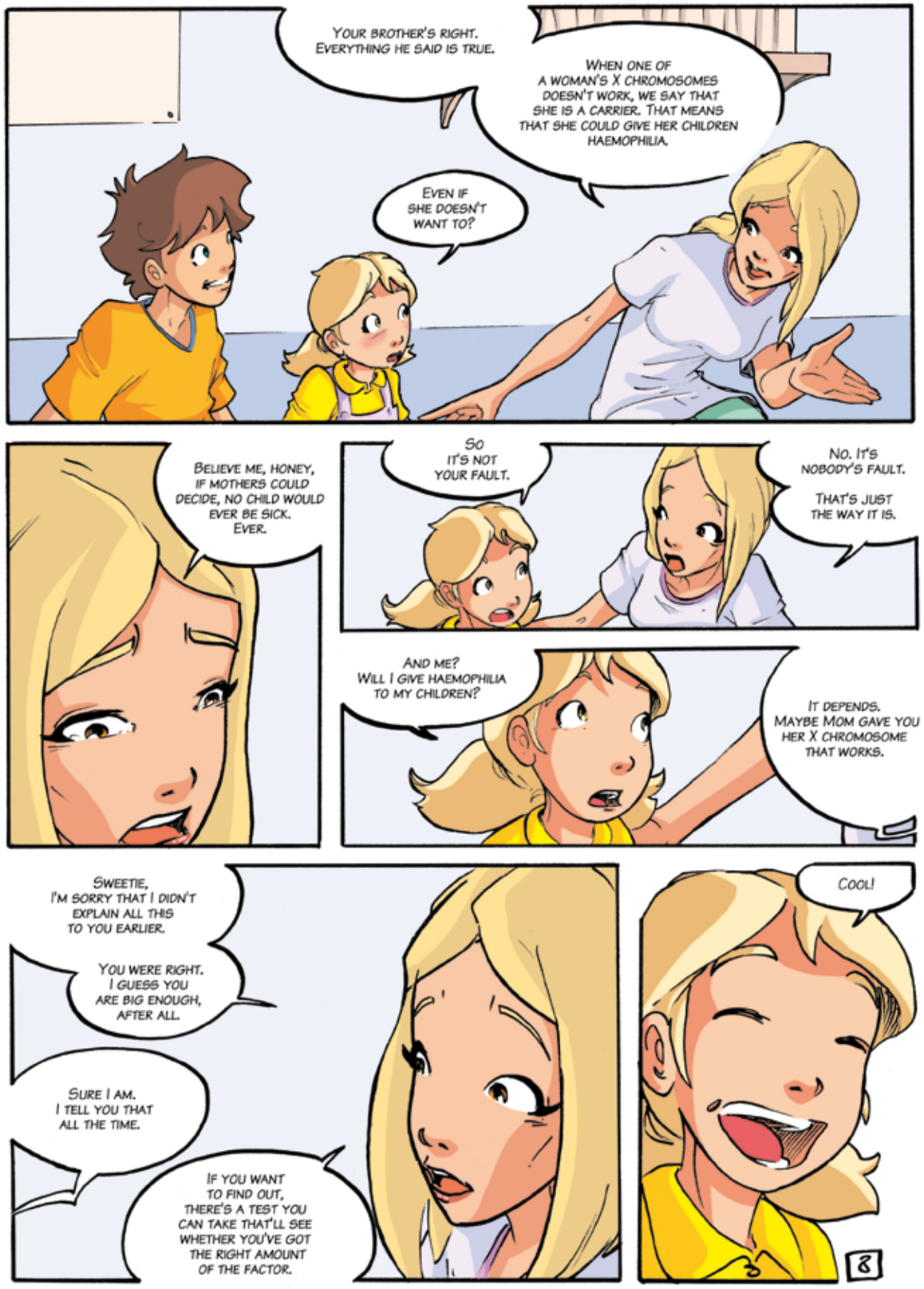
BUT WHAT ABOUT ME?

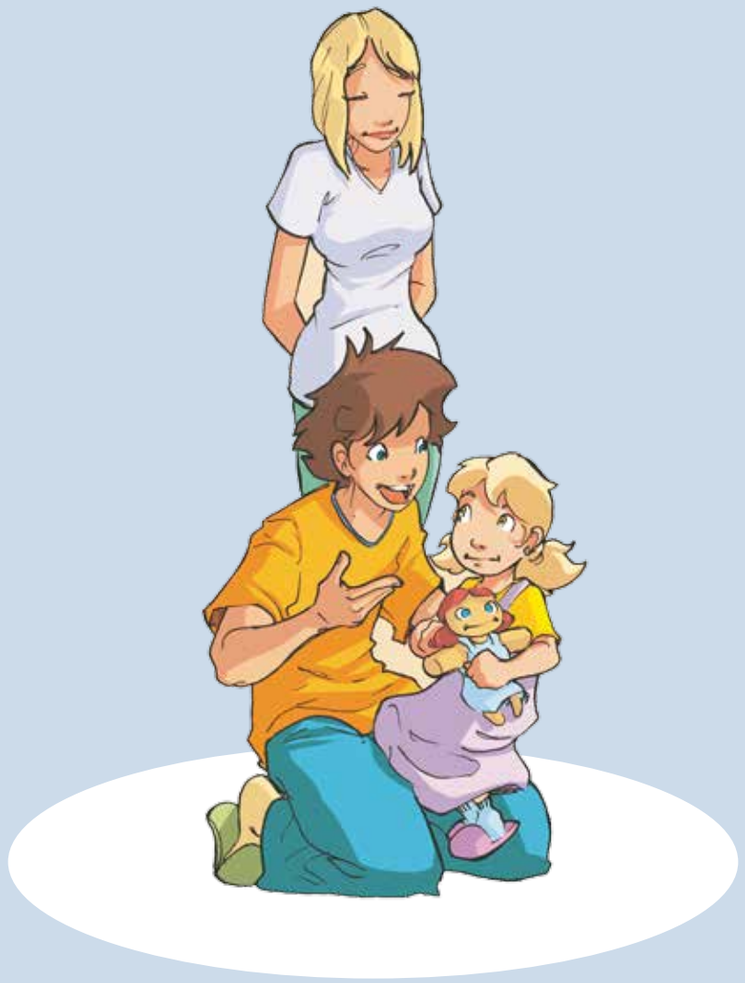
Papi Roger X Y — Maman X X — PAPA XY — ALEXANDRE XY — JULIEN XY — AMANDINE XX

YOU' VE GOT TWO XS; DAD'S PROTECTS YOU FROM GETTING HAEMOPHILIA.

BUT WILL I GIVE THE X THAT DOESN'T MAKE THE FACTOR TO MY CHILDREN?

ALEXANDRE, MAY I ANSWER THAT QUESTION?


YOUR BROTHER'S RIGHT. EVERYTHING HE SAID IS TRUE.
WHEN ONE OF A WOMAN'S X CHROMOSOMES DOESN'T WORK, WE SAY THAT SHE IS A CARRIER. THAT MEANS THAT SHE COULD GIVE HER CHILDREN HAEMOPHILIA.
EVEN IF SHE DOESN'T WANT TO?
BELIEVE ME, HONEY, IF MOTHERS COULD DECIDE, NO CHILD WOULD EVER BE SICK. EVER.
SO IT'S NOT YOUR FAULT.
NO. IT'S NOBODY'S FAULT.
THAT'S JUST THE WAY IT IS.
AND ME? WILL I GIVE HAEMOPHILIA TO MY CHILDREN?
IT DEPENDS. MAYBE MOM GAVE YOU HER X CHROMOSOME THAT WORKS.
SWEETIE, I'M SORRY THAT I DIDN'T EXPLAIN ALL THIS TO YOU EARLIER.
YOU WERE RIGHT. I GUESS YOU ARE BIG ENOUGH, AFTER ALL.
SURE I AM. I TELL YOU THAT ALL THE TIME.
IF YOU WANT TO FIND OUT, THERE'S A TEST YOU CAN TAKE THAT'LL SEE WHETHER YOU'VE GOT THE RIGHT AMOUNT OF THE FACTOR.
COOL!
8



octapharma

For the safe and optimal use of human proteins

Octapharma AG
Seidenstrasse 2 · 8853 Lachen · Switzerland
Tel. +41 55 4512121

Octapharma France S.A.S.
62bis Avenue André Morizet · 92100 Boulogne Billancourt · France
Tel. +33 1 41318000

Scenario: Severine Gauthier
Illustration: Thomas Labourot
Colour: Christian Lerolle

www.octapharma.com