

# Annual Report 2012



**octapharma**

For the safe and optimal use of human proteins

## Company Snapshots

- Global, independent, Swiss-based, human protein manufacturer
- 30 years focus on human proteins
- Manufacturing facilities in 5 countries
- Sales in more than 80 countries
- Sales of 916 million Euros in 2012
- 16% compound annual growth rate since 1995

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This special 30<sup>th</sup> anniversary annual report reflects on

Octapharma's past, present and future. It shows the

human nature of the family owned organization which

has a patient centered focus developing lifesaving

products from human proteins. This report gives

insights into the careers of some of our valued

**30<sup>th</sup>**  
ANNIVERSARY

**octapharma**

colleagues who have demonstrated loyalty and

commitment over decades and applied their skills and

talent to the company's impressive growth. Although

individuals are highlighted, Octapharma's success is a

result of team work, of the combined contribution of

all employees, what we call "the human factor".



## Foreword by Wolfgang Marguerre

This year we celebrate Octapharma's 30th anniversary. Octapharma was founded on the principle of enhancing safety for patients; the "octa" is derived from the Greek and Latin word for eight, named after the factor which is deficient in haemophilia A patients. Our inaugural product, octavi<sup>®</sup>, was the first FVIII concentrate using what was then innovative solvent detergent virus inactivation technology. I am proud to say that over these 30 years we have remained focused on improving the lives of patients. Over the coming year we expect to submit a series of products to the FDA and EMA, including, with a rather pleasing symmetry, our first recombinant product, the human cell line recombinant FVIII. Our clinical studies have successfully concluded and we will submit the Biologic License Application during the course of 2013 in both Europe and the US.

In 2012, which has been a successful year, we have invested heavily in major projects, improving capacities in all plants to facilitate our long term growth. We aim to build on our successes to target opportunities in encouragingly promising markets with the aim of enhancing revenues for all products and continuing to optimally utilize our resources.

Since its conception in 1983, the company has grown to 5,000 employees. With this growth we do not forget the responsibility for each of our employees. We have created a new global Human Resources function based in our headquarters in Lachen, Switzerland, to build a world class global HR organization to support Octapharma's business strategies as the company continues to grow.

As well as living up to the responsibilities for our employees, we collectively take responsibility for the trust instilled in us by physicians and patients. The philosophy of Octapharma is that we have a responsibility for transparent and open communication with all our stakeholders. We operate in a very delicate segment of the biopharmaceutical industry and our fundamental core qualities are trust and reliability. These fundamental principles led to the comeback of the corporation's star product, octagam<sup>®</sup>. The successful return of this product, which is highly appreciated by all markets, was the result of efforts throughout the company, demonstrating a perfect sense of team spirit and the qualities which define us.

The board recently identified the strategic pillars which will lead to achieving our long term ambitious goals. The foundation of our 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. These strategic pillars, we believe, will lead to further successes and profitable organic growth, significantly increasing our revenues from this year's healthy figure of almost one billion Euros.

The 30 year milestone is an opportunity to feel pride in what we have achieved so far, to appreciate how far we have come and to look to the future. There will come a day when my sons will take over the leadership of the family business and continue to strive to uphold and strengthen the values of Octapharma well into the future.

**Wolfgang Marguerre**  
Chairman of the Octapharma Group



## The Management Board of the Octapharma Group



## At a Glance

### Founded

in 1983

### Mission

“For the safe and optimal use of human proteins“

### Employees

4,939

### Net Sales

916 million Euros

### 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

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### Markets

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

### Brands

(registered trademarks) albuminativ®, alunorm®, 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





## Interview with Frederic Marguerre

### In what ways has Octapharma influenced your life?

I remember sitting at the dinner table listening to the early ideas for the company before its inception. I listened as the budding concepts developed and gained shape, becoming real. In many ways Octapharma has been a member of the Marguerre family since my teenage years. This has given me a sense of responsibility and purpose. I knew from an early age that I would have the opportunity to join the family business. I spent the initial part of my professional career in other industries, which provided me with a different perspective and context. During this time I gained management experience which can be applied across a spectrum of industries. This experience has given me a deeper understanding and appreciation of the significance of our business, the purpose of which is to produce lifesaving therapies.

### Are there any important lessons you have learnt from your father?

Timing is always of the essence; if we don't achieve our goals within given timeframes, we cannot accomplish our objectives. The importance of a consistent detail-orientated mindset; to follow up on all projects; to avoid politicking; to remain business-focused and to act with integrity. We strive to place people first: patients, stakeholders and employees, above short-term gains. The temporary voluntary withdrawal of one of our key products serves as a perfect example because we did not lose track of the long term. We did not make short-term decisions which would have prevented us from growing in the manner as set forth in this report. We were confident that we would resolve the withdrawal and could rely on the expertise and unwavering loyalty of our employees.

### What are the key Octapharma values for you?

Octapharma's patient centered approach is the essence of the company. For me, it is very important never to lose sight of what we set out to achieve and to continue to grow in a healthy and realistic manner. In the end, patient safety is always more important than growth.

### Octapharma now employs 5,000 people, how do you feel about this responsibility as the company continues to grow?

Our core value of nurturing a healthy organization with proud and talented employees becomes increasingly even more important as the company grows. As a result, we are focusing on implementing organizational structures to provide a fair and professional framework which enables career progression and opportunities. Octapharma now has a truly global footprint and employees can recognize opportunities in other areas within the company in which they can further excel.

### The foundation of Octapharma's strategic vision is our patient-oriented corporate culture. What does this mean to you?

Life is very precious and fragile; you become aware of that every time you visit the end users of the products we manufacture. Whenever I travel on business, I generally also plan to meet with our stakeholders in the hospitals where they are based. These visits are a constant and humbling reminder of the importance of our work.

### Can you tell us about the importance of the partnership between you and your brother?

My brother and I have a good partnership. Whilst I am responsible for the very beginning of the production process, i.e. the sourcing of our precious raw material, Tobias looks after the manufacturing process of our finished products. We are also both engaged in different regions in which we

supply these products, enabling us to be sensitive to the needs of the markets. Simultaneously, we each look after different corporate functions as well as different product areas from an international marketing point of view. Overall, there is a good balance because we are different yet complimentary in our approach: his hand fits mine.

### How do you want to shape the Octapharma of the future?

Octapharma has achieved so much in 30 years. I would like to see Octapharma become a company that on the one hand retains the flavor and flexibility of a family business, on the other hand, one which operates efficiently in a business focused, self-driven manner. There are many advantages to being privately owned in terms of decision making and taking a genuinely long-term view with regards to growth and stability. I would like to shape the company towards the continued empowerment of my colleagues, creating structures which enable each of them to make wise and intelligent business decisions to drive the company into a profitable and stable future.



## Interview with Tobias Marguerre

### In what ways has Octapharma been a member of the Marguerre family for these 30 years?

Whenever we are together as a family, we discuss Octapharma. Many of the early meetings took place in our home in Paris. The company was always a natural part of family life, in any get-together the company was the topic of discussions: on a trip, in the car, over breakfast. Octapharma has been a real presence throughout my life. I have been personally active in the company for 13 years. Today, Octapharma is part of my life every second. I am in a lucky situation because my wife and family understand this and they support me 100% in giving the necessary attention to Octapharma.

### How has Octapharma shaped your life?

Before the company was called Octapharma, when it was more of a concept than a company (we didn't have a product or a plant) my father was offered to sell his part of the business. When he told the family I told him I didn't want him to sell because I wanted to work for the company when I grew up. I was 11 years old and I knew that I wanted to work for my father. I knew that if I really wanted to work for his company, I had to prove to be the right person for the job. With this in mind, I chose my education so that it would fit with a future with Octapharma. I also wanted my education to leave me enough room to be flexible and not become too specialized. I studied economics, marketing, management and finance, which gave me a broad knowledge and a good foundation for my career with the family business.

### Will Octapharma remain a family company?

As a family we are very dedicated to the company. Continuity is important. It is quite clear that what we have created

over these 30 years is something very special indeed, therefore my brother, my sister and I are committed to keeping Octapharma in the family.

### Are there any important lessons you have learnt from your father?

The devil lies in the detail, when there is a problem if you dig into the detail the solution often reveals itself. It is not about being right; it is about taking the right decision for the company. Finally, responsibility is not something you get, it is something you take.

### Can you tell us about the importance of the partnership between you and your brother?

I believe that it is very important to have a good balance. When my father decides to take a step back, our partnership will be increasingly important. I think what is key is that there is a shared respect. We complement each other in our personalities and organizational responsibilities. I look forward to a closer collaboration with my brother.

### Wolfgang Marguerre talks about the importance of not forgetting the responsibility for all employees. How do you feel about this responsibility as the company continues to grow?

One of our strategic visions is a healthy organization; we should have the right resources in the right place at the right time. With our new global HR function we are demonstrating that we want to create a company which lives by certain shared values. 5,000 is a number, but each of our employees is an individual, each with their own goals and visions for their career. I am proud to work with such qualified and competent colleagues. We strive to create a challenging and rewarding workplace whilst providing an economically sound environment for our colleagues and their respective families. We must continue to make robust decisions and remain financially healthy, in order to continue to make good investments and to grow.

### One of Octapharma's strategic visions is our patient centered approach, is it rewarding for you to know that what we do improves the lives of patients?

We develop and produce lifesaving therapies and deliver programs that are increasingly patient focused. The standard of care is very diverse in many of the countries in which I work. It is in the countries where treatment is not widely available that you really come to appreciate and understand the significance of our purpose. With access to proper treatment, patients' lives can be significantly improved. For example, we launched a major primary immune deficiency program in Eastern Europe supporting 16 immunological centers with grants.

### How do you want to shape the Octapharma of the future?

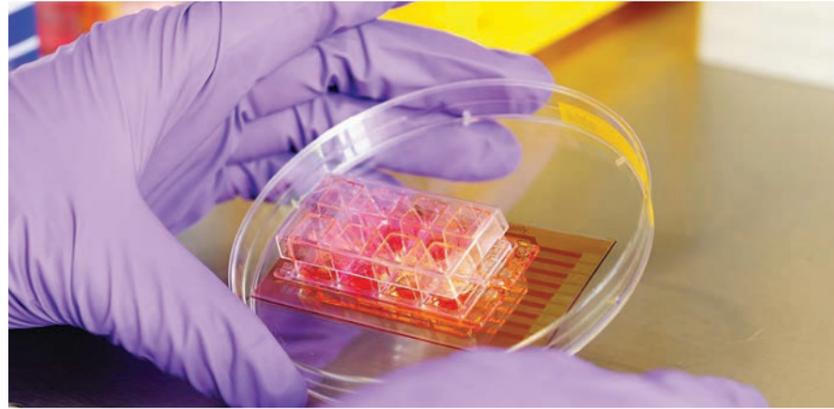
We are approaching the next stage in Octapharma's development. We have huge growth opportunities and now is the time when we must prepare for the next phase. To prepare we need to have the right structures in place. To achieve our objectives we need to optimize processes and systems. As a family owned company we can take fast decisions. When someone identifies opportunities, we say, "Yes, let's try". As the company grows this becomes more difficult because to take decisions you need the whole picture: for this we need to have the right systems in place providing the right information at the right time. This becomes increasingly challenging as you grow. At the same time we must maintain our entrepreneurial spirit and outside-the-box thinking. We must take well judged business decisions associated with commercial risks, which is part of the entrepreneurial spirit we wish to maintain. We need to keep our flexibility as a core, maintain our closeness with the market and ultimately keep our finger on the pulse. This will be about striking the right balance.

# Research and Development

The year 2012 has seen significant advances in several major projects involving Octapharma's Research and Development activities. All of our development projects for new therapeutics have made significant progress towards their most important milestones, i.e. filing of regulatory dossiers and market approval. Our scientists continually strive to improve our existing products as well as search for new and better therapeutic uses of innovative products derived from source blood plasma. Our daily source of energy is the quest to improve patients' lives and health.

Cutting edge analytical techniques, including fluorescence microscopy, flow-chamber experiment and HPLC chromatography system





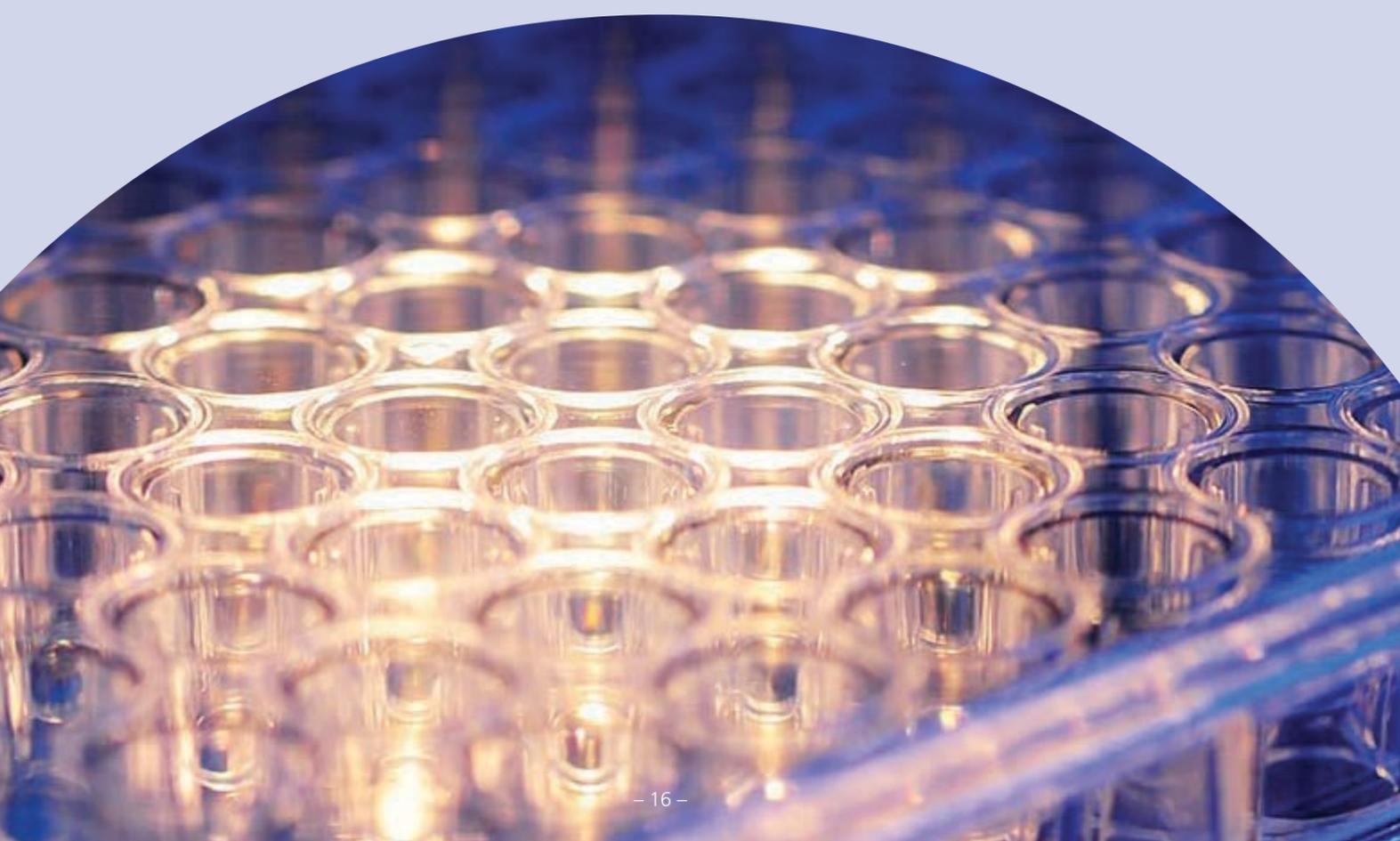
Brand new research facility for the Molecular Biochemistry group in Berlin, showing scientists discuss results, handling of cell culture and MALDI-TOF mass spectrometer

### Torben Schmidt Head of Virus & Prion Validation

Octapharma has always been a pioneer in viral safety; notably being the first company to implement solvent detergent (S/D) treatment in a FVIII product in the 1980s. Over recent years Octapharma has put focus on pathogen safety. My team is responsible for this important area for all Octapharma products which is incredibly motivating. We are proud every time a product comes to market. Our work is scientifically very interesting covering a wide spectrum of virus and prion safety activities. We perform laboratory studies with a validated downscale model of production. The proudest achievement of the department so far has been to secure our Good Laboratory Practice (GLP) status in 2001-2002. As a result, our viral safety work is always under GLP and every three years we are audited by our GLP monitoring authority to retain this status. In 2013, key activities include the Human-cl rhFVIII submission in the US, as well as preparing safety studies for the submission of our new immunoglobulin product. The team I joined in 2000 as a Research Scientist has now doubled in size. As the company grows we will continue to maintain our high standards for pathogen safety of our products and to protect our patients.

### Christoph Kannicht Head of Molecular Biochemistry

I joined Octapharma in the beginning of 1997, before that I already worked as an employee of the Free University Berlin funded by a grant from Octapharma. The opportunity to establish an Octapharma research lab in a university surrounding was appealing and challenging. This spirited decision exemplifies Octapharma as a privately owned company with the freedom to be pioneering and unconventional. Today, our team of highly skilled scientists and technicians is working in our brand new research facility for the Molecular Biochemistry group in Berlin, which was opened in November 2012. Over the last 15 years, we have developed and established cutting edge analytical techniques: difference gel electrophoresis, dynamic light scattering, flow-based VWF assays, surface plasmon resonance-based measurement of protein interactions and mass spectrometry for analysis of posttranslational modifications – to name just a few. Besides our work for the development of new products, we offer assistance on existing products and marketing activities, including publishing our results in peer-reviewed journals and presenting data at symposia. The huge breadth of activities and tasks immediately brings to light the main challenge for my team: to apply cutting edge know-how, self responsibility and flexibility in order to react immediately and professionally on urgent priorities.



# Heidelberg Facility



New home of Octapharma Biopharmaceutical Research Center in Heidelberg, Germany

Octapharma invested €25 million to build this striking facility bringing all our recombinant R&D technology together in one state-of-the-art building. The 10,000 m<sup>2</sup> building resembles the shape of a ship, representing our voyage into a new era for Octapharma. The building now homes all recombinant research activities with laboratory and office space, as well as a state-of-the-art GMP clean room production facility in which we will perform technical upscale and production of clinical samples of new recombinant therapeutic proteins produced from a human cell line. The advancement of our Human-cl rhFVIII project to a more mature stage allowed for a transfer of know-how from the R&D group in Stockholm to Production and Quality departments. From now on, all research and development activities for FVIII and all other recombinant projects take place in Heidelberg. OctaBio's new home is in the centre of a highly renowned academic and biotechnology cluster, surrounded by research institutions and biotech start-up companies. This marks an important step signaling the recombinant branch as a key factor in Octapharma's future.



## Carola Schröder

Senior Vice President, Recombinant R&D and General Manager Octapharma Biopharmaceuticals

I am proud to have led Octapharma Biopharmaceuticals ("OctaBio") from a small biotech start-up to a high tech pharmaceutical company. I lead a group of highly motivated scientists building up a GMP facility from scratch and implementing the requirements for pharmaceutical drug development. We are up-scaling our production processes to the clinical scale in our new shining stainless steel fermenters. OctaBio still has the feel of an entrepreneurial biotech company; a think-tank of creative and intelligent people. Having the full support of the wider company allows us to focus on populating our research pipeline and strengthening our recombinant portfolio produced from a human cell line. We moved to our new home in April when construction was ongoing. On one occasion, alarms of our high-tech monitoring systems went off during the night and I arrived to find it was a false alarm; I also found I was not the only one who had made that night time journey. I think I speak for all of the highly motivated employees when I say, "you feel like the owner of the house". We feel responsible for every corner of the building.

In 2013, we have two major target milestones: the submission for the marketing authorization for Europe and the US of Octapharma's first recombinant product produced from a human cell line, Human-cl rhFVIII; and gaining the manufacturing license in the new facility for producing clinical material for the very promising Granulocyte colony-stimulating factor (HES-GCSF) project. It is rare in your professional life in research that you bring a product to the market. I am happy to have such highly professional colleagues in my team including those who have known our "baby-rhFVIII" from the very beginning.



## Maya Tiemeyer

Scientific Head of Octapharma Biopharmaceuticals

We were presented with the rare opportunity to plan the optimum laboratories for our needs. It is great to finally be in our new facility. Heidelberg R&D is responsible for the first steps in the development of the recombinant pipeline. The R&D department consists of five groups; together with the Clinical Production department we work on the concepts to generate new products for the pipeline. Our focus is to lay the foundation to establish a robust process for commercial production. Part of the concept is the human to human philosophy by using a human cell line for commercial production with the aim of ensuring better tolerability for the patients. Human-cl rhFVIII is the first recombinant product in which we have implemented this strategy. Clinical studies so far have shown a very good tolerability and efficacy confirming our approach. The product is currently prepared for submission. Bringing a product from conception to market will be a fantastic achievement.

## Holger Pfründer

Project Manager

I joined as a Line Manager responsible for developing purification processes for recombinant products. Soon after, I was asked to take over the position of Project Manager for the development of our HES-GCSF product. I am co-ordinating all activities and ensure timelines are met. I was highly involved in the planning of the Heidelberg facility where we are building up clinical production in parallel to the development of new products and the life-cycle activities of our Human-cl rhFVIII. I studied process engineering before specializing in biotechnology and did my PhD in bioprocess engineering.

I like to work with technical systems: this is the basis of our work. However, working with proteins and living cells, very complex biological structures and systems, is what really excites me. OctaBio offers a diverse environment allowing me to get involved in a variety of activities. It is rewarding to know that our work here in Heidelberg is important for the wider Octapharma Group.



## Cathleen Wegmann

Research Associate

I was the lucky one who isolated the cell clone, one in several million! This was the result of team work, but I am proud to have played a role in the foundation of our future recombinant portfolio. I joined in 1999 and am now a member of the fermentation team.

We are responsible for laboratory based tasks including fermentation, cell culture, sampling, testing, recording and analyzing results. As Lab Assistants we are fortunate to be in this beautiful building. The team was previously split into two buildings with limited space in our old rented site in Munich. The space here is fantastic! It is a pleasure to work on such an exciting project which has brought people together and creates a good working environment. This year I am looking forward to moving to the next stage into production.





**Armin Tiemeyer**  
Head of Production

Our activities in our previous home in Munich were pure R&D: selecting clones and developing new products. We were producing up to 25 litres for pre-clinical scale. Now we are switching to clinical production, which involves implementing new quality standards for GMP and implementing processes that comply with authority requirements. I am responsible for setting up the production line and scaling up the production process. We moved into an empty building with areas still under construction. It was a lot of work to get everything up and running; the whole team worked together which adds to the sense of this building becoming our new home. The decision to build this facility shows that the owners have strong trust in recombinant technology. We are part of the company's future. It's a once in a lifetime opportunity to see the whole project from concept to market. OctaBio is special because it is a small site but with the support of a larger company.

I spent 14 months in 2011/2012 working in Stockholm on the technology transfer of the FVIII project. This was a great opportunity to get to know how the business is run on a larger production site; in many ways recombinant and plasma do not differ in terms of engineering and clean rooms.

Octapharma is special in that it is a large privately held and run company. The owner family is strongly visible in our daily work which makes things more personal, more human.



**Ying Wang**  
Line Manager

I joined in 2002 as a Scientist in the purification group. At that time there were around 12 of us. We began looking into protein expression and gene therapy, after which we focused on recombinant protein expressed in a human cell line. My previous experience was all academic before I joined Octapharma. I completed my PhD in biotechnology in China and my post doc in Germany. Along with many of my colleagues who have come from the universities I was given a fair chance. Selecting people from academia is important because R&D is the link between academic research and GMP. It doesn't matter where you come from or who you are, if you are qualified you are given the chance to shine in Octapharma. We now have many more resources in Heidelberg and being located in one place makes our R&D more efficient. It is a great milestone that we now have GMP status. Octapharma creates an environment which encourages you to contribute and to believe that there are no limitations to what you can do. R&D today defines Octapharma's production of tomorrow. We all want to bring great benefit to society and to the patient. Preparing to release our Human-cl rhFVIII for market authorization is a big milestone. It is what we have worked all these years to achieve!



Various activities including quality control, storage of analytical samples, clean room operations and upstream process development



# Lingolsheim Production Plant



Located near Strasbourg, France, the facility was acquired in April 1999 from Aventis. In less than a year, the plant was integrated into Octapharma operations by the transfer of technology for the production of FVIII, immunoglobulins and albumin, using intermediate plasma fractions from the basic fractionation plant in Vienna. Later, Lingolsheim started fractionating plasma and producing Factor IX (FIX) and octaplex®. Octapharma has entrusted Lingolsheim to be in charge of producing the new generation of immunoglobulin. This challenge will also be the occasion for the site to obtain its first FDA license. The site employed 80 staff pre-acquisition and now employs 370 people. Two major projects will be finalized this year: the production of the new immunoglobulin which is planned to be launched in the US and in Europe in 2015 and the first phase of the new logistics platform. Lingolsheim is also preparing for its next major projects: a new utilities building and further investments to increase the site capacities in fractionation and aseptic filling.



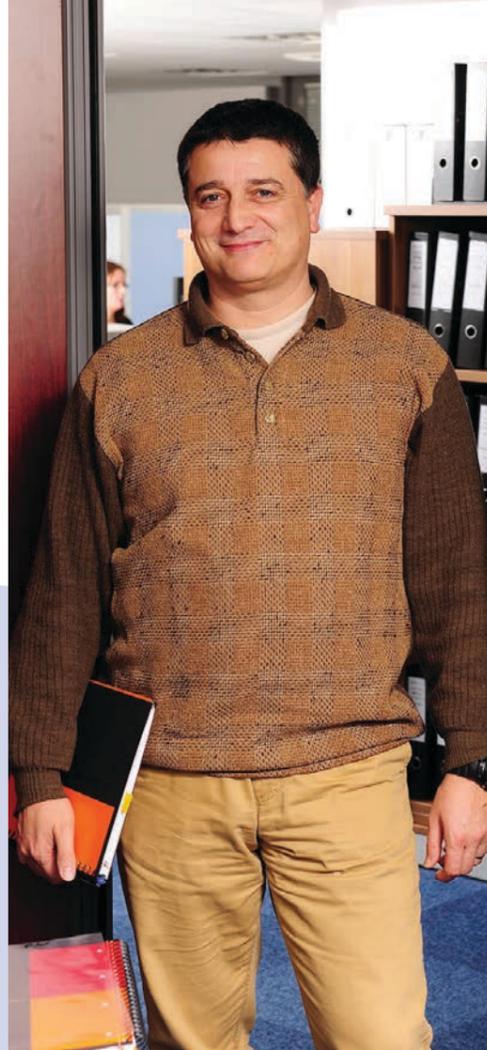
Ion exchange chromatography system, team working on the implementation of the new immunoglobulin product equipment and process and the new ultrafiltration system

## Frédéric Bal

### Head of Quality Unit

My roots are in R&D. I discovered blood fractionation during university and fell in love. I developed my expertise during a traineeship in the blood transfusion center in Lille. When I joined Octapharma in 1989 there was no plant, no production and limited administration. I worked at the Red Cross fractionation center in Germany doing R&D projects for Octapharma. After the first plant was purchased I moved to Vienna. My role was lab development and upscale/transfer to production. As the company grew and colleagues joined I had to speak English and learn German. I accompanied Octapharma's immense growth both personally and geographically, living in Germany, in Austria and then moving back to France. As the company grew and developed, so did I; I am an Octapharma product myself! The personalities of the owners and the humanity and visibility of the management means that we still behave and feel more like a family than a 5,000 head company. Personally, I have enjoyed discovering and sharing in cultures that are not mine by birth. As a result, I am not 100% French anymore. Professionally, I am proud to have developed the octanine® manufacturing process, as well as the first generation of what is now octaplex®. I also contributed to the Heparin Sepharose step which solved the octagam® issue.

Our new immunoglobulin project is probably the biggest project in Lingolsheim's history. This is our masterpiece. This is not just an adaptation of another production line; this is a brand new state-of-the-art line with new equipment and new technological steps. The first phase activities are technology transfer and implementation of the process, the equipment and the first validation batches. The second phase is to apply for the FDA license. This will be Lingolsheim's first FDA licensed product and will be a great milestone for us. We are challenging ourselves to do better than ever before and we are looking forward to future opportunities for other new products.



## Danielle Ulmer

### Purification Activity Manager

I joined Lingolsheim 30 years ago as a Technician, progressing over the years to head of department. Along with the project team, I am responsible for co-ordinating the transfer to the new production process of our new immunoglobulin product. This is a great challenge for my team: a new product and a new process with the goal of obtaining FDA license. Things have changed considerably since being integrated into the Octapharma Group. Today we produce five products and have grown from 80 people to 370, with my own team having grown five-fold. Octapharma invest in employees and advance talented staff, the promotion of Frédéric Cambecèdes to Site Manager is a good example. Octapharma always look to the future, investing in production and the development of new products to treat more patients. My greatest pride has been to show, with my colleagues, that the site is able to overcome challenges. In 2011, we worked incredibly hard to successfully resume production of octagam®, we also implemented corporate harmonization processes between the four production sites. Together with my production team and all support services our energy in the near-term future will be devoted to securing FDA license.



## Alain Millot

### Methods Officer & Project Manager

I joined Lingolsheim in 1991 as Production Technician working in plasma thawing, basic and fine fractionation, and in the aseptic areas. Since 2003, my role is Methods Officer and Project Manager in the Production Support department. In the past, I implemented the first automatic aseptic filling line in Lingolsheim for albumin. Today, I am very proud to be Project Manager for the new generation of immunoglobulin; Lingolsheim will be the first site to produce this new product. My role is to co-ordinate project tasks for all departments and to work closely with other sites and sustain a very close relationship with the Technology Transfer department. We started with a blank sheet of paper and created new production rooms in basic and fine fractionation, procured new equipment including chromatography, ultrafiltration, tanks and separator. We are qualifying all new rooms and all new and modified equipment and are preparing for the first validation batches in the first half of 2013.

For more than 20 years, I have been able to develop within the company in positions which were rewarding both personally and professionally, without falling into a boring routine. Before 1999, we experienced some difficult years because the activity of the site was not sustainable. When Octapharma took over it became clear the intention was to invest and maintain employment. During these fourteen years, the investment on the site has only strengthened this feeling of security which gives me the desire to succeed in my role within company projects. Octapharma value employees who demonstrate expertise and skill and encourage employee development.





Octapharma Lingolsheim's quality control laboratory for raw materials, environment and products



**Carine Delannee**  
Deputy Transport & Warehouse Manager

I joined Lingolsheim in 1983 as QC Technician and later moved into Quality Assurance. I worked with Supply Chain to implement GMP and enjoyed the diversity of activities. I was happy to move into Supply Chain as Deputy Transport & Warehouse Manager in 2012. What we do here is pivotal for all activities on-site; we are responsible for material flow, traceability, quality, temperature control, purchasing, material management, and distribution. In my new role I must first master how Supply Chain works, I will then look to improve and simplify processes where I can. As a result of my background I appreciate the importance of quality in everything we do. Construction has started on our new logistics platform. The Lingolsheim plant is in the centre of town so it is difficult for trucks coming in and out and it makes increasing our capacities complex. At the moment we are renting cold room storage in two locations. This new platform will optimize our process because all activities will be located in one place. Before Octapharma there was uncertainty because we didn't have a lot of work. When the Chairman first came here he spoke to everyone (in French!). He makes no distinctions between people; you feel valued no matter what your role.

The Marguerre family is deeply attached to their business. Octapharma is more human than a faceless corporation. It is unusual for a company to be led by members of a family, but perhaps Octapharma is like a member of their family.



**Alice Dorsi**  
Team Leader, Aseptic Production

For 38 years I have worked in the production of clotting fractions. I lead a highly dedicated team which ensure the aseptic filling of albumin; octanate®; octanine® and octaplex® is fulfilled according to the instructions of batch records. I love my job because we are in perpetual progress, and we continue to evolve. Since being acquired by Octapharma we manufacture more products and this is great for us to be challenged and to adapt. My proudest achievements have been to help in the introduction of octagam® production and to see the advent of octanine®.

Octapharma is a human company because the staff feel recognized, the individual is not a number, employees feel connected to the business and this is motivating. It is a family company, even in my own case; twelve years ago my daughter did an internship and has been working for the past decade as a Service Technician in Quality Control. 2012 was definitely a good year; Lingolsheim was chosen to be the site for the production of the new generation immunoglobulin product. This gives us a lot of momentum and we are embracing the challenge.

## Joseph Schwartzmann

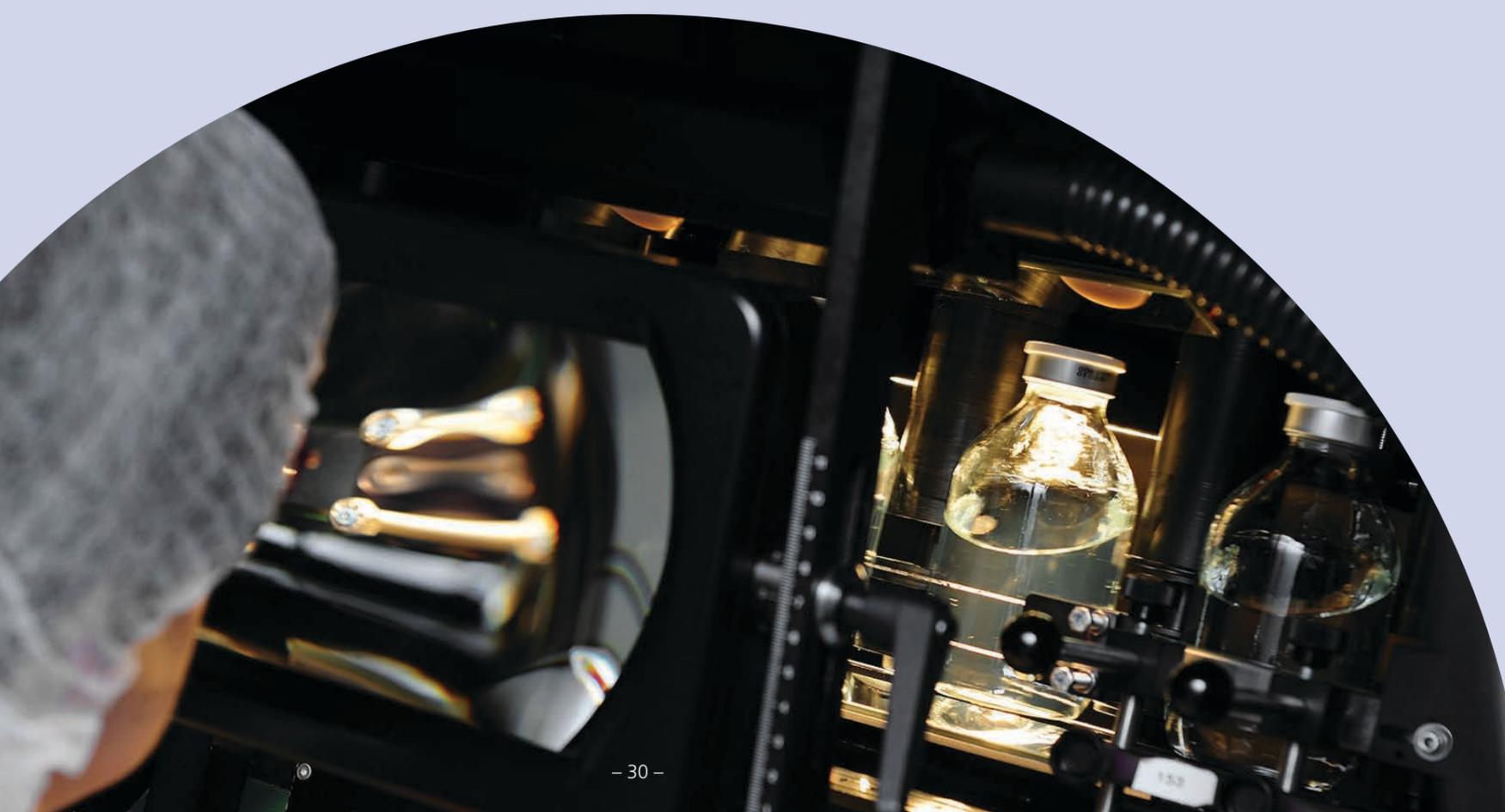
### Head of Engineering

As head of the engineering department, my work includes all industrial and building projects on the Lingolsheim site: qualification (design, installation, operational) and hygiene, security, environment issues (HSE). In 1989, I became the maintenance manager at the Regional Blood Transfusion Centre encompassing process, engineering, site maintenance and HSE. When Octapharma acquired this production unit in Lingolsheim in 1999, this was the beginning of a period of work and challenges on an unprecedented scale in order to adapt the facilities to the products, quality and capacity needs of the fast-paced and constantly evolving world of Octapharma. Significant investments in line with company cash flow have been made over the years. Mr Wolfgang Marguerre once told me: "As my father used to say: only spend what you have". The involvement of family members in the daily running of the business ensures continuity and gives us confidence in the future of our site. Octapharma believe in investing not only in state-of-the-art production technology but also in people.

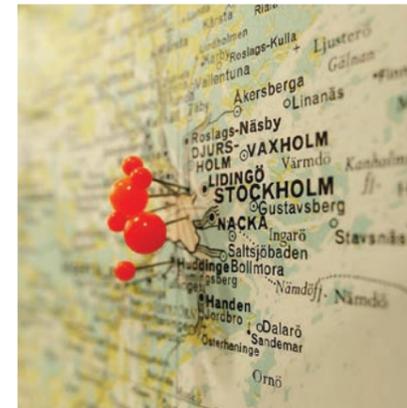
Constant growth and career opportunities make Octapharma an attractive place to work. The highlights of my career are when Octapharma acquired the site, the challenges of adapting the installations to the Octapharma products and increases in production capacity. 2013 will see the finalization and production of the new generation immunoglobulin, the opening of the new logistics platform, planning for the construction of a new utilities building and the extension of the production building. I will be involved in documentation compliance and adapting equipment and facilities to FDA standards.



Pharmaceutical production activities in Octapharma SA, Lingolsheim



# Stockholm Production Plant



Reception area, Octapharma AB, Stockholm

Located at Lake Mälaren in the west of Stockholm, Sweden, and originally owned by Kabi (later Pharmacia, and then spin-off Biovitrum), the site has been involved in plasma fractionation since the 1940s. The first plasma protein, albumin, was supplied to the market in 1949 followed by gamma globulin in 1950. In the mid-1960s, Kabi was one of the first commercial companies in the world to introduce a Factor VIII concentrate. Octapharma acquired the plant, which was at that time the Plasma Products Division of Biovitrum, in July 2002. The production facilities were subsequently converted to enable the continuous production of both Biovitrum's existing plasma products as well as Octapharma's product range. Ongoing investments of more than € 150 million into the acquisition and adaptation of expanded premises, such as the historic brewery building, as well as installation of state-of-the-art production equipment, have increased the plant's annual capacity seven-fold from 2002–2012. Today, there are 600 employees in Stockholm.



The "Stora Bryggeriet" (the Old Brewery) was built in 1892 and marked the beginning of a biotechnology era in Stockholm. Renovation will make it a representative headquarters for the Octapharma business in Stockholm which will facilitate laboratories and other support functions

## Olivier Clairotte Plant Manager, Stockholm

I joined Octapharma Vienna in 1998 in technology transfer and process development, working on the transfer of processes to Octapharma's newly acquired second plant, Lingolsheim. I returned to Vienna to work for the newly created pre-clinical research group. Later, I was involved in the Brazilian self sufficiency project. I returned to Lingolsheim in 2002 to manage production from plasma thawing to bulk products.

In 2006, I became Plant Manager for Stockholm. I can certainly speak from experience when I say, when you are located in only one site it is easy to think local, but when you get to know the different plants and countries you see things differently. In Octapharma production plants gain a lot from sharing and benchmarking between sites, especially since the process of harmonization began, led by Gerold Rempeters. Cultures might differ, but technical people speak the same language. The Marguerre family continue to keep track of everything on both a strategic and detail level, it's quite amazing actually.

Here in Stockholm we are privileged to have amazing access to investment; the small volume parenterals (SVP) project is the biggest investment in the plant's history and one of the biggest clean room projects in Europe. Octapharma is a business built on innovation; founded upon the idea of building virus inactivation methods into the production of a FVIII product. Today, virus inactivation is a given, but the fact that it is industry standard now is something of which we can be proud. Despite now being a global company, Octapharma retains its flexibility and pragmatism, allowing us to continue to be innovative and set new standards in safety and quality.



## Jörgen Roslund

Head of Pharmaceutical Production

I have worked in plasma since 1994 when I joined the plant which was later acquired by Octapharma in 2002. We are implementing state-of-the-art equipment as part of the Filling-Lines and Freeze-Dryers (FLFD) project. Aseptic filling has a high process complexity and a low tolerance which makes it a challenge to maintain a good process capability. We are decreasing the risk of contamination by separating the human being from the product using an isolator. After filling we will have automotive transportation to the freeze dryer, automatic loading and unloading and then capping. We are controlling the aseptic environment up until we crimp the vial. The process, from filling to capping, will be fully automated. This not only increases the safety of products but creates better working conditions for employees as well as higher output of the line. It is great to know that the owners want to make investments in state-of-the-art production lines. Mr Marguerre and his sons are on the production floor asking the right questions, they speak to the employees and they want to see where the money goes. It is like in your own home when you buy a new washing machine and you want to see it working.

There is a lot of contact with the family and the board, they listen and they challenge you. The big objective in 2012 was to finalize the filling line and technical documentation. This year, the project moves to the realization and implementation phase.



## Joakim Schöld

SVP Project Manager

By 2014, Stockholm will have a brand new ultra-modern production line for aseptic filling of freeze dried products. Octapharma has invested nearly €30 million to build this new sterile production plant. Launched in 2008, the small volume parenteral (SVP) is the largest investment project in the Stockholm plant's history. This state-of-the-art highly automated installation will significantly improve the working environment, productivity and efficiency. The six identical freeze dryers will allow us to almost double the filling and freeze drying capacity in Stockholm by 2014. Filling takes place in an isolator which is a totally enclosed area where no foreign particles can enter. This new equipment lives up to both regulatory requirements and market demand for flexibility and safer products. The main motivator for this investment was to replace older equipment with a state-of-the-art production line which will reduce risk of contamination of product and facilitate the demands of our new recombinant production. This project is part of a global strategic project implementing new harmonized filling lines and freeze dryers on the four European Octapharma production plants. When I see what we have achieved so far, I feel a real sense of pride.

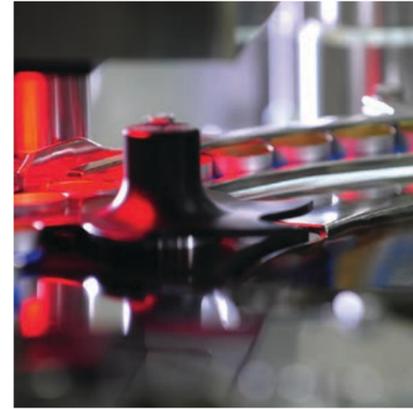


The new SVP filling line: vial washing machine, signal cables, automatic unloading cart for emptying the freeze dryers and 25m unloading corridor for emptying the freeze dryers





Aluminum caps for final closing of vials, commissioning activities, vision camera checks caps, first isolator filling machine now installed in Stockholm



### Roland Löfgren Head of Bulk Production

I joined Kabi in 1976 as a Process Technician. Over the years, I worked my way up to my current role. My responsibilities include base and fine fractionation/ purification and octaplas® production. Before Octapharma there was a lot of uncertainty, we went through a number of owner companies. When the Marguerre family first visited Stockholm, they spoke to us in Swedish. They spoke to us not only in our country's language, but also in our technical language. We knew then that finally we have owners that are really interested in what we are doing: owners focused on fractionation. It was a culture shock at first; we had to change and conform to the same organization and working practices as the other plants. Initially there was competition between the sites, but over time this evolved to positive competition and co-operation. We can all learn from each other because we speak the same language of fractionation.

Octapharma has invested highly here in Stockholm: we built the octagam® line, the new line for octanate®, and now the brand new shiny state-of-the-art octaplas® line. There was a lot of work this year to finalize the FDA license. As a result, along with Vienna, we now have the license to sell octaplas® in the US. What is most important for me personally is to create a good working environment for the 150 people for which I am responsible. What we do here is complex, challenging and interesting work. Even after all these years, I am still learning today.



### Lena Engman Quality Assurance Manager

I joined Kabi's R&D coagulation laboratory in 1972 to perform FVIII assays. In 1977, I became Group Manager for the coagulation lab. Later, I moved into development of all biochemical assay methods as Group Manager. In 1999, I was appointed Regulatory Affairs Manager, which was very interesting work. My proudest achievement has been the development of gammanorm®. There was a market demand for subcutaneous treatment and I came up with the idea for an immunoglobulin from normal plasma and also invented the name. Today, my main task is writing product quality reviews, a requirement for European and US regulations. We write reviews for each product covering how manufacturing has been performed, assays, deviations, in process controls, etc. These reviews are for management and are available for GMP inspections. I am a half time pensioner now but after 40 years working with plasma products, I am still learning every day. Did you know that FVIII activity in plasma differs in summer and winter? We found this in the 1970s when we used "normal" plasma, collected from 30 colleagues, as standard for FVIII assays, before an International Standard was available.



### Stefan Winge Senior Advisor

In 1984, I started to work in the purification development group at the plasma company Kabi and since then I have been working in the R&D area. I was presented with an Invention Award by Octapharma because I invented a technique used in the production of our Human-cl rhFVIII. In 2004, I had the idea to apply a specific extraction technique to increase the yield of FVIII out of a human cell line. I often try to think outside the box, which in some cases gives interesting results. I went to the laboratory to try out the idea and, as it happened, it resulted in an almost 10-fold increase of the process yield. This was a completely new and innovative method; we applied for a patent and introduced the method into production.

I have been playing chess since I was a little boy, to quite a high level. There came a time when I had to make a decision: try to pursue a career in professional chess, or search for more traditional work. The mindset of chess has been very useful in my professional life: thinking strategically, planning, imagining what is coming next and being one step ahead of your opponent.

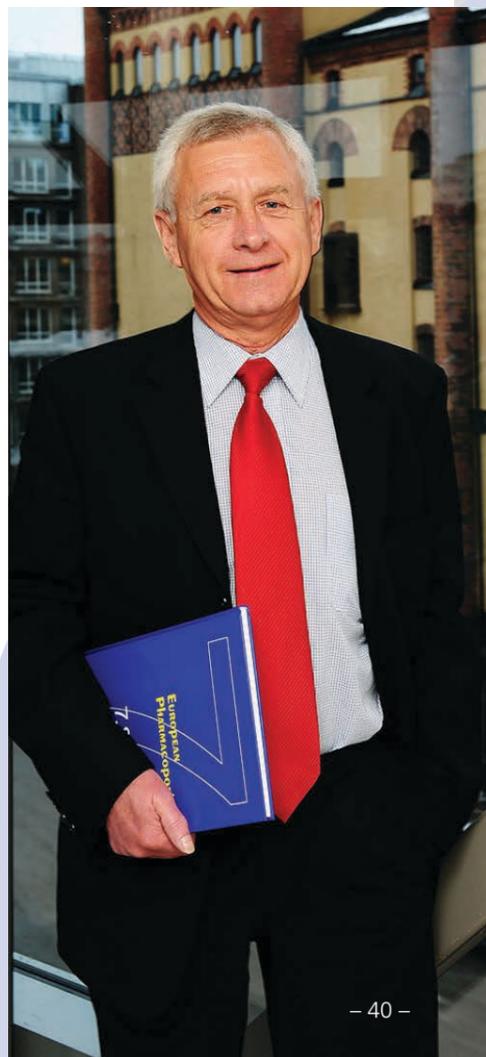
It has been a big milestone for Octapharma to go into the recombinant field, added to that is our special concept of working with the human cell line. As a researcher and process developer it is always a dream to participate in a project from the beginning and to see a product with the capability of helping other people reach the market. It takes approximately 10-15 years for the development of a product, but not all projects in the development phase reach the market for one reason or another. When the first bottle is sold that will be a real milestone for me and for Octapharma.



## Göte Carlebjörk

Head of Quality Assurance Plasma/ Plasma Supply

I researched coagulation disorders at the Karolinska Institute in the 1970s where I was privileged to work with Margareta Blombäck and Inga Marie Nilsson, both well known researchers and worldwide opinion leaders. I joined Kabi in the early 1980s as the global HIV crisis unfolded. I became responsible for all activities related to plasma: negotiation, purchasing, logistics, quality and release. There is a great power in the knowledge that the work we all perform has a direct link to patient lives. Plasma is a very precious material which cannot, like other raw material, be ordered from a shelf. I see plasma as a living being which holds the difference between life and death. Plasmapheresis machines revolutionized the industry in the late 1980s, offering automation and large scale production of plasma for fractionation; I was involved in the evaluation and development of these machines and also became head of one of the first automated plasma centers in Europe. In the late 1990s, we already had Polymerase chain reaction (PCR) for direct virus tests in Stockholm, later I participated in the development of the PCR lab from a local to a global lab serving all of Octapharma. As Head of Plasma Supply, I co-ordinate plasma related activities from donors to plasma released for production, including business development, agreements, plasma supplier auditing, logistics, viral testing and quality control/release. All my years in plasma have been very intense, stimulating and rewarding. The Marguerre family, when acquiring the plant, had an ambitious vision of how they wanted to develop on the experience in Stockholm. These were not just empty words, they really did it. With large investments in procedures, equipment, tech transfers, adding to the existing pool of experience in Stockholm, Octapharma has accomplished something very special here with great perspectives for the future.



## Jan Glindre

Head of Quality Unit

I joined the plant in 1980 as a QC Analyst, later working in R&D as a Laboratory Engineer in method development with a focus on plasma related analyses. I was involved in establishing the PCR laboratory in 1997-1998 and was responsible for the new lab which grew to 34 people processing as much as three million samples annually. The development of the PCR technique made it possible to detect extremely low levels of viruses. We receive individual samples of each donation labeled with a unique identity code. We create mini pools with a possibility to trace back to a positive donation. A personal highlight of my career was when the PCR lab became the corporate minipool testing facility for all Octapharma plants. I was Department Manager until my promotion to Head of Quality Unit in 2011. If you asked someone 10 years ago, they would not have been able to imagine the big investments and dramatic changes Octapharma brought to this site. Strategic investments continued even during tough years. Our work helps people live a life which is not possible without these products. If you keep the patient in mind, you understand that the importance of quality in everything you do is essential.



## Inger Antonsson

Director Medical Marketing

I joined Kabi in 1969 in the position of Medical Writer after which I moved into immunoglobulins and became International Product Manager. I eventually became Group Product Manager for the whole plasma range. I am proud to have been responsible for the projects to introduce S/D treatment in Kabi's IVIG product in 1989 and PCR testing in Stockholm in the mid 1990s. These 10 years with Octapharma have been very interesting. Prior to the acquisition, Pharmacia had a big pharma culture, and then in came this smaller, entrepreneurial, family-owned company. It was challenging at first; the organization had to change, but we recognized the big commitment of Octapharma to develop the site. Wolfgang Marguerre had extensive experience in the plasma industry, and in fact had done business with Kabi in the 1970s and appreciated the competence in the organization. Since Octapharma took over there has been (and still is) a lot of investment to develop the site. The development for Octapharma Nordic has been extremely interesting and we now have colleagues in almost all eastern European and former Soviet states. These countries are developing fast and the market is growing through access to better diagnosis and treatment.

Sweden has always been pioneering in the field of haemophilia. I knew Inga Marie Nilsson well, as well as Margareta Blombäck (still active) who, along with her husband, discovered FVIII when purifying fibrinogen. By the end of the 1950s they could treat haemophilia patients and in the 1960s they turned to Kabi to produce on an industrial scale. The blood crisis in the 1980s was a devastating time that affected patients, relatives, and also the doctors who prescribed the medicine, as well as the industry as a whole. This dark period pushed the industry to develop better and safer products. Octapharma was a pioneer in the early 1980s and has continued to be innovative with a priority on patient safety. The new recombinant area is an important new leg for Octapharma, but plasma will continue to play a strong role.



# Vienna Production Plant



Entrance to administration building 3 and main entrance to administration building 1, Octapharma Vienna, Austria

The Vienna plant was the first Octapharma-owned production site. The premises were acquired in 1989 from the state-owned Heilmittelwerke Austria/Chemie Linz, the first to manufacture a solvent detergent (S/D) treated FVIII preparation and later the first virus-inactivated plasma for transfusion. The size of the premises has nearly doubled to 54,000 m<sup>2</sup>, the original buildings have been upgraded, equipment has been installed with the latest in production and laboratory technology and new buildings have been constructed. The plant's annual fractionation capacity has grown seven-fold since 1989. In the beginning, there were 80 staff, the plant now employs around 740 people. Recent projects include the implementation of a state-of-the-art isolator filling line for small volume parenterals as well as the implementation of an additional robot loaded freeze dryer. Both systems will be in operation during 2013. In addition to these activities, we also have further exciting plans for the future.

## Rita Fabits

### Quality Assurance – Training

I joined the site in 1985 and hope that my work and engagement over the years has had a positive effect, as the proverb says “Steter Tropfen höhlt den Stein”, meaning “constant dripping wears away the stone”. Today, I am responsible for many aspects of the organization’s training program. I joined Schwab & Co in 1985 as Assistant to the Head of Production. When Octapharma acquired the site in 1989 there were 80 of us, everybody knew each other and there was a very personal atmosphere. Through the fast growth of the company, priorities inevitably evolved. This required adjustments to adapt to the new culture of departmental focus and thinking. I moved into the Personnel office working in payroll and labour law. Post-maternity leave, my role changed to assist in the Marketing Department, later becoming Assistant to the individual responsible for the introduction of octagam® in Austria.

In 2002, I joined Quality Assurance to support the preparation of the first FDA inspection and then supported the department in the collection of training data, eventually taking over training responsibilities. A personal highlight was the successful implementation of the Training Database. As a result of changing to this new process there were increased training activities in 2012, it has been a busy year. In 2013, I would like to continue my education in the GMP and training sector.

## Karol Dlugosz

### Shift Leader - Large Volume Parenterals (LVP)

I was hired by Schwab & Co in 1986 as a production worker in Cohn-Basis fractionation. My next position was as management personnel in sterile filtration and bottling. I have had a very interesting career development with Octapharma over the years. My job is supervision, control, and of course working with my team. The department is responsible for sterile filtration and transfer for albumin and octagam®. My responsibilities include preparation of sterile equipment and sterile packaging material. Every action is documented. Product and material movement is managed using our company manufacturing execution system (OctaMES). A shift lasts 12 hours: in this time up to 16,000 bottles of Albumin 50 ml are filled, two to three bulk filtrations are performed and we must complete extensive documentation. We have always worked in a team and developed many projects and improvements.

Octapharma is a very human company, for example if there is a continuous shift operation the Corporate Christmas party for shift workers will be rescheduled. I am sure that 2013 will be a very good year for Octapharma.



New warehouse with ambient temperature storage area, integrity testing of final product vials and setup of SVP filling line 2





**Gerhard Tuma**  
**Head of Aseptic Production -**  
**Small Volume Parenterals (SVP)**

I began my work in the pharmaceutical industry in 1969 and in 1977 had my first experience in plasma processing. In 1980, I moved to the site which Octapharma would later acquire. I began my career at Octapharma in a position responsible for sterile filtration, filling and freeze drying. I am very proud to have been involved in 1985/86 in the planning and establishment of the production plant. New structures had to be established and developed. When you are part of a company from the very beginning strong bonds of loyalty are welded. Together we overcame challenges and have a strong connection with Octapharma. Being family owned has always been an advantage because flexibility and relatively short decision paths make us very efficient, I think this is the biggest difference to other companies. Octapharma is always fair to employees; job security has always been a high priority and this has been maintained even in times of crisis. One highlight in 2012 has been the successful acceptance test for the SVP filling line 4. This was installed as part of the FLFD Project, the first time such a project was implemented at a corporate level bringing together from all four production sites different mentalities, philosophies and technologies. Through this we have created a very good foundation for future projects. In 2013, I look forward to the successful commissioning and acceptance by the authorities of the new filling line. I will also begin the handover of my position to my successor in preparation for my retirement.

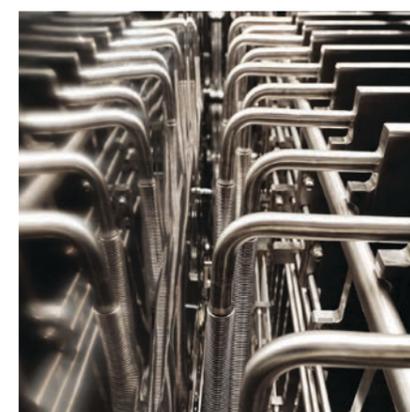


**Alexandra Mader**  
**Technology Transfer**

I am an Assistant in Technology Transfer, doing administration and organizing travel for my colleagues. I started in 1986 in the QC department as administrator for documentation and batch records. I joined the Technology Transfer department in 1999. As the company has grown so have our regulatory requirements, as a result there is more paperwork. In 1986, we could not have imagined that Octapharma would become one of the world's major plasma producers, or that the Vienna site would be expanded so generously and that Octapharma would have additional sites in Europe. A major milestone was FDA approval for octagam®. Over the years, much has changed in terms of regulations across the industry. Although in 1986 the Vienna site was state-of-the-art, you cannot compare the QC protocol of 1986 with today! We have all contributed in our own ways over the years. Now that Octapharma is truly an international company we all think globally and are not focused solely on regional facilities. There is a feeling of togetherness and tolerance. In the beginning, each employee knew each other personally, nowadays, with 5,000 employees this is no longer possible, but nevertheless there remains the shared and indefinable "Octapharma spirit".



Qualification and validation of new SVP filling line 4 and additional freeze dryer 6. Both devices will be in operation in 2013



Octapharma Vienna has a special place in Octapharma history as the first company owned production site. On site we have in total 61 colleagues who have been with Octapharma for 20 years or more. These individuals hold either local or corporate functions. Corporate areas include R&D, Corporate Engineering and Technology Transfer dealing with interesting projects throughout the Octapharma sites. Other long serving individuals work in administration, as technicians or in production as shift leader or department heads. Some are in the Quality unit within QC or dealing with assessment and release of our products, others work in Supply Chain. All of them have contributed in their own way to the development of the organization over the years.

- Sylvia Macourek
- Jana Heckova
- Alexandra Mader
- Rita Fabits
- Susanne Mücke
- Mirsad Durmic
- Gerhard Tuma
- Lutz Hoffer
- Thomas Weiss
- Monika Stadler
- Werner Gehringer
- Richard Rebec
- Raimund Schütz
- Barbara Mika
- Alexander Groschl
- Walter Budin
- Shyam Sunder Chadha
- Ronald Fröschl
- Andreas Schotzko
- Hans Sachse
- Claudia Fritzen
- Robert Kastenhofer
- Elisabeth Tomaz
- Richard Buchberger
- Mihayil Ocak



- Rene Akimesko
- Karol Dlugosz
- Prabh Singh
- Rhoda Cortes
- Walter Meister
- Janja Brainovic
- Christian Korger



Operations in visual inspection and packaging department



Haemophilia A is a congenital X-linked disorder which affects around 1 in 5,000 people. In the 1950s patients were treated with whole blood or fresh frozen plasma, often leading to haemolysis or insufficient factor replacement with the risk of serious internal bleeding. Common causes of death among people with haemophilia were bleeding in the brain or after minor surgery or injury. Cryoprecipitate was discovered by Dr Judith Pool in 1965. It was found that the precipitated protein content at the bottom of plasma after thawing was rich in Factor VIII (FVIII) and von Willebrand Factor (VWF). Infusion to treat haemophilia A and von Willebrand Disease patients was a lengthy procedure. Industrialization meant that in the 1970s Factor concentrates became available. These freeze dried powdered concentrates opened the possibility of at home treatment. In 1958, Sweden began prophylactic treatment in boys with severe haemophilia under the hypothesis that early prophylactic treatment was the best route to allow patients to lead normal lives and to avoid arthropathy. It is now accepted that the preventative approach is best, and furthermore, to prevent haemophilic arthropathy, continuous prophylaxis should be given from an early age.

Prophylactic replacement therapy has revolutionized the lives of people living with haemophilia A, however the development of inhibitors is the most serious complication. Antibody eradication is the ultimate goal of inhibitor management. Immune Tolerance Induction (ITI) is the only clinically proven strategy for inhibitor eradication.

## Key milestones in 2012

### octanate®

- Human plasma derived FVIII naturally stabilized with VWF.
- Used for the treatment of haemophilia A (HA).
- Proven efficacy based on more than 14 years of clinical experience and over five billion IUs infused.
- Since 2006, 145 patients worldwide have received ITI therapy using octanate®.
- Octapharma is due to publish a study in a largely poor-prognosis cohort of 48 patients who completed ITI, this will provide the largest prospective data for a single product.
- Incidence of clinically relevant inhibitors in PUPs is only 5.1%.
- Geographic market: Global (approved in 81 countries).

### Human-cl rhFVIII

Octapharma's human cell line recombinant Factor VIII (Human-cl rhFVIII) has been developed with the aim of reducing the most serious clinical risk for HA patients: the development of FVIII inhibitors:

- First truly human rhFVIII
  - produced in a human host cell line.
  - devoid of antigenic animal epitopes\*, which can be found in rhFVIII produced in hamster cell lines.
- Completed four clinical trials in >130 adult and pediatric patients with excellent clinical results demonstrating not a single case of inhibitory antibody development. All studies are on track for submission to authorities.



- No case of product-related serious adverse events and no allergic reactions.
- Clinical study in previously untreated patients (PUPs); the first patient enrolled at the end of 2012.
- The registration dossiers are planned to be submitted to supervisory authorities (EMA and FDA) during the course of 2013.

\*sialic acids of N-glycolylneuraminic acid type and antigenic Gala1,3Gal carbohydrate

### wilate®

Von Willebrands Disease (VWD) is the most common inherited hemorrhagic disorder affecting both males and females. It is caused by a deficiency or dysfunction of von Willebrand factor (VWF). Defects in VWF can cause bleeding by impairing platelet adhesion or by reducing concentration of FVIII. Diagnoses can occur from infancy to adulthood. There is a great variability in the severity of bleeding problems: type 2, type 2N patients can have spontaneous joint bleeds (hemarthrosis). VWD remains under diagnosed and under treated; Octapharma organizes educational courses with physicians to improve diagnoses and discuss treatment. Diagnoses can occur after excessive bleeding after surgery, dental work or trauma.

- wilate® was developed as the first next generation VWF product to set a new standard in VWD treatment. The global introduction of wilate® 500/1000 started in EU markets and is currently available globally.
- Ongoing trials: WIL-24 wilate® use during surgical procedures is currently recruiting; WIL-20 post marketing surveillance program to extend the general experience with wilate® in VWD treatment
- Geographic market: Global (approved in 52 countries).

### octanine®F

- octanine®F is a leading plasma derived factor IX product for the treatment of haemophilia B.
- octanine®F provides an excellent track record with no known cases of rare inhibitor formation or thrombosis after 14 years.
- Improvement of therapy for haemophilia B patients i.e. higher relevance of prophylactic treatment, is a key driver for further growth of the product.
- Geographic market: Global (approved in 58 countries).

## Interview with Mark Skinner

Mark Skinner, President of the World Federation of Hemophilia (WFH) from 2004-2012, is a Washington-based Attorney with an extensive background in public policy. He was chair of the NHF Advocacy Committee responsible for successfully championing funding for compensation of people with haemophilia who were infected with HIV by blood products in the US



### What was your experience of growing up with haemophilia?

I was born in 1960 and diagnosed with severe haemophilia A at birth. My older brother had been diagnosed when he was two so they knew to test me as a newborn. We grew up in a small town in rural Kansas. Apart from my brother, I didn't meet anyone with haemophilia until I was a teenager.

When I was born, the prognosis was not good. My parents were told there was a strong likelihood we could die young or would grow up severely disabled. As children we were never told this. However, around the age of 6, I was fitted for a leg brace due to significant joint damage. I was then told that I would likely never walk again without assistance or would need a wheelchair.

It felt isolating at times. I remember sitting on the swings watching my classmates jumping on the trampoline, or playing baseball and soccer. But looking back, I can say I had a relatively normal childhood, largely due to the support of my family and friends, especially my mother who was a very strong, practical and matter-of-fact person.

### Can you tell me about your treatment growing up?

The nearest treatment center, the University of Kansas Medical Center, was four hours away. Cryoprecipitate was discovered in 1965 and our local physician learnt to make cryo for us. The first clotting factor concentrates came in the 1970s, although not highly purified they certainly were the next step up from cryo. They started producing lyophilized products, which we kept locally, but we were still reliant on replacement donations.

Had it not been for my parents, it would have been easy to fall behind in school due to the time spent in bed or hospital. The importance of education was highly stressed. As children we were taught the importance of our minds over our bodies. Don't plan a physical career, we were told. I had three uncles who were lawyers. They were great role models. I always had an interest in government and public policy. By the 1980s I was in law school and working for the state legislature.

### Can you tell me about your experience of the HIV/AIDS crisis?

When factor concentrates were introduced commercially there was a golden era when quality of life improved and a more normal life seemed possible. Then in the early 1980s it became obvious that there was a problem with the blood supply. As we were the canary in the mine shaft, it showed up first in the haemophilia community. Developed countries were hit the hardest because of the wide use of factor concentrates. I was one of the 10,000 people with haemophilia in the US who contracted HIV. I was told not to disclose my HIV status. I told my parents, but no one else; I didn't tell my friends not even my brother. There was a huge stigma and fear. There was a lot of discrimination at this time. The famous example is Ricky Ray and his brothers who were kicked out of school; out of fear hundreds of parents had petitioned against them being allowed to attend. Their house was burnt down and they were forced to leave town. Ricky Ray died in 1992, but his story came to represent the injustices of that time and in 1998 Congress passed the Hemophilia Relief Fund Act, making a compassionate payment to those who contracted HIV from tainted blood supplies.

### How did this crisis change treatment?

I am a perpetual optimist. What happened to the Haemophilia community in the 1980s and early 1990s was tragic, but what was also remarkable is the strength of the national network built upon this tragedy; the collation and advocacy in communication it inspired. It propelled forward the need for research for safer products. So many diseases do not have the excitement that still goes on today, for a rare disease group there is so much going on in research and development.

### How has treatment changed in your lifetime and what is treatment like today?

Treatment has evolved considerably in my lifetime. Firstly, the discovery of Cryoprecipitate in 1965 by Judith Pool, and then in the 1970s the arrival of the first commercially available FVIII. After the terrible events of the 1980s, the introduction of virus inactivation and new technologies was an enormous step forward in treatment. Plasma products today are remarkably safe and remain an important treatment option.

However, treatment is expensive and thus access remains a significant global challenge. In the US health insurance coverage has been a significant problem. Pre-existing conditions such as haemophilia have been very difficult to cover and until recently many policies had lifetime limits on coverage.

The WFH has achieved significant progress toward achieving its vision of "Treatment for All" people living with bleeding disorders, regardless of where they live. The WFH is working to close the gap between the estimated and the actual number of people living with bleeding disorders, the gap between the amount of products needed and those available, and the gap between those born with haemophilia and those who reach adulthood.

#### What do you hope to see in the future of treatment?

While access to prophylaxis is life changing, it presents health economic challenges. Every patient dreams of, if not a genetic cure, then a therapeutic cure. Until then, what is important today is optimizing and personalizing care. Today, the risk of inhibitor development is the most significant adverse event, far eclipsing the risk of viral infection. We need to continue the efforts to reduce and eliminate this risk.

#### Octapharma

In the mid 1980s Octapharma introduced an innovative heat treated and S/D product, entering this space at an incredibly challenging time. This has defined their presence and character. I have been impressed from the very beginning of the culture and the philosophy of Octapharma. There is something special about being family owned: the ownership and leadership are personally invested in the company and what it represents. There is a human face to this global corporation. I imagine that Wolfgang Marguerre feels that Octapharma reflects on him personally, and it seems that it is with this mentality that he approaches business. I have really enjoyed getting to know the company and the senior leadership over these 14 years. Octapharma is an important part of a big global family.

#### What do you think about Octapharma's move into recombinant technologies?

I am really intrigued by Octapharma developing a recombinant treatment from a human cell line. I think they will have a niche. It is innovative and it will be really interesting to see how it compares, in particular how it works in terms of inhibitors. Conceptually it is very attractive. I think Octapharma has a balanced approach, although developed markets tend to shift to recombinant, plasma therapies remain incredibly important.



#### Martina Jansen

##### Senior Clinical Project Manager

Together with Wolfgang Frenzel we "founded" Octapharma's Clinical Research & Development Department (CR&D) in Vienna in 1996. The early days at Octapharma were without any technical equipment, just paper and pencils. We designed and implemented clinical research systems and SOPs from scratch. The CR&D department has grown from four to almost 30 people today. We run clinical studies with clinicians from all over the world conforming to international guidelines and regulatory requirements. For over twelve years my main clinical research area is haemophilia, a rare disease affecting around 1 in 5,000 people. We have known the doctors participating in our studies for many years, and often the personal stories of our patients.

In a company like ours you get the chance to follow the product from research to the market. It is rewarding when the first sold vials reach patients. Our priority is always the patients' safety and welfare! Each of our marketed products today started clinical success with our studies: octanate®, octanine® and wilate®.

For almost eight years we support ObsITI, a study in patients with inhibitors to FVIII. With octanate® we were able to show high efficacy rates and have cured many patients.

The next important milestone will come soon – the Human-cl rhFVIII. This represents a new chapter in Octapharma's corporate history. My high priority project today is a study in previously untreated patients with severe haemophilia A. This study will hopefully confirm that we have developed a less immunogenic and safer product for the worldwide market. Everybody is looking forward to see the first results.

## Bärbel Helmich

### Product Management Haemophilia

I joined Octapharma in 1991. I am responsible for the haemophilia portfolio in Germany – namely wilate®, octanate® and octanine®F. The haemophilia community's history has created a special importance on confidence and trustworthiness. Patients and physicians trust in Octapharma and that is the achievement of continuous partnership over many years. As coagulation disorders are mostly inherited, patients normally need lifelong treatment. Therefore trust, not only in the product but also in the company, is of utmost importance. In the mid 1990s there were various companies offering coagulation products. After a phase of mergers and acquisitions many of those disappeared. Octapharma is still Octapharma.

It is very special for a company of this size to be owned by one family visible in day-to-day activities. As the company has grown we have become more centralized and more structured. I have witnessed and participated in this evolution, which has been very exciting.

One of my proudest achievements has been my role as Product Manager for the successful introduction of wilate® in a market environment historically dominated by one product. In addition, even in developed countries like Germany, von Willebrand Disease is still under diagnosed with patients often suffering a long history of bleeding complications before eventually being diagnosed in their 30s. Therefore, we also allocate substantial resources to support improvements in diagnosis and training projects for physicians, especially gynecologists and pediatricians, in order to raise awareness of the disease.



Octapharma's Human-cl rhFVIII signals a new era for Octapharma. I saw how this product was developed and it is fantastic to see the very promising first clinical results. Our move into recombinant proteins should not be seen as a replacement for plasma but as the optimal completion of our product range. For some haemophilia A patients octanate® will remain the product of choice, for others it will be the new Human-cl rhFVIII. That is what is so exciting: we will be in the position where we can offer tailored solutions to our patients.

## Dr Anna Klukowska

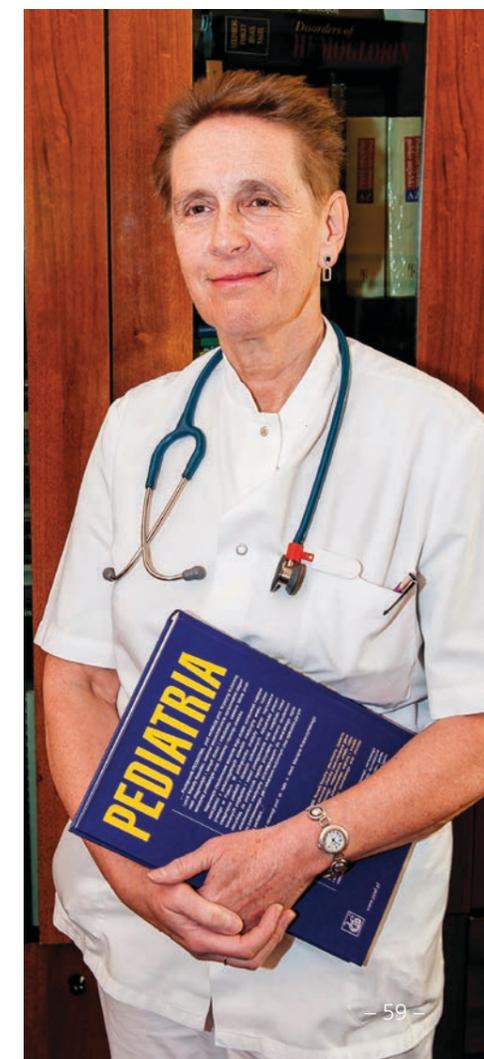
### Medical University of Warsaw Department of Pediatrics, Hematology and Oncology

I have worked in the pediatric department focused on haematology since 1980. When I started, our haemophilia B patients were treated with fresh frozen plasma and haemophilia A patients with "cryo". There was no other treatment available in Poland. Some FVIII was introduced in 1990, but not enough so many patients were still treated with cryo. Patients were treated on demand; if they had a bleed they infused factors, but repeated bleeding impaired joint function. Prophylaxis is the treatment of choice for all children with severe haemophilia; in Sweden it was tradition for 50 years, but of course it is expensive.

In 2008, Poland introduced prophylaxis in all children with severe haemophilia. Young patients treated from age 2–3 have experienced no joint bleeding so have very healthy joints and can go to school and do physical activities. Even 10 years ago we had a lot of patients who had to stay in hospital for weeks, with every bleed treated in hospital. After the introduction of prophylaxis all that changed, for example during the last several weeks we have had no hospitalized patient. As doctors this gives us great satisfaction. However, the development of inhibitors is a severe complication of haemophilia A. In the beginning, we could offer nothing for treatment; immune tolerance induction (ITI) was not a possibility. Patients who developed inhibitors spent a lot of time in hospital in our department.

In 1999, we began studies with octanate® to assess the immunogenicity of the product in previously untreated patients (PUPs) with severe haemophilia A. The rate of clinically relevant (symptomatic) inhibitors was only 5.1%. In light of our good experience with the product, the overall low immunogenic profile and the very good data on octanate® in ITI in patients with poor prognosis from other countries, we initiated ITI using octanate®, as well as other FVIII concentrates, for patients with inhibitors. This was a big step forward for our patients and we have extremely good results. My patients are very satisfied with ITI; most of them can stay at home instead of being in hospital. They can share and enjoy a normal childhood with their friends, they can attend school and they can go on holiday with their parents, taking the concentrates with them.

We work very closely with Octapharma, with the HQ, the presence in Poland and the clinical department; other studies in co-operation with Octapharma include the recombinant FVIII concentrate as well as clinical studies with wilate®. Octapharma also organizes educational meetings for doctors and patients.



## Interview with Prof. Erik Berntorp

Professor at Malmö Centre for Thrombosis  
and Haemostasis, Lund University in Sweden



### Can you reflect on the prognosis for someone with haemophilia when you first started in medicine?

When I studied medicine in the late 1960s, I remember an old textbook on haematology which had a brief chapter on haemophilia with a picture of a severely disabled child; it said "Haemophilia is a life threatening disease".

### How has the outlook changed?

The outlook has changed dramatically since that time, and Sweden has been a pioneer. Convinced early that starting prophylaxis treatment at a young age was the best way to treat patients, Sweden was the first country to introduce lifelong treatment which started in a small scale in the 1950s and then on a large scale in the 1970s. Prophylaxis changed patient's lives dramatically. When I joined the coagulation department of the Malmö Centre in 1985, I worked with Inga Marie Nilsson until she retired in 1990. We published a large study on prophylaxis in 1992 and I did a lot of work with her on inhibitors. After she retired I took over her role as head of department and conducted local studies with prophylaxis and inhibitors. Today in Sweden life for a person with haemophilia is very similar to the normal population with life expectancy at 75 compared to only 30 in the 1950s. People can now attend school, work, do athletics and do not need major orthopedic surgery.

### How did the HIV/Hepatitis crisis affect the haemophilia community?

In the mid-eighties, I conducted primary studies in HIV's epidemiological aspects. At that time it was very shocking and new. It is important to remember that haemophilia involves lifelong treatment; doctors get to know their patients very well over many years. It was very hard for the physicians who had prescribed these products. Many people died, including young children, it was a very dramatic situation. HIV/AIDS not only impacted the health of the patient, but a psychological burden was placed on them with newspapers and television full of incorrect and dramatic descriptions of HIV. Patients felt like they had the plague and were afraid to disclose that they had HIV. It is not easy for young people today to really understand what that time was like.

### How did the HIV/ Hepatitis crisis change the plasma industry?

This period dramatically changed everything and catalyzed the development of safer products of improved purity. It improved testing and selection of plasma and led to the development of recombinant products. The introduction of viral testing and viral inactivation steps in manufacturing were incredible steps forward.

### What are the challenges facing the haemophilia community today?

Despite the advances made in treatment, there remains a serious risk for patients on prophylaxis: the development of inhibitors which neutralize the infused FVIII, meaning the patient can develop joint disease and essentially be reverted back in time to a life with haemophilia 60 years ago. Octapharma strongly supports the international Observational Immune Tolerance Induction (ObsITI) study which evaluates the success rate of ITI in haemophilia A patients with newly developed or already existing FVIII-inhibitors.

### What has been your experience of Octapharma over the years?

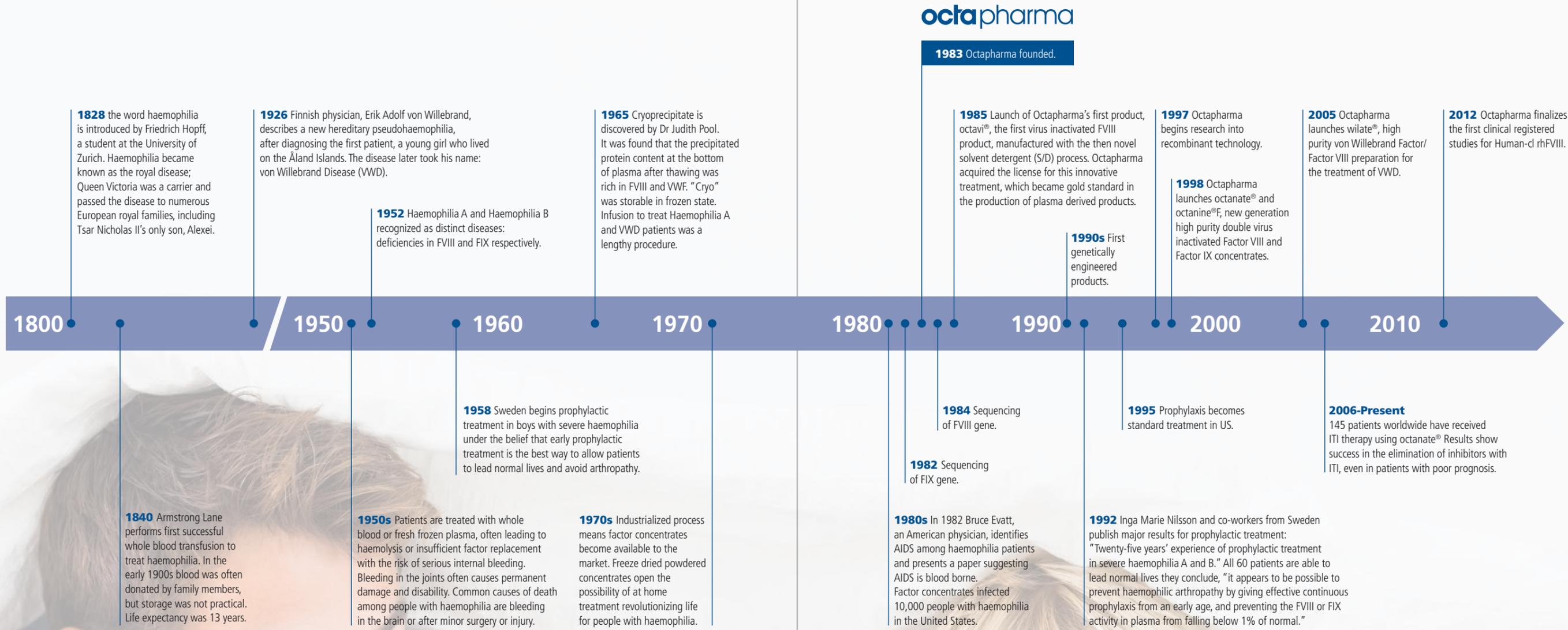
I have met Wolfgang Marguerre several times. Octapharma differs from other pharma companies. It is open to new ideas, it may be smaller than others, but Octapharma focuses on development of innovative new products and has a short track between idea and action.

The contribution of Octapharma in von Willebrand disease has been tremendous, not only for the development of a concentrate but in educational programs. Von Willebrand disease is underdiagnosed and undertreated. Octapharma is the sole sponsor of the Åland Island Meetings where physicians meet to discuss basic and clinical aspects of von Willebrand disease. We publish a supplement after these meetings in the Journal of Hemophilia. The fact that these meetings are held on the Åland Archipelago, halfway between Finland and Sweden in the Baltic Sea, is historically significant because it was here in 1924 where Erik von Willebrand diagnosed the first patient.

Another fascinating development with Octapharma is the recombinant FVIII, in which I have been involved since the early stages. Because the recombinant FVIII is from the human cell line, it could mean that it has lower inhibitor risk than other recombinant products. It is a new concept.

**“ For it was taught: If she circumcised her first child and he died,  
and a second one who also died, she must not circumcise her third child”**

4th century, Babylonian Talmud: Tractate Yebamoth



octapharma

1983 Octapharma founded.

# Immunotherapy

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ANNIVERSARY



In 2012, we celebrate 60 years since the first patient with an inherited immunoglobulin deficiency was described by Col. Dr Ogden C. Bruton at the Walter Reed Hospital in Washington DC. The eight year old boy had a medical history comprising 19 episodes of clinical sepsis over a five year period and was treated experimentally with an immunoglobulin concentrate subcutaneously. With monthly infusions for more than a year, new sepsis attacks were completely prevented. Dr Bruton published his case in the journal 'Pediatrics' (1952) and this is regarded as the birth of immunotherapy with plasma-derived immunoglobulins. Thirty years later, Octapharma was founded. The use of plasma-derived immunoglobulins for the treatment of patients suffering from inherited (or acquired) immunodeficiencies was fairly small; the worldwide consumption in 1984 was only 7.5 tons of immunoglobulins for intravenous (IVIG) and subcutaneous (SCIG) products combined. The immunoglobulin concentrates used at that time were not virus inactivated and the number of side-effects following the use of these freeze-dried products was high. In addition, there were few indications for which IVIG or SCIG were used.

### octagam®

Octapharma's first IVIG, octagam®, was launched in 1994. This was the world's first double virus inactivated liquid ready-to-use IVIG. During the 18 years up to 2012 the total immunoglobulin world market grew more than four-fold to approx. 120 tons. Polyvalent IVIGs and SCIGs cannot be genetically engineered (i.e. no recombinant products exist); they are fully dependent on human blood plasma as raw material. Thus, plasma supply, production capacity and high immunoglobulin yields per litre plasma are key drivers for the plasma fractionation industry. The enormous growth in the market has led to increased prices and today 40-50% of the total turnover per litre plasma comes from immunoglobulins. Should the growth continue uninterrupted over the next five years, the total world market for immunoglobulins may reach as much as 160 tons by 2017. As the world's fourth biggest immunoglobulin supplier, Octapharma's future task will be to contribute to this growth.

Our IVIG octagam® has been a very important product for Octapharma's development during the last 18 years and its strong clinical record demonstrates very good tolerability on top of the impeccable efficacy. Gammanorm® is an excellent counterpart in terms of clinical performance for subcutaneous administration at home, which allows more freedom in lifelong therapy.

Octagam® (5% and 10%) resumed commercialization in all major markets in 2011. The return of octagam® was highly appreciated by both physicians and patients and the monthly sales during autumn 2012, both volume and monetary wise, reached and passed the levels from before the marketing authorisation suspension in late 2010. Our main plasma-derived product, in terms of turnover, is back and stronger than ever, which will contribute to further investments into our future generation of immunoglobulins.

### gammanorm® and rhesonativ®

Over the last two years we have also seen good growth for the other two products in the immunotherapy family: gammanorm® 16.5% (SCIG) and the hyperimmune anti-D immunoglobulin (rhesonativ®), used for the prevention of haemolytic disease in newborns. Gammanorm® and rhesonativ® have been a part of Octapharma's immunotherapy product portfolio since the acquisition of our plant in Stockholm from Biovitrum back in 2002. Over the last years the



growth per year of these products was 21% and 11%, respectively. By the end of 2012 we are at a level of more than 800,000 standard treatment doses annually from the immunotherapy portfolio.

To keep up with the rapid increase in the use of immunoglobulins and our commitment to supply immunotherapy to patients around the world, Octapharma has developed two new immunoglobulin preparations, one IVIG and an SCIG. The goal of this major product development is to gain 25-30% more immunoglobulins out of every litre of plasma, but at the same time replicate the very convincing clinical record demonstrated by both octagam® and gammanorm®. Together with the ramp-up in plasma throughput of 50% planned for the next five years, our immunoglobulin supply to the world market will double. The IVIG version of gammanorm® is about to complete the clinical trials needed for marketing authorization and the launch is expected early 2015 in both the US and Europe. In addition to these activities, we are pursuing new indications for example through the support of a pre-Alzheimer study in the US.

## Interview with Dr Leena Kainulainen

Turku University Hospital, Finland

Research Unit, Department of Pediatrics



### Overview of background and research activities

In my out-patient clinic I have 70 patients (pediatric and adult) with Primary Immunodeficiency (PID). My research activities are mainly focused on PID: pulmonary changes and respiratory infections.

### How has treatment developed over the years?

I collected data of Finnish patients with PID as part of my doctoral thesis on Common Variable Immunodeficiency (CVID) in 1996. Most were receiving intravenous immunoglobulin (IVIg), some intramuscular immunoglobulin (IMiG), and some were without any replacement therapy. The serum IgG concentration was below 5 g/l in most of the patients at that time. Fortunately, the treatment has improved during recent years.

### You were involved in the first subcutaneous treatment in Finland with gammanorm®. Can you tell us about that?

The patient was diagnosed with CVID in 1981, but she refused to have replacement therapy with IVIg. She was first on IMiG, a Finnish Red Cross immunoglobulin product, which was given every two weeks. I have to give credit to the patient, she was very active. She had heard that in Sweden it was possible to get immunoglobulin subcutaneously. She initially obtained a Finnish Red Cross immunoglobulin subcutaneously, but the preparation of this product was discontinued. Gammanorm® was not at that time used in Finland and it needed some effort to persuade the officials to allow her to get the product in 2002. She has been on gammanorm® ever since.

### What is your experience of gammanorm®?

Gammanorm® gives patients more freedom; there is no absenteeism from work or school due to replacement therapy. The patients do not usually get any adverse reactions related to the subcutaneous treatment. I give patients with primary hypogammaglobulinemia freedom to choose between SCiG and IVIg. Most of my patients on immunoglobulin replacement therapy are patients with PID. Most of the youngsters choose subcutaneous, overall these patients are pleased with the treatment. They usually take care of the infusions themselves, or in some instances parents do the infusions.

### What has been your experience of Octapharma?

Octapharma is an active and reliable company that has been very active in arranging important educational courses in Finland, and in this way has contributed to increasing the awareness of PID.

## João Coelho

Unit Business Manager, Octapharma Portugal

There were four of us when I joined as the sole sales representative in 1994. As the team grew I became Sales Manager, then Product Manager and Marketing Manager. I now manage the Immunology Unit developing strategies for octagam®, gammanorm®, rhesonativ® and albumin in Portugal, working mainly with the sales force, key opinion leaders, patient associations and physicians.

Over these 20 years Octapharma has evolved from a European company to a truly global organization. Growth brings new ideas and new approaches. There is still a high level of responsibility to take decisions on a local level: bigger companies usually lose that flexibility. Octapharma still recognizes the



importance of the individual having freedom to share ideas and challenge the status quo. People are important. Everybody feels like part of the company.

One of the key steps in the history of the plasma industry was the introduction of virus inactivation/removal methods. Octapharma introduced the double virus inactivation/removal concept in the majority of products and this will always be linked to the Octapharma name. Quality and safety have always been our key priorities. These core values were demonstrated in our most challenging period: octagam® suspension and re-launch. The response to the situation and the extraordinary comeback of octagam® is a powerful example of what makes Octapharma special. The swift decision was made to voluntarily suspend the product and to solve the issue. As I am responsible for the product in Portugal, I worked closely with customers taking them with us step by step. We approached the situation honestly with transparency which I think fortified the confidence our customers have in Octapharma. 2012 has taught me how much our customers respect and trust us.

# Intensive Care & Emergency Medicine

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ANNIVERSARY



Intensive Care & Emergency Medicine (ICEM) is a medical speciality, in which physicians care for patients with acute illnesses or injuries that require immediate medical attention. The medical conditions treated in both emergency rooms and intensive care units require a range of remedies, including targeting instabilities in vital blood coagulation, clotting inhibition and fluid balance. In addition, therapeutic plasma exchanges are commonly used as interventions in patients with complex disorders of blood coagulation as well as acute neurological diseases and intoxications.

Octapharma has been one of the major suppliers of lifesaving plasma-derived pharmaceutical products to emergency rooms and intensive care units worldwide for many years. Due to the medical urgency and the strong desire to reduce the number of variables for these patients, a well defined product profile, a fast onset of action and excellent tolerability are mandatory features of these biopharmaceuticals: all of our ICEM products are compliant with these requirements. As many as 3.5 million standard treatment dosages of Octapharma's four ICEM products are used worldwide each year.

**octaplas®**

In 1989, following extensive research and development, solvent detergent (S/D) technology was successfully applied to virus inactivation of transfusion plasma, later licensed as octaplas®. Octaplas® is the only pathogen safeguarded plasma of pharmaceutical quality available in the world and since this product comprises all fully active plasma proteins, it is used for many different clinical settings.

For over 20 years, there have been more than 8 million units of octaplas® transfused internationally, in more than 2.6 million patients. Octaplas® is indicated for life-threatening oedemas, complex coagulation disturbances, the management of preoperative or bleeding patients who require replacement of multiple plasma coagulation factors, patients with coagulation deficiencies due to hepatic disease and patients undergoing cardiac surgery or liver transplantation. At the beginning of 2013 the FDA approved octaplas® including the indication for transfusion or plasma exchange in patients with congenital or acquired thrombotic thrombocytopenic purpura (TTP), a rare blood disorder with an incidence of 3.8 per million.

In terms of life-cycle management, the conversion to octaplasLG® (specific prion removal step included) will continue and we are thrilled to finally launch this product in the US. We also expect a lyophilised version of octaplasLG® to be launched in 2013.

**octaplex®**

The prothrombin complex concentrate octaplex® is used for the treatment of complex coagulation disturbances and for rapid reversal of anticoagulation treatment. Octaplex® has had a fantastic average annual growth rate of more than 130% over the last 15 years.

A new generation octaplex® will soon emerge based on a new and even more efficient virus filter for a further improved pathogen safety profile, as well as with a new and larger filling size for better logistics and faster administration. As well as entering the new and exciting US market towards the end of 2013, we intend to pursue some interesting emerging markets and unexplored opportunities for octaplex®. Today, therapeutic plasma is used for some indications for which octaplex® is a better medical alternative but not yet implemented. The increase in elderly patients with heart diseases and an intensified focus on the detailed treatment of trauma patients and liver disease will influence future prothrombin complex concentrate use.

**atenativ®**

Atenativ®, our antithrombin product, is used for the inhibition of over-coagulation. Atenativ® was one of the products which joined the portfolio following the acquisition of our Stockholm plant in 2002. New indications in transplantation surgery could mean a revival for this product.

**Albumin**

Albumin is mainly used for fluid disturbances and exchange liquid for therapeutic plasma exchanges when normal coagulation is not an issue. Albumin was one of the first plasma-derivatives Octapharma launched in the 1980s, as one of the three main products harvested from every litre of plasma. The fast growing world population and the challenges in developing medical equivalents to albumin will increase the need for this product in the years to come.



The ICEM scientific area is huge and the stakeholders are many. We organize activities, both at local and international levels, to educate physicians and nurses about the developments in this area of medicine and the opportunities provided to them by our products. The continued contact with our customers helps us to understand their needs better and, based on this, to improve and expand our ICEM product portfolio.

All our ICEM products are licensed in most of the relevant markets of the world. Global plasma consumption has increased over recent years. New protocols for treating trauma patients have shown emergency room doctors how valuable these products are in bleeding control and lifesaving therapy of severely injured patients.

In terms of product life-cycle management, our newly developed double virus safe-guarded fibrinogen product is about to enter the clinical development phase and we expect this product to enter the markets in Europe and the US during the next five years. In addition, we have planned for more phase IV studies to extend the indications of some of our existing products and more ICEM products are in the pipeline for the years beyond 2017. It is expected that our ICEM portfolio will grow substantially during the next decade.



**Łukasz J. Krzych**

**Associate Professor in Anesthesiology and Intensive Care  
1st Dept. of Cardiac Surgery, University Hospital, Katowice, Poland**

Perioperative care of cardiac surgical patients is one of the most challenging issues in modern intensive therapy. In the era of a growing number of patients who require heart valve surgery and therefore anticoagulant treatment, the problem is gaining particular importance. It is not only the valve implantation itself but also the risk associated with atrial fibrillation that makes an absolute indication for this treatment.

The introduction of prothrombin complex concentrate (PCC) into everyday practice has considerably improved and facilitated the process of therapy. The benefit for the patient is earlier surgical intervention; for the healthcare professional team, earlier treatment outcomes; for the health care system, shorter hospital stay and lower risk of nosocomial infection. It can be concluded that in this respect PCC has dramatically changed our approach to the possible reversal of the effect of oral

anticoagulation. It must be kept in mind that one of the most important problems encountered in everyday practice is the need for rapid therapeutic measures that must be taken to control postoperative bleeding.

Recently a few interesting papers have been published that report on the efficacy of point-of-care coagulation tests in guiding therapy. In my opinion PCC is becoming an inherent part of this branch of cardiac surgery, effects of which I can see also at the center where I work.

# The Human Factor



From human to human:

Octapharma is a human company in many ways. We are a family owned organization developing lifesaving products from human proteins, traditionally from plasma and now also from the human cell line. All our activities are made possible by our most valuable resource: our people.

Within the pages of this report we are offering insights into the work and careers of some of our valued colleagues across the breadth of the business. These individuals have demonstrated loyalty and commitment to Octapharma over decades, they are just some examples of the people throughout Octapharma who have applied their skills and talent to the company's impressive development. Their combined contribution we are calling "the human factor".

As a result of Octapharma's tremendous growth over these 30 years, and the future aspirations of the organization, it was decided that the time was right to establish a global human resources organization to support, strengthen and build on the talent already present in Octapharma and to nurture a healthy organization with proud and talented employees.

## Interview with Beverley Cox

Vice President, Global Human Resources



I recently joined our global headquarters in Switzerland as Vice President, Global Human Resources. In my previous role I was Senior Director, Human Resources of Octapharma Plasma Inc. (OPI) based in North Carolina. I joined in 2009 and developed a strong HR team establishing practices to support OPI's growth strategy including implementing a companywide Human Resource Information System.

I am thrilled to take on this global role and to have the opportunity to build a world class human resources organization in Octapharma. My goal is to support Octapharma's business strategies by developing HR practices and systems that drive organizational performance, attract and retain the best candidates and provide learning and career development opportunities for our employees.

### **Octapharma has grown rapidly in a relatively short period and now employs 5,000 people. What is your approach to such growth?**

Our company is growing fast and is poised to double its sales over the next five years. Much of our growth in the past has been through acquisition which brings with it challenges of harmonization and synergy. My goal is to set the global HR strategy but also ensure flexibility on a local level, giving power to local plant managers and HR to do what needs to be done locally to support the global position.

### **Octalent: how does Octapharma attract the best talent?**

Octapharma develop and produce medicines that make a real difference to people's lives. Many people today want to work for a company that is making a difference in the world, so our mission is quite compelling to prospective employees. I also think we have a reputation for providing opportunities for employees to learn and develop in an innovative and challenging environment and that is also important to candidates.

### **Octapharma has many employees who have been with the company for decades, why do you think that is?**

People are loyal to organizations that show loyalty to them. Octapharma is a privately owned company; the emphasis of the family has always been on people. Their commitment and connection to the business is something employees feel and share. Octapharma invest in career development, training and education. When people feel they are learning and growing they want to stay. Our function is not simply to attract the best qualified and brightest candidates, but to also provide a stimulating and challenging environment in which they can pursue a long term career. Octapharma also has a strong track record of promoting within which is a fantastic motivator; I am a product of that myself.

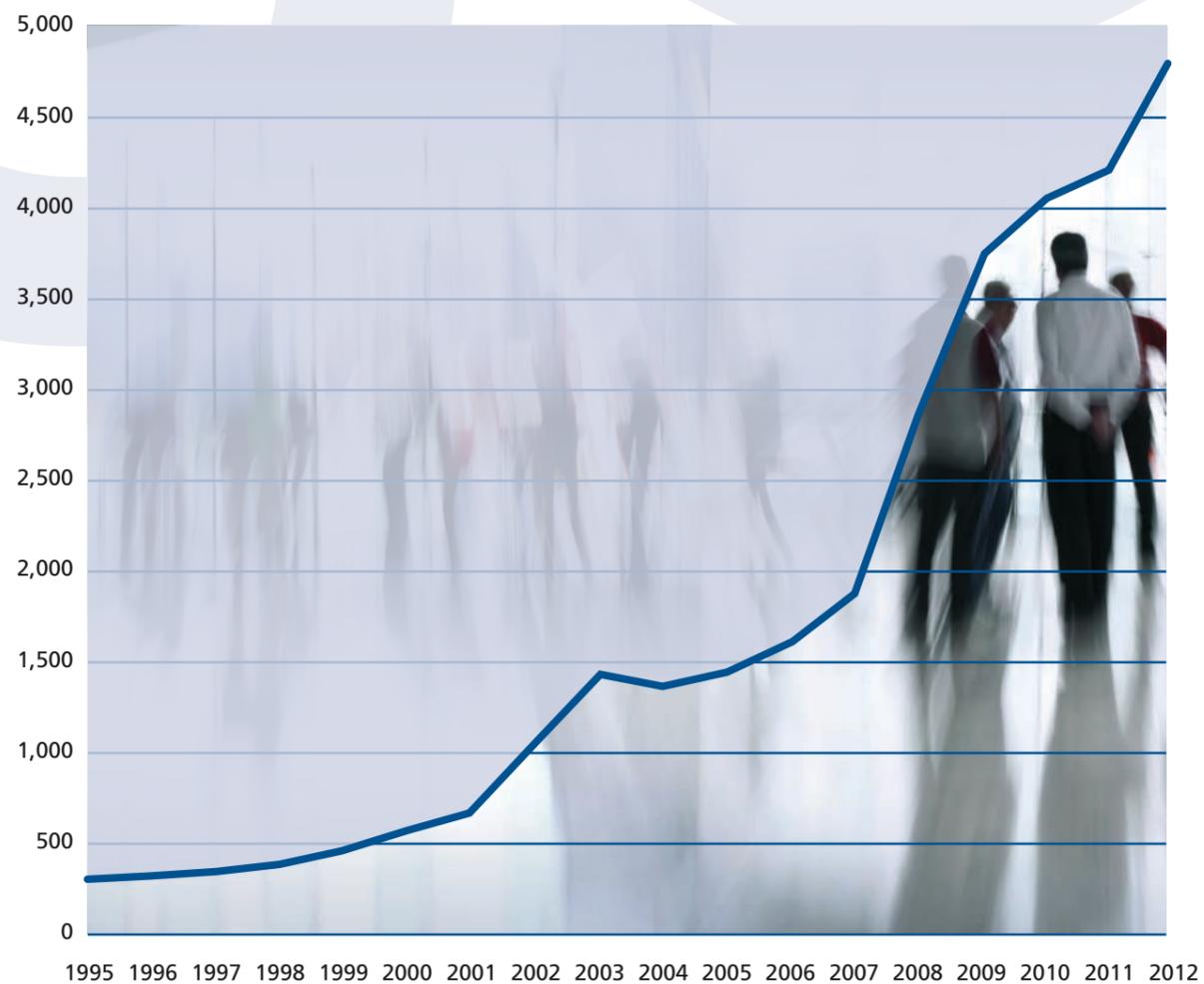
### **Why are people proud to work for Octapharma?**

People are proud to work for Octapharma not just because of what we do, but how we do it. To work for a company that is so focused on safety and quality is a source of great pride. Octapharma's culture is defined by these two principles and the company's response to the temporary withdrawal of one of our key products is the paradigm of how Octapharma always responds responsibly and puts patients and safety first. Once routine Pharmacovigilance revealed an issue, we voluntarily withdrew the product from the market and immediately acted to establish what happened and why, resolving the issue and at the same time establishing a new gold standard in safety. It is not difficult to imagine a different scenario in a large public pharmaceutical company where the first reaction would most likely have been severe cost cutting, which translates on the human level to mass redundancies. Although we did not hire to a great extent during this time, we still filled critical positions. There was a trust that the people in place were the people best placed to resolve the situation. The results since the product returned to market speak for themselves. Our response emphasized our dedication to safety, quality, our patients and employees.

### **What is your vision for the coming years?**

I am engaging with management and board members to identify their most important HR priorities and will establish strategic and tactical plans to address them. We have great employees, good processes and excellent HR teams around the world; we need to capitalize on these to evolve to the next stage in our company's growth. Ultimately, I want to build a world class human resources organization.

Average headcount



**Shirley Meyer**  
Assistant, R&D

As I enter my 20th year with Octapharma I can look back and reflect over a wealth of experiences, many of which have impacted my life in a meaningful way. The working environment has been one of the main reasons why I have stayed with the company for so long. The past few years have really taught me the value of working together with a positive and enthusiastic group of colleagues. It has been great to share in the journey of the company, to witness major milestones and see the company continue to grow and develop. However, what I really appreciate is despite the fact that Octapharma is now a major global organization, there still exists a very relaxed and familiar environment and on the occasions when our Chairman visits the headquarters here in Lachen he always has time to stop and say hello.

Since January 2011, I have been working as Assistant to Ulrich Thibaut in the area of Research & Development, a position I value highly. As I work on a part-time basis and have three children at home, I appreciate the flexibility offered by Octapharma. Knowing that your contribution to the workplace is valued continues to be a real motivator.



**Cristina Gonçalves**  
Export Executive

Octapharma has been parallel to my personal life for 20 years and, before my son was born, took absolute priority over my personal life. I was hired by Paulo Castro in Portugal. I remember being shown a dining table covered in papers and being asked to start the filing to organize the Octapharma vault. I was involved in so much: translating submission documents, submitting registration dossiers and on one occasion personally delivering product to hospitals! I then had the responsibility for the finance and administrative department. At that time, all Latin America markets worked through Portugal. The phones didn't stop ringing. I later moved to Switzerland to work in the newly created corporate controlling department. The company was growing fast and only had a limited database and system; we had to build everything from scratch. One of our responsibilities in controlling is to provide accurate reports to management so that decisions can be made. There were many things happening over a short period and our growth was fast with the acquisition of production plants; I remember reading brochures from the newly acquired Stockholm plant, reading about gammanorm®, atenativ® and about this amazing woman Inga Marie Nilsson. I was thinking I would have so much to remember. I still have these brochures and they bring back nice memories of this time.

In my current role as Export Executive I am split 50% for Latin America and 50% Brazil. I am there for customers to optimize service and manage shipments. I have had immeasurable support from Wolfgang Marguerre and Paulo Castro over many years. With Octapharma it is personal, not only with employees, but customers, and of course with our patients who are always at the forefront of what we do.

## Angel Sosa

Country Manager, Octapharma Mexico

I am responsible for the complete commercial and manufacturing operation in Mexico. In 1994 Octapharma had a prominent role in Europe and was beginning to globalize. Mexico was one of the first relevant markets outside of Europe. In 19 years we have gone from zero to the leader in the plasma products market in Mexico, with one of the most complete portfolios. In many ways this is thanks to the board's decision to invest in a local manufacturing site in 1999. Being a local manufacturer differentiates us from our competitors.

The presence of the family is vital: they are only a phone call away when it comes to important and swift decisions. Great value is placed by the board

on the innovative ideas, creativity and initiative of the people. We have a remarkable freedom to manage the company; this is a main motivator for me. This year we have invested in the renewal of our offices and QC laboratories.

As a result of my chance meeting with Wolfgang Marguerre at the WFH congress in Mexico in 1994, the past 19 years have been incredibly rewarding. I can proudly state that Octapharma has not only been a witness to the development of the Mexican blood derivatives market, but a main actor, working together with patients, doctors, authorities and health providers.

One of my personal highlights was Octapharma Mexico's 15 year anniversary celebration: we organized a concert in one of the most important historic sites in Mexico, Chapultepec Castle. And speaking of music, the appreciation for culture is typical of Mr Marguerre and his family; it is a real pleasure for me to share in the rich cultures of my colleagues around the world.



## Patricia Morey

Vice President, Corporate Brand Management

I joined Octapharma in 2002 in the role of Business Development Manager for the UK and Ireland. Since then my responsibilities have increased in line with the growth of the organization, resulting in my recent relocation to Octapharma's HQ to lead the newly established corporate branding department.

Octapharma is immensely successful in attracting and recruiting high calibre individuals and I have over the past decade been privileged to work with many highly talented people across the organization. I have seen the company expand substantially in recent years, however, I feel the passion and enthusiasm within Octapharma remains compelling and the venturesome culture cultivated continues to inspire like-minded people. Over the past 10 years I have personally learnt and developed so much from working in this environment. Looking to the future, with the planned introduction of the Human-cl rhFVIII and the establishment of the global HR department, I feel this is an exciting time to be involved in the next phase of the company's growth and evolution.



## Helena Direito

Regulatory Affairs and Technical Director, Octapharma Portugal

I have worked for Octapharma since 1993. My role encompasses regulatory, quality, customer service and human resources. The complexity of these activities has evolved over time with increasingly demanding regulations. The plasma industry has changed dramatically over these 20 years; in the beginning blood derivatives were not considered medicines. When they were reclassified more demanding dossiers and more complex registrations improved the industry. After the problems with HIV and Hepatitis the introduction of viral inactivation steps changed everything. Today viral safety is standard; our efforts are therefore now focused on efficacy, tolerability and product/plasma supply. One project of which I am particularly proud is when I was responsible for the Brazil self sufficiency program. Octapharma was able to improve the quality systems at the blood banks, implementing procedures for collecting and handling plasma and increasing yields.

In Octapharma the importance placed on individuality makes all the difference. We are proud that Octapharma continue to be innovative by investing in recombinant and inhibitor treatment. Despite the growth, Octapharma has kept the flexibility to adapt to changing circumstances and we remain, as we always have been, committed to safety and quality.

# Annual Accounts



An impressive return of octagam® 5% and 10% consolidated the financial performance and financial position of the Octapharma Group in the year 2012. Significant increases in net sales combined with a good performance in the collection of trade receivables and sound investment decisions allowed the Octapharma Group to end the year 2012 with increased profitability, significantly without bank loans.

Net sales for 2012 are reported at 916 million Euro, which represents an increase of 183 million Euro or 25% compared to the 2011 figure. In response to our unprecedented situation in 2011, plasma sales were very high. If we exclude the atypical figure for plasma sales in 2011, the increase from 2011 to 2012 is 262 million Euro, an exceptional increase of 40%. The significantly higher volumes sold in the Immunotherapy area, together with the continuously robust development of the sales in the Haematology and Intensive care area, led to this very satisfying result in net sales.

Gross profit in 2012 was 285 million Euro, 80 million Euro higher than in 2011. Although the gross margin increased from 28% in 2011 to 31% in 2012, it includes extra costs for re-gaining the octagam® 5% and 10% market share, in addition to the general price pressure in some markets in the Immunotherapy area.

Operating expenses were 148 million Euro, 7 million Euro higher than in 2011. Investments into Research and Development were 37 million Euro in 2012. The Sales & Marketing expenses increased by 9 million Euro, as a consequence of the efforts made to secure the successful return of octagam® 5% and 10% and to achieve the significant increase in net sales.

Earnings Before Interest and Tax (EBIT) can be reported at 137 million Euro or 15% of net sales. This reflects a 114% increase compared to 2011, which itself was reported as 164% higher than 2010. Benefitting from a tax item from previous years on the income tax line, the net income after tax is 136 million Euro.

The Octapharma Group reports a positive net cash position of 32 million Euro at the end of 2012 and is again free of any bank debts. Despite the 25% increase in net sales, the trade receivable position remained almost unchanged at 306 million Euro. This includes a significant improvement of the payment situation in certain Southern European markets.

Net inventory increased by 55 million Euro in 2012. In relation to cost of goods sold, we expect that the inventory will start decreasing from the second half of 2013 onwards.

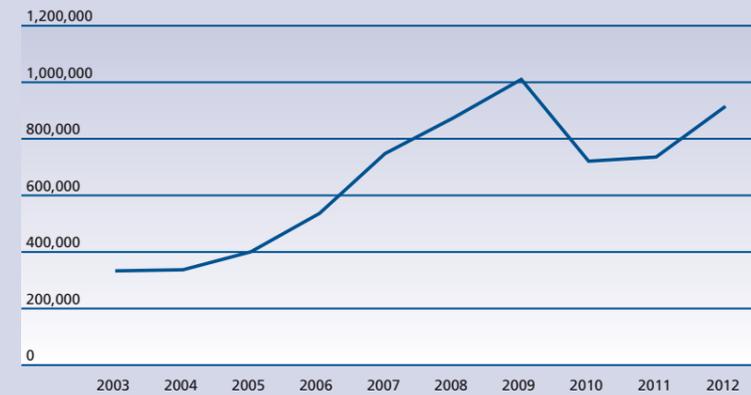
The investment in fixed assets amounted to 61 million Euro in 2012. This is 13 million Euro or 26% more than in 2011 and encompassed the completion of important projects as well as signalling the beginning of the 2013-2017 development plan of our six modern production plants.

The equity ratio further improved to 82.6% at the end of 2012.

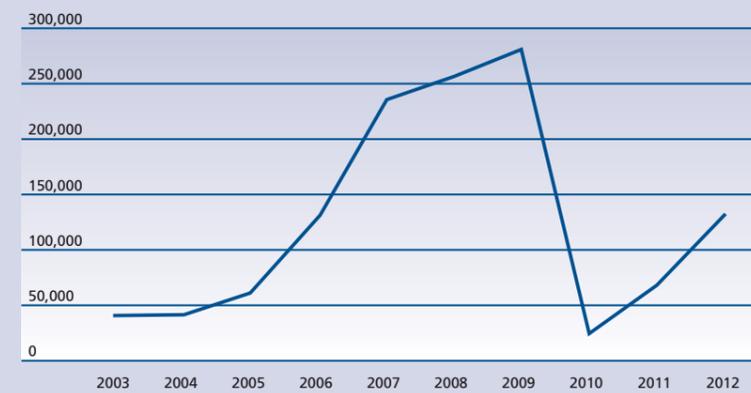
This solid financial basis will support the overall goals for 2013: further strengthening the market position of the Octapharma product portfolio; completely re-gaining the octagam® 5% and 10% world market share and, as a consequence; further increasing profitability.

## Key Figures of the Octapharma Group

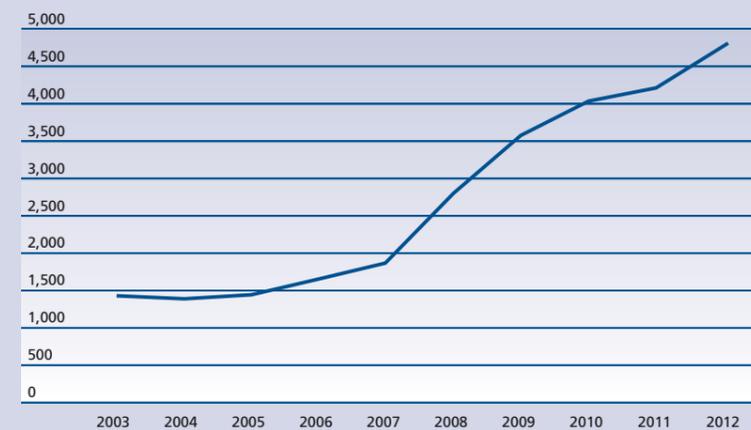
## Net sales in 1,000 EUR



## Operating income in 1,000 EUR



## Average headcount



(monetary figures are in 1,000 EUR)

	2012	2011	2010	2009	2008
<b>Operating income</b>	<b>136,540</b>	63,758	24,140	278,320	256,045
<b>Net profit of the year</b>	<b>135,538</b>	72,082	45,807	253,533	231,018
<b>Year-end headcount</b>	<b>4,939</b>	4,514	4,238	3,977	3,037
<b>Return on average equity</b>	<b>12%</b>	7%	5%	29%	35%
<b>Profit from operations per employee</b>	<b>28</b>	15	6	78	92
<b>Current ratio</b>	<b>591%</b>	463%	533%	517%	468%
<b>Days of sales in receivables</b>	<b>115</b>	145	106	93	101
<b>Average days to sell the inventory</b>	<b>379</b>	396	282	173	135
<b>Cash flow from operations</b>	<b>131,559</b>	-43,501	-62,003	169,433	208,180
<b>Expenditures to ensure future prosperity</b>	<b>97,637</b>	91,660	151,114	175,346	140,549
• Research and development	<b>36,741</b>	43,491	40,347	38,502	25,115
• Capital expenditures and investments in activities	<b>60,896</b>	48,169	110,767	136,844	115,434

## 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, 2012, the summary balance sheet and the summary cash flow statement for the year then ended, aggregating non-material financial statement captions.

## Consolidated Income Statement of the Octapharma Group

January–December

(all figures in 1,000 EUR)	2012	2011
<b>Gross sales</b>	<b>970,117</b>	758,309
Sales deductions	-54,465	-26,108
<b>Net sales</b>	<b>915,652</b>	732,201
Cost of sales	-630,795	-527,230
<b>Gross profit</b>	<b>284,857</b>	204,971
Research and development	-36,741	-43,491
Selling and marketing	-67,643	-58,494
Regulatory affairs/quality audit	-8,111	-8,536
General and administration	-36,719	-33,751
Other income	2,107	3,720
Other expense	-1,210	-661
<b>Total operating expenses</b>	<b>-148,317</b>	-141,213
<b>Operating income</b>	<b>136,540</b>	63,758
Non-operating income and expenses	2,542	-274
<b>Profit before taxes</b>	<b>139,082</b>	63,484
Income tax	-3,544	8,598
<b>Net profit of the year</b>	<b>135,538</b>	72,082

**Consolidated Statement of Financial Position of the Octapharma Group**

at 31 December

(all figures in 1,000 EUR)	2012	2011
<b>Assets</b>		
Cash and cash equivalents	32,060	26,521
Trade receivables	305,869	301,387
Other receivables	11,929	2,815
Inventories	636,328	581,225
Other current assets	24,641	16,526
<b>Total current assets</b>	<b>1,010,827</b>	928,474
Financial investments	8,850	2,820
Deferred tax assets	62,958	53,241
Loans to related parties	821	814
Investments in associates	0	3,848
Intangible assets	0	191
Property, plant and equipment	344,384	335,843
Other non-current assets	130	0
<b>Total non-current assets</b>	<b>417,143</b>	396,757
<b>Total assets</b>	<b>1,427,970</b>	1,325,231

(all figures in 1,000 EUR)	2012	2011
<b>Liabilities and equity</b>		
Trade payables and other payables	70,056	62,949
Payables to related parties	107	12,524
Bank loans	0	45,000
Income tax payable	13,074	6,336
Accruals and current provisions	87,925	73,907
<b>Total current liabilities</b>	<b>171,162</b>	200,716
Deferred income	2,258	3,504
Provisions	45,749	46,313
Deferred tax liabilities	28,722	28,157
<b>Total non-current liabilities</b>	<b>76,729</b>	77,974
<b>Total liabilities</b>	<b>247,891</b>	278,690
Share capital	100	100
Retained earnings	1,174,493	1,048,955
Hedging reserve	0	-5,615
Currency translation adjustments	5,486	3,101
<b>Total equity attributable to owners of the Company</b>	<b>1,180,079</b>	1,046,541
<b>Total liabilities and equity</b>	<b>1,427,970</b>	1,325,231

**Consolidated Statement of Cash Flow of the Octapharma Group**

January–December

(all figures in 1,000 EUR)	2012	2011
<b>Net profit for the year</b>	<b>135,538</b>	72,082
Depreciation on tangible and intangible assets	55,994	68,272
Change in fair value of non-current assets	-12,166	-11,529
Share of (profit) loss of associates	-5,869	-1,273
(Profit) loss on sale of property, plant and equipment	86	21
Changes in long-term liabilities and provisions	-886	256
Unrealised foreign exchange (gain) loss	-1,150	-137
<b>Cash flow before changes in working capital</b>	<b>171,547</b>	127,692
(Increase) decrease of working capital	-39,988	-171,193
<b>Net cash from operating activities</b>	<b>131,559</b>	-43,501
Acquisition of property, plant and equipment	-60,896	-48,169
Proceeds from associates, current and non-current financial investments	1,512	1,280
Proceeds from sales of property, plant and equipment	886	96
<b>Net cash used in investing activities</b>	<b>-58,498</b>	-46,793
Dividends paid	-22,471	-2,529
Increase (decrease) of bank loan	-45,000	45,000
<b>Net cash used for financing activities</b>	<b>-67,471</b>	42,471
<b>Net change in cash and cash equivalents</b>	<b>5,590</b>	-47,823
Cash and cash equivalents beginning of period	26,521	74,371
Effect of exchange fluctuation on cash held	-51	-27
<b>Cash and cash equivalents end of period</b>	<b>32,060</b>	26,521



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**REPORT OF THE INDEPENDENT AUDITOR ON THE SUMMARY FINANCIAL STATEMENTS****Octapharma Nordic AB, Stockholm**

The accompanying summary financial statements on pages 88 to 92, which comprise the summary balance sheet as at 31 December 2012, 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 2012. We expressed an unmodified audit opinion on those financial statements in our report dated 28 February 2013. 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 88 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 2012 are consistent, in all material respects, with those financial statements, on the basis described on page 88 of this report.

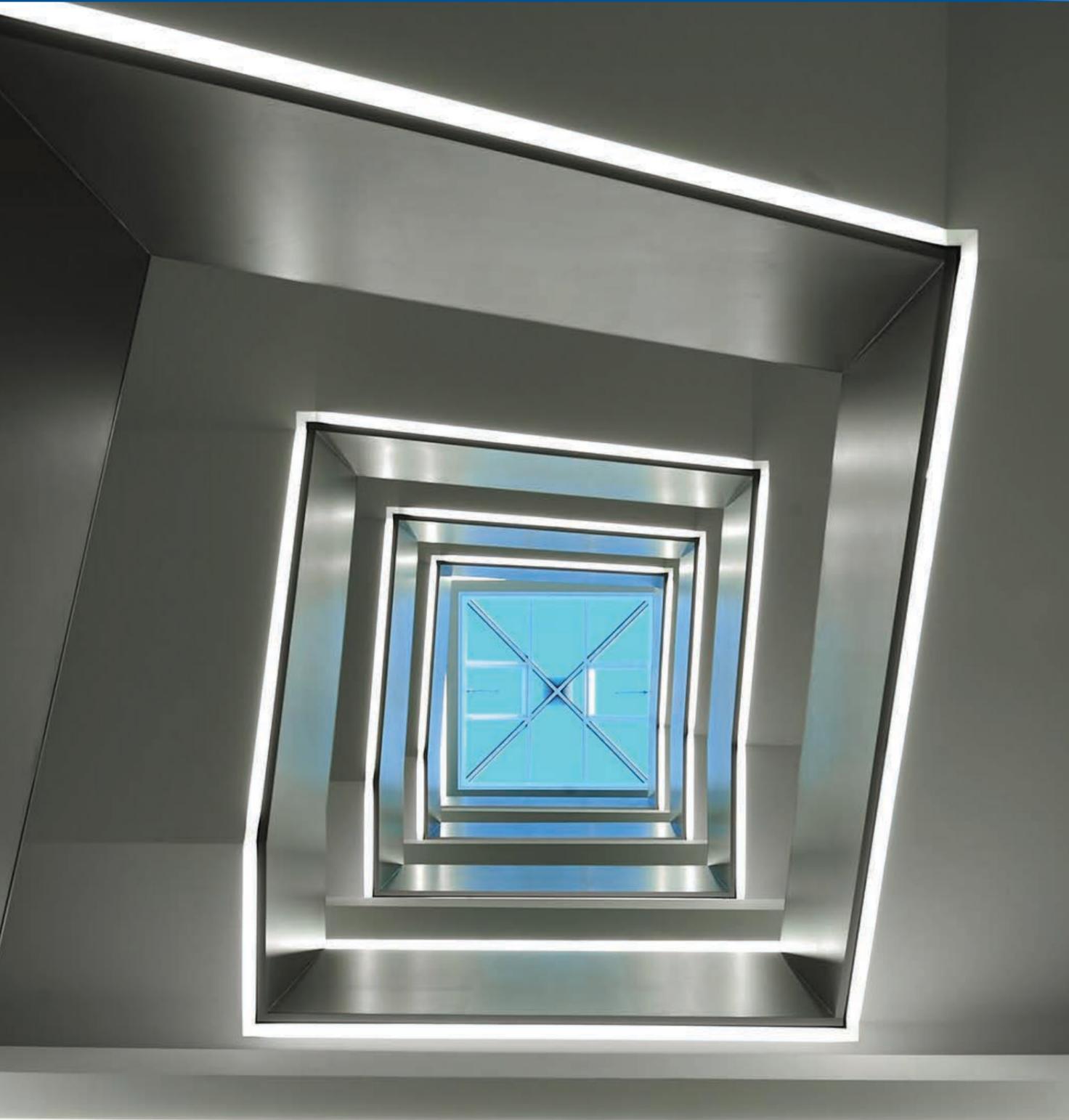
KPMG Ltd

  
Orlando Lanfranchi

  
Markus Ackermann

Zurich, 28 February 2013

# Company Perspective



This special anniversary has provided the opportunity to reflect on the past 30 years of Octapharma and to communicate the vision for the future. In 2012, we invested 61 million Euro in fixed assets including the completion of major projects. These investments will support improved capacities in our production plants to facilitate our long term growth.

The foundation philosophy of the company is our patient-oriented approach. In this report we have shown the breadth of activities centered towards patients, including research and development into new products and indications. It reflects on the historical retrospectives on how treatment has changed over 30 years and the role Octapharma has played in these changes. With the encouraging development of our Human-cl rhFVIII we are ever closer to fulfilling our aim of entering the recombinant sector successfully with our human to human philosophy. Our Heidelberg facility is now home to all research and development activities for FVIII and all other recombinant projects.

The Company goal is to expand products and indications so we can optimally utilize every litre of our precious plasma raw material, with the strategic aim of increasing plasma availability and throughput and increasing our product portfolio to access the global market. The philosophy of Octapharma is that we have a responsibility for transparent and open communication; the establishment of our Corporate Brand Management team will further contribute to this aim.

Overall, Octapharma has achieved so much in 30 years and is now primed and ready to enter the next phase of our development and growth over 2013-2017.

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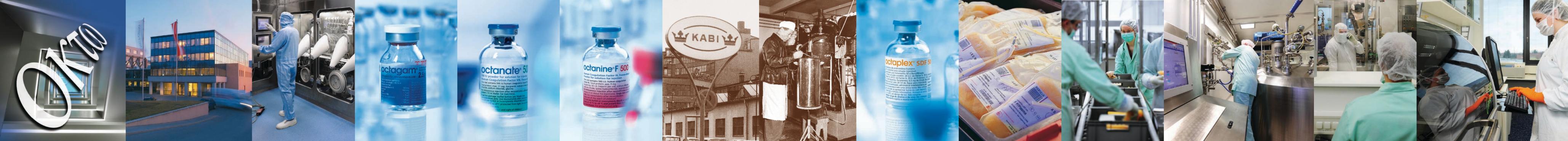
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## 1983

Octapharma is founded. The "octa" in the name is taken from the Greek word for eight, the factor deficient in people with haemophilia A.

## 1990

Octapharma opens its first production facility in Vienna, acquiring the fractionation plant from Chemie Linz.

## 1994

After several years of development, the intravenous immunoglobulin octagam® is launched.

## 1998

Launch of a new generation of high purity, double virus inactivated FVIII and FIX concentrates, octanate® (replacing octavi®) and octanine®F, respectively.

## 2002

Octapharma acquires Biovitrum in Sweden, gaining increased manufacturing capacity and incorporating Biovitrum's product portfolio. Octapharma also benefited from Kabi's 60 year history of plasma product expertise.

## 2004

octaplex®, a state-of-the-art prothrombin complex concentrate (PCC) is launched.

## 2006

Octapharma acquires Deutsche Gesellschaft für Humaplasma (DGH) plasma centres, paving the way to secure plasma supplies from our own sources.

## 2008

Octapharma acquires a fractionation plant in Springe, Germany, from the German Red Cross.

## 2010

octagam® is voluntarily withdrawn from markets after routine Pharmacovigilance revealed a lot dependent cluster of thromboembolic events. The manufacturing process was amended and an innovative assay introduced which confirms the successful removal of any pro coagulant activity.

## 2012

Octapharma opens the new Institute for Recombinant Protein Research and Development in Heidelberg, Germany.

1983



octapharma

2013

## 1985

Octapharma launches its first product, octavi®, the first virus inactivated FVIII product, manufactured with the then novel solvent detergent (S/D) process. Octapharma acquired the license for this innovative treatment, which became gold standard in the production of plasma derived products.

## 1992

Laboratory in Frankfurt established for the validation and documentation of virus inactivation methods.

## 1997

Octagene, now Octapharma Biopharmaceuticals, is founded in Munich to develop a human cell line for the production of recombinant FVIII.

## 1999

Octapharma acquires a second plant in Lingolsheim, France, from Aventis. 80 staff pre-acquisition, the site now employs 370 people.

## 2003

Expansion into North America: Octapharma begin sales in the US, the world's largest pharmaceutical market, and continues to expand operations in North America by acquiring a fractionation plant in Mexico.

## 2005

wilate®, a high purity von Willebrand/ FVIII preparation is launched.

## 2007

Octapharma establishes its plasma service company, Octapharma Plasma Inc. (OPI).

## 2009

Sales exceed € 1 billion.

## 2011

octagam® 5% and 10% resume commercialization in all major markets. Elsewhere, Octapharma launches a global plant harmonization project.



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From human to human  
[www.octapharma.com](http://www.octapharma.com)



1983 – 2013



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For the safe and optimal use of human proteins

