Grifols is a world-leading healthcare company since 1940 Grifols has contributed to improving people’s health. Grifols employs 13,200 people, who share the mission of improving people’s health and well-being through the research, development, manufacture and distribution of plasma-derived biological medicines, clinical diagnostics systems and pharmaceutical preparations for hospital use.

Since 1940 Grifols has contributed to improving people’s health. Grifols is one of the leading companies in the world in the production of plasma proteins, with a global market share of approximately 20%. Following the acquisition of the Novartis diagnostics unit in January 2014, Grifols completed its range of immunological diagnostics and is a world-leading company in transfusion medicine.

A leader in the manufacture of plasma-derived biological medicines and in transfusion medicine. Grifols business model is one of vertical integration, enabling it to control the entire production cycle, starting with the collection of raw material in the form of plasma through an extensive network of donor centers in the United States, and ending with the finished product. In the area of diagnostics Grifols offers comprehensive solutions that contribute to transfusion safety for clinical laboratories, blood banks and transfusion services.
KEY DATA

SALES REVENUE OF 2,741.7 MILLION EUROS IN 2013
• 92.4% OF INCOME IS GENERATED IN INTERNATIONAL MARKETS
• A STRONG PRESENCE IN THE USA AND CANADA, WHICH ACCOUNTS FOR OVER 63% OF SALES; 21% GENERATED IN EUROPE AND MORE THAN 15% IN OTHER REGIONS

GLOBAL DISTRIBUTION WITH PRODUCT SALES IN MORE THAN 100 COUNTRIES

150 PLASMA DONOR CENTERS IN THE USA

13,200 EMPLOYEES IN THE WORLD
• 73% OF THE WORKFORCE BASED IN THE UNITED STATES

LISTED IN THE TOP 100 MOST INNOVATIVE COMPANIES IN THE WORLD

ONGOING COMMITMENT TO R&D, WITH AN ALLOCATION OF 4.5% - 5% OF ANNUAL INCOME

FUNDING OF PORTFOLIO COMPANY R&D PROJECTS IN AREAS SUCH AS ALZHEIMER’S AND IN THE FIELD OF PERSONALIZED MEDICINE

EXPERTS IN THE MANUFACTURE OF LIFESAVING BIOLOGICAL MEDICINES, INCLUDING:
• IMMUNOGLOBULINS, PARTICULARLY INTRAVENOUS IMMUNOGLOBULIN (IVIG), TO TREAT IMMUNOLOGICAL DISORDERS
• ALBUMIN, TO RE-ESTABLISH AND MAINTAIN BLOOD VOLUME
• FACTOR VIII, FOR THE TREATMENT AND PROPHYLAXIS OF HEMOPHILIA
• ALPHA-1-ANTITRYSIN, TO PROTECT AGAINST THE DETERIORATION OF LUNG TISSUES (PULMONARY EMPHYSEMA)

SPECIALISTS IN CLINICAL DIAGNOSTICS
• A WORLD LEADER IN TRANSFUSION MEDICINE
• LEADING MANUFACTURER OF INSTRUMENTS AND REAGENTS FOR IMMUNOLOGY AND HEMOSTASIS

DIRECT GEOGRAPHIC PRESENCE IN 25 COUNTRIES THROUGH WHOLLY OWNED SUBSIDIARIES

MANUFACTURING FACILITIES IN THE UNITED STATES, SPAIN, AUSTRALIA AND SWITZERLAND
As of December 2013, Grifols share capital amounts to 119.6 million Euros. The share capital is made up of 213,064,899 ordinary shares (Class A), with a nominal value of 0.50 Euros per share, and 130,712,555 non-voting shares (Class B), with a nominal value of 0.10 Euros per share.

Grifols ordinary shares (Class A) are listed on the Spanish Continuous Market, where they form part of the Ibex-35 (GRF), Spain’s leading share index, while its non-voting shares (Class B) are also listed on the Continuous Market (GRF.P) and on the NASDAQ (GRFS) via ADRs (American Depositary Receipts). One Grifols ADR represents one Class B share.

In 2013, Grifols resumed the payment of cash dividends as the means of compensation to all shareholders. The policy on dividends is maintained and the target payout stands at 40% of net profit.
THREE DIVISIONS TO MEET THE NEEDS OF PATIENTS AND HEALTHCARE PROFESSIONALS

BIOSCIENCE DIVISION

SPECIALIZING IN PLASMA-DERIVED PRODUCTS FOR THERAPEUTIC USE

ACCOUNTED FOR APPROXIMATELY 90% OF INCOME IN 2013

The Bioscience division is Grifols’ principal line of business; it draws on the legacy of over 70 years of delivering human plasma proteins that improve the quality of life for patients with potentially life-threatening diseases.

The main plasma derivatives are:
• Intravenous immunoglobulin (IVIG)
• Factor VIII
• Albumin
• Alpha-1-antitrypsin (A1-AT)
• Other hyperimmune immunoglobulins

The company’s main products lead sales worldwide

<table>
<thead>
<tr>
<th>Plasma protein</th>
<th>Market share</th>
<th>Position in world ranking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyvalent IVIG (Intravenous immune globulin)</td>
<td>27%</td>
<td>1</td>
</tr>
<tr>
<td>Alpha-1-antitripsina</td>
<td>66%</td>
<td>1</td>
</tr>
<tr>
<td>Coagulation factor VIII</td>
<td>18%</td>
<td>2</td>
</tr>
<tr>
<td>Albumin</td>
<td>14%</td>
<td>3</td>
</tr>
</tbody>
</table>

In addition, Grifols is world leader in plasma collection capacity. The company owns and operates a network of 150 plasma donor centers in the United States, which daily receive more than 26,000 plasma donations, to obtain more than 6.4 million liters of plasma per year. Grifols therefore ensures a constant and reliable supply of raw material to meet the growing demand for plasma protein treatments.

For the fractionation process, plasma protein separation and purification, and the dispensing of the final product Grifols uses manufacturing sites in the United States and one in Spain. Grifols’ overall fractionation capacity currently stands at 9.6 million liters of plasma per year.

Key business indicators 2013

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nº of donation centers</td>
<td>150</td>
</tr>
<tr>
<td>Nº of plasma donations/day</td>
<td>+ 26.000</td>
</tr>
<tr>
<td>Nº of donations analyzed (annual capacity)</td>
<td>+ 15 million donations</td>
</tr>
<tr>
<td>Liters of plasma obtained</td>
<td>6.4 million liters/year</td>
</tr>
<tr>
<td>Nº of fractionation plants</td>
<td>3</td>
</tr>
<tr>
<td>Fractionation capacity installed (2014)</td>
<td>9.6 million liters/year</td>
</tr>
</tbody>
</table>
THREE DIVISIONS TO MEET THE NEEDS OF PATIENTS AND HEALTHCARE PROFESSIONALS

HOSPITAL DIVISION

THE HOSPITAL DIVISION BRINGS TOGETHER NON-BIOLOGICAL PHARMACEUTICAL PRODUCTS AND HEALTH SUPPLIES FOR HOSPITAL PHARMACY

APPROXIMATELY 3.5% OF THE SALES REVENUE EN 2013

The division’s main products include parenteral solutions (fluid therapy), enteral and parenteral clinical nutrition products, and hospital logistics systems.

Since 2005, the division’s plants in Barcelona and Murcia have offered third-party manufacturing services through its Grifols Partnership service. Such arrangements ensure that Grifols maximizes use of its high-tech facilities and makes the company’s experience and knowledge of the production of sterile solutions and other health products available to third parties.

DIAGNOSTIC DIVISION

A WORLD LEADER IN TRANSFUSION MEDICINE

ACCOUNTING FOR 20% OF SALES AS FROM 2014

Diagnostics also contribute to healthcare by helping medical practitioners in the decision making process. The Diagnostic Division provides reagents and automated analyzers for transfusion medicine, hemostasis and immunology that meet the parameters of accuracy, reproducibility, and sturdiness to deliver highly reliable results that are essential for clinical diagnosis.

The range of products for transfusion medicine is reinforced with the addition of genomic amplification systems to detect the presence of infection in blood or plasma donations. Together with the already consolidated conventional blood typing systems genotyping contributes to ensuring safe transfusions.

Some of the Division’s most important analyzers for the immunohematology laboratory include Wadiana® and Erytra®; the Procleix® platform for blood banks and transfusion centers, the Triturus® system for the immunology laboratory and the hemostasis analyzer Q.
ILLNESSES TREATED WITH PLASMA-DERIVED MEDICINES

The plasma derivatives produced by the Bioscience Division are essential lifesaving biological medicines used in the following areas:

**IMMUNE DISORDERS**

Grifols’ immunoglobulin range, in particular those administered intravenously (IVIG) are used to treat people born with a variety of immunodeficiencies, such as the primary immunodeficiencies. They are also used to provide replacement therapy for patients with chronic lymphatic leukemia or recurrent infections.

**Primary Immunodeficiencies**

Primary immunodeficiencies (PI) encompass a group of 150 diseases that are inherited or caused by genetic errors in the cells that constitute the immune system. As a result, the immune system that protects the body against bacteria or viruses does not function properly. Individuals with an immune deficiency disease are susceptible to infection, both mild and severe, and take longer to recover.

There are different treatments for the different types of primary immunodeficiency. One of the most common treatments is intravenous immunoglobulin (IVIG), which is able to help some patients by temporarily replacing the antibodies needed to fight infection. The IVIG replaces the antibodies that the body should be producing, but does not help the patient’s immune system to create more. This is because replacement therapy works by helping to combat infections in patients with immune deficiencies.

**Kawasaki Disease**

Grifols immunoglobulins are also used to treat Kawasaki disease, a systemic inflammation of the blood vessels (vasculitis) of unknown cause that affects primarily pediatric patients. Children of Japanese or Korean descent are at increased risk of developing the disease.

**Neurological Disorders**

Gamunex® is the only intravenous immunoglobulin approved by the FDA for the treatment of chronic inflammatory demyelinating polyneuropathy (CIDP), a rare neurological disease that causes progressive muscular weakness in the arms and legs.

**Plasma Volume Replacement Therapy**

Human albumin is one of the essential proteins and is the largest single component of plasma. In intensive care it is used in patients who have suffered from shock or trauma with a significant loss of blood, as a treatment to re-establish plasma volume. Grifols biological medicines such as albumin are administered to re-establish and maintain blood volume.

**Clotting Disorders**

Grifols also manufactures biological medicines indicated for the treatment and prevention of diseases that cause excessive bleeding or abnormal clotting, including hereditary diseases such as hemophilia, von Willebrand’s disease and anti-thrombin deficiency.

An absence of factor VIII produces hemophilia A, while the lack of factor IX causes hemophilia B. Grifols produces specific clotting factors to meet the needs of patients suffering from deficiencies of either of these plasma proteins.

**Alpha-1 Antitrypsin Deficiency**

Also known as AATD or alpha-1, this is a hereditary disorder that causes a significant reduction in the naturally occurring protein, alpha-1-protease. Alpha-1 is the most common cause of genetic emphysema in adults, and the most common cause of liver disease in children. People who suffer from this deficiency often develop chronic obstructive pulmonary disease (COPD), leading to incapacity and early death.

Grifols is the world’s leading producer of alpha-1 protease inhibitor, used to provide replacement therapy for alpha-1-antitrypsin deficiency (AATD) in patients with pulmonary emphysema.

**Fatal Infections**

Grifols produces a range of hyperimmune immunoglobulins that provide rapid, temporary immunity against a series of potentially fatal infections such as rabies, tetanus, hepatitis B and Rh incompatibility.
One of the company’s strategic cornerstones is international growth. During recent years, Grifols has consolidated its presence in the United States, where its subsidiary Grifols Inc. acts as the parent company for the group’s subsidiaries in that country. Grifols took its first steps towards consolidating its business structure in the North American market with the acquisition, in March 2002, of its first 48 plasma donor centers. Through a combination of acquisitions and the opening of new centers, this network now consists of 150 centers.

Other corporate operations, including the acquisition of Talecris Biotherapeutics, have seen Grifols’ presence in the United States grow steadily, together with the incorporation of Canada as a major new market with its own subsidiary. Approximately 85% of sales are concentrated in Europe and the United States, although other emerging areas such as Latin America and the Asia-Pacific region are gradually gaining in importance. Grifols has a strong presence in Latin America, with subsidiaries in Argentina, Chile, Mexico, Brazil and Colombia. In Europe it has subsidiaries in Spain, Portugal, France, the United Kingdom, Italy, Germany, the Czech Republic, Slovakia, Poland, Switzerland and Scandinavia, and in the Asia-Pacific region it has established subsidiaries in Japan, Thailand, Malaysia, Singapore, China and Australia. Additionally, in 2013 Grifols established its office of representation in Dubai to launch its entry to the Middle East.
MANUFACTURING FACILITIES IN USA AND EUROPE

GRIFOLS’ PLASMA DERIVATIVES, CLINICAL DIAGNOSTICS PRODUCTS AND HOSPITAL PRODUCTS SHARE A SINGLE PURPOSE: TO SERVE THE NEEDS OF MILLIONS OF PATIENTS AND TO SUPPORT THE WORK OF HEALTH PROFESSIONALS

ALL OF THE MANUFACTURING PLANTS APPLY THE HIGHEST QUALITY AND SAFETY STANDARDS

INVESTMENT IN MANUFACTURING FACILITIES WILL TOTAL OVER 450 MILLION EUROS DURING THE PERIOD 2014-2016
The manufacture of plasma-derived medicines is a highly technological process. Grifols has a track record of improving and modernizing its facilities for the fractionation and purification of the various therapeutic plasma proteins in order to maximize the safety and efficacy of these products.

**PLASMA PRODUCT MANUFACTURING PLANTS**

**PARETS DEL VALLÉS**  
(BARCELONA, SPAIN). ONE OF THE LARGEST PLASMA FRACTIONATION PLANTS IN EUROPE. CAPACITY TO FRACTIONATE 4.2 MILLION LITERS OF PLASMA PER YEAR

**LOS ANGELES**  
(CALIFORNIA, UNITED STATES). CAPACITY TO FRACTIONATE 2.2 MILLION LITERS OF PLASMA PER YEAR

**CLAYTON**  
(NORTH CAROLINA, UNITED STATES). CAPACITY TO FRACTIONATE 3.2 MILLION LITERS OF PLASMA PER YEAR

Grifols’ fractionation capacity currently stands at 9.6 million liters of plasma per year. Future plans provide for this to increase to over 12 million liters by 2016.
Grifols is one of the leading Spanish manufacturers of enteral and parenteral solutions in flexible and glass containers.

It manufactures products for intravenous therapy in accordance with the highest quality standards, and its plants hold environmental, quality and workplace safety certification: ISO 9001, ISO 14001, ISO 13485, OHSAS 18001.

**MANUFACTURING PLANTS: PHARMACEUTICAL PREPARATIONS AND HEALTH PRODUCTS**

**PARETS DEL VALLÈS**
(BARBELONA, SPAIN). PRODUCTION PLANT FOR INTRAVENOUS SOLUTIONS FOR PARENTERAL NUTRITION IN GLASS CONTAINERS

**LAS TORRES DE COTILLAS**
(MURCIA, SPAIN). PRODUCTION OF INTRAVENOUS SERUM IN FLEXIBLE CONTAINERS AND BLOOD CONSERVATION BAGS. HOLDS FDA HEALTH PRODUCT APPROVAL

**DEVELOPMENT AND MANUFACTURING PLANTS: DIAGNOSTIC PRODUCTS**

**PARETS DEL VALLÈS**
(BARBELONA, SPAIN). DIAGNOSTIC PRODUCTS MANUFACTURING PLANT

**DÜDINGEN**
(SWITZERLAND). MANUFACTURING PLANT FOR MDMULTICARD® RAPID BLOOD GROUP TYPING CARDS

**MELBOURNE**
(AUSTRALIA). DG GEL® CARD MANUFACTURING PLANT

**SAN FRANCISCO**
(CALIFORNIA, USA). PRODUCTION OF ANTIGENS FOR IMMUNOLOGICAL DIAGNOSTIC REAGENTS.
MANUFACTURING FACILITIES IN USA AND EUROPE

PLASMA SUPPLY

The production of plasma-derived medicines depends on a supply of high quality plasma. Grifols is the world’s leading plasma supplier, and has built up an extensive US-based organization, Grifols Plasma Operations, consisting of:

**150 PLASMA DONOR CENTERS**
DISTRIBUTED THROUGHOUT THE UNITED STATES, WHICH PROVIDED GRIFOLS WITH 6.4 MILLION LITERS OF PLASMA IN 2013

**CENTRALIZED PLASMA ANALYSIS LABORATORIES**
in the United States: San Marcos and Austin (Texas), with the capacity to process 60,000 plasma samples per day

**PLASMA LOGISTICS:**
3 CENTRAL WAREHOUSES FOR THE STORAGE AND DISTRIBUTION OF PLASMA TO THE DIFFERENT MANUFACTURING CENTERS
PREVIOUS PAGE

MANUFACTURING FACILITIES IN USA AND EUROPE

RECONCILING MANUFACTURING WITH THE NEEDS OF THE ENVIRONMENT

The increased production of plasma derivatives by the Bioscience division, Grifols’ main area of activity, has been achieved on a responsible basis that minimizes the potential environmental impact. This has been made possible by applying the company’s environmental policy and objectives, the key features of which are set out in the Corporate Plan for strategic action on energy.

At all Grifols’ manufacturing facilities, key objectives focus on recovering compounds, as in the case of ethanol, increasing the recycling of waste, both general and plastic, through more efficient separation, and reducing atmospheric emissions. Grifols participates in the Carbon Disclosure Project (CDP), which recognizes the measures adopted by various companies to reduce emissions and mitigate the risks of climate change. In 2013, the company obtained a score of 90 out of 100, making Grifols the fifteenth highest placed company of the 125 largest companies in Spain and Portugal, and the leading company in the health sector.
Plasma is the liquid component of human blood. Around 90% of plasma consists of water, and approximately 7% of the remainder consists of essential proteins and antibodies that help maintain the vital functions of our body. These are what are called plasma proteins.

A deficit of any of these proteins, such as albumin or the immunoglobulins, causes diseases that can only be treated through the administration of plasma-derived products. Proteins converted into medicines are the standard treatment for millions of people who need them to stay alive. Grifols develops and produces these blood-derived treatments and distributes them in almost 100 countries.

Some of the most important biological medicines obtained from plasma include albumin, clotting factors (such as factor VIII), intravenous immunoglobulin (IVIG) and alpha-1-antitrypsin.

In order to produce the necessary quantities of these lifesaving plasma-derived proteins, a considerable quantity of human plasma is required as raw material, because not all of the proteins are present in the same proportion in plasma.

From collection of the plasma unit until distribution of the final product takes between 9 and 11 months. This cycle is managed by Grifols from start to finish, and the company’s integrated production model enables it to guarantee every stage of this complex process.
THE PROCESS FOR OBTAINING BIOLOGICAL MEDICINES FROM PLASMA

Plasmapheresis is the process most widely used to obtain donated plasma. This is a method by which plasma is separated from the other blood components (red blood cells, platelets and other cells), which are injected back into the donor during the donation process. For this reason, we always talk about plasma donations, not blood donations.

Plasmapheresis was developed by Dr. José Antonio Grifols Lucas in 1951, and is the most effective system for obtaining the amounts of plasma needed to extract the different therapeutic proteins through industrial fractionation.

Grifols obtains almost all of the plasma through its donor centers in the United States; the plasma is fractionated to obtain each of the proteins with a therapeutic use. The plasma supply chain is validated by the FDA and the EMA. Grifols only obtains plasma from qualified repeat donors. At each center, the donors must undergo a yearly medical examination and the routine tests at each donation. Grifols does not use plasma from sporadic donors.

Grifols has also fractionated excess plasma from Spanish hospitals for over 20 years. Through this service, Spanish plasma is converted into plasma-derived products for use by the Spanish health system. Similar agreements for plasma fractionation exist with blood banks and hospitals in Canada, the Czech Republic and Slovakia.

Production consistency depends not only on the analysis of the final product, but also on controlling the raw material and monitoring the entire production process. The procedure starts with industrial fractionation to extract the different proteins that have a therapeutic use. Plasma fractionation involves subjecting it to various changes in temperature, pressure and chemical conditions, among other procedures, in order to force the separation of each protein.

Each protein is purified and subjected to viral inactivation and elimination procedures and then dispensed under sterile conditions in order to conserve all of the therapeutic properties.

The main plasma derivatives manufactured by Grifols are intravenous immunoglobulins, coagulation factor VIII, albumin and alpha-1-antitrypsin.
THE PROCESS FOR OBTAINING BIOLOGICAL MEDICINES FROM PLASMA

FINISHED PRODUCTS

INTRAVENOUS IMMUNOGLOBULIN (IVIG)

Intravenous immunoglobulins are considered to be the most important plasma derivatives. For the last twenty years their administration has become a fundamental therapy in clinical medicine. These are the purified plasma fraction containing the antibodies that provide the body with its immune defenses. Although originally developed for use as antibody replacement therapy, it has been demonstrated that their use has other clinical benefits.

IVIG is generally indicated for the treatment of primary immunodeficiencies, certain secondary immunodeficiencies, various autoimmune diseases and in allogenic bone marrow transplant.

Grifols produces the first and, to date, only IVIG approved in the United States and Canada to treat chronic inflammatory demyelinating polyneuropathy (CIDP), a neurological disorder characterized by progressive weakening and deterioration of the sensory function in the arms and legs. This immunoglobulin is also registered in the United States for subcutaneous use in the treatment of primary immunodeficiencies.

ALBUMIN

Albumin is indicated for re-establishing and maintaining blood volume in situations due to traumatic shock or hemorrhage. Replacing human albumin can speed up recovery and increase the survival rate of intensive care patients.

COAGULATION FACTOR VIII

Factor VIII is indicated for the treatment and prevention of hemorrhage in patients with hemophilia A and acquired factor VIII deficiency. Future market growth for factor VIII is ensured due to the rise in prophylactic treatments, combined with the large number of hemophiliacs who still do not receive treatment. According to the World Federation of Hemophilia, only around 20% of the world’s hemophiliacs receive treatment with factor VIII concentrates.

One of the versions of factor VIII produced by Grifols is the first and only high-purity concentrated factor VIII/ von Willebrand factor complex to incorporate a double inactivation stage in its production process. It has been approved by the FDA for use in the treatment of congenital von Willebrand disease.

ALPHA-1-ANTITRYPsin

Alpha-1-antitrypsin is a protease inhibitor that is indicated as a replacement therapy for people with alpha-1-antitrypsin deficiency, which is a genetic disorder that can cause chronic obstructive pulmonary disease (COPD) such as emphysema and chronic bronchitis.

OTHER HYPERIMMUNE IMMUNOGLOBULINS

Grifols’ portfolio of plasma derivatives includes various specific hyperimmune immunoglobulins for the treatment of potentially fatal infections such as rabies, tetanus, hepatitis B and Rh incompatibility.
Grifols’ diagnostic division specializes in instrumentation and reagents for blood banks, transfusion services and clinical laboratories. In recent years, Grifols has made significant investments in the transfusion medicine line of products. The company is now strategically positioned in this segment.

**DIAGNOSTIC DIVISION PRODUCTS**

**AREAS OF SPECIALIZATION**

**TRANSFUSION MEDICINE**

Grifols offers instrumentation to automate blood typing techniques and patient-donor blood compatibility tests for blood banks, transfusion services and immunohematology laboratories. The instrumentation is used to process blood typing cards using column agglutination technology.

The range of products for transfusion medicine is reinforced with the addition of genomic amplification systems to detect the presence of infection in blood or plasma donations.

**HEMOSTASIS SYSTEMS**

Grifols offers a wide range of products that covers instrumentation, an extensive range of reagents and software applications. The hemostasis automatic analyzer Q conducts coagulation, chromogenic and immunoturbidimetric tests. It has been designed to adapt perfectly to the requirements of the hemostasis laboratory.

**IMMUNOLOGY**

Grifols specializes in the immunological diagnostics of infectious and autoimmune diseases using ELISA techniques based on antigen-antibody reactions.

Triturus® is an open system that automates the ELISA technique using microplates.

Instrumentation of this type is essential for clinical laboratories in order for them to deliver precise results. The system must also be flexible and at the same time work automatically to conduct large numbers of tests.
Through its Hospital division, Grifols supplies standard parenteral solutions for intravenous therapy, preparations for clinical nutrition, and a wide range of sterile products and medical devices. In addition, the division provides technological platforms for hospital logistics management, designed to ensure that citizens receive safe, high-quality healthcare. These include cutting-edge products for the management of medicines.

**Fluid Therapy: Solutions for Intravenous Therapy**

The intravenously administered therapeutic solutions to restore or maintain fluid and electrolyte balance that Grifols offers to hospital pharmacy services are available in a range of pharmaceutical forms. The company also develops systems for the preparation of intravenous solutions under sterile conditions, such as the Misterium®-Modular Clean-Room and the Grifill® 3.0 filling device.

**Clinical Nutrition**

Clinical nutrition affects patients’ quality of life and contributes to their rehabilitation. Grifols produces a full range of special diets and formulations for parenteral nutrition and enteral (oral or nasogastric) nutrition.

**Medical Devices for Interventional Therapy**

This line includes advanced instrumentation, medical devices and disposable material for a range of hospital services, including hemodynamics, urology, anesthesiology and cardiovascular surgery.

**Hospital Logistics**

The Grifols model for the integrated management of medicines consists of a wide range of high-tech products that cover every stage of the medication process, from the central pharmacy all the way through to individualized registration of administration to patients at the bedside. This model is designed to ensure maximum quality and safety of patient care.

The range includes the BlisPack® system, which automates the preparation and electronic identification of medicines and can prepare 85% of solid medicines for use in a unit dose setting and in hospital units, and the Pyxis® system, used to automate the control of stocks of medicines and health material on the ward.
R&D: A PRIORITY

GRIFOLS PROMOTES INNOVATION THROUGH RESEARCH INTO NEW THERAPEUTIC PLASMA PROTEINS AND THE INVESTIGATION OF NEW INDICATIONS FOR EXISTING PROTEINS

IN 2013 GRIFOLS INVESTED MORE THAN 123 MILLION EUROS IN R&D AND FUNDED RESEARCH PROJECTS IN ITS PORTFOLIO COMPANIES
R&D: A PRIORITY

PRINCIPAL RESEARCH LINES

INTEGRATED ALZHEIMER’S RESEARCH STRATEGY

Faced with the progressive aging of developed societies, Grifols is committed to increasing research into Alzheimer’s disease. The company’s strategy for conducting research into Alzheimer’s disease follows two pathways: one is directly handled through the company and the other is through Araclon Biotech. This means that a comprehensive approach is taken in the three main areas of activity: new treatments aimed at slowing the progress of the disease, an early diagnosis and the development of a preventive vaccine.

In 2013 the first patients were enrolled on the AMBAR study (Alzheimer Management by Albumin Replacement). This clinical trial uses a combined therapy involving plasma exchange and apheresis together with the administration of plasma proteins, in particular albumin in different doses and regimens. The first results are expected to come available in 2015.

Through Araclon Biotech, Grifols is working on the validation of a diagnostic kit and on the development of a vaccine against Alzheimer’s disease. In order to obtain sufficient data to validate the diagnostic kit, various collaborative studies are currently being performed with groups in Australia, United States and Europe, in which more than a thousand individuals have taken part.

The vaccine has passed the animal experimentation stage and in September of 2013 the Spanish Medicines Agency gave its approval for phase I of clinical trials in humans. Patients were enrolled on the study in 2014. Phase I will evaluate the tolerability and the safety of the vaccine in patients with mild to moderate Alzheimer’s disease, but not its effectiveness. This clinical trial is coordinated by the ACE Foundation and expected to finish in 2015.

FIBRIN BIOLOGICAL GLUE

Biosurgery represents a new specialist research line, pursued as an interdisciplinary R&D project. Research is focusing on the development of a hemostatic and tissue sealant for vascular, liver, soft tissue and connective tissue surgery. Four clinical trials are currently under way: two in vascular surgery, and two in liver and soft tissue surgery, in Europe, Canada and the United States.

ALBUMIN IN HEPATOLOGY

This is a clinical study to evaluate the effects of the prolonged administration of human albumin on cardiovascular and renal function in patients with advanced cirrhosis and ascites.

OTHER STUDIES

The trials investigating the use of plasmin in cases of acute peripheral arterial occlusion will continue. The clinical trial to evaluate the safety and tolerance of treatment of cystic fibrosis with an inhaled formulation of alpha 1-antitrypsin is currently in phase II.

ANTI-THROMBIN IN CARDIAC SURGERY

This is a clinical study to demonstrate the clinical efficacy of Anbinex® anti-thrombin (AT) in patients undergoing heart surgery.
Grifols promotes biotechnology initiatives through its participation in research companies.

Grifols itself is not a biotechnology company, as Grifols’ plasma-derived medicines are manufactured from extracted plasma, and not as a result of biotechnological processes. However, Grifols’ pioneering spirit and its commitment to patients have led the company to pursue a presence in biotechnology projects.

Grifols has a presence in the biotechnology field through:

1. Its pharmaceutical engineering company, Grifols Engineering, specializing in the development of medical biotechnology (also known as red biotechnology) basically in the area of recombinant proteins and antibodies, as well as in cell and tissue therapies.

2. The acquisition of shares in companies and R&D projects in fields of medicine lying outside the scope of its main activities.

Grifols primarily channels its part-ownership of research companies through Gri-Cel, a group company that manages and coordinates research in gene and cell therapy conducted by spin-off companies such as Nanotherapix or VCN Biosciences.
Grifols is involved in the following fields and companies:

In the field of **advanced therapies**, an innovative and important area with strong potential for the treatment of diseases for which there is currently no effective treatment:

### Nanotherapix

Nanotherapix is a company specializing in the field of gene therapy (human gene-based medicines). Its main project is the development of a platform based on the use of adenoviruses as vectors to introduce genes into cells. Nanotherapix uses the latest generation of adenoviral vectors to increase the safety and efficacy of this class of treatment.

The Nanotherapix project grew out of collaboration between researchers at the Autonomous University of Barcelona and the Hospital Germans Trias in Badalona.

### VCN Biosciences

VCN Biosciences is dedicated to the research and development of new therapeutic approaches to tumors for which there is no effective treatment, using a technological platform based on oncolytic adenoviruses. Its most advanced project is the VCN-01 adenovirus, which has been designated as an orphan drug by the European Medicines Agency (EMA) to treat pancreatic cancer. The clinical phase is due to start in 2013. VCN Biosciences is a company that emerged from the Virotherapy Group at the Catalan Oncology Institute (ICO).

### TiGenix

This company specializes in cell therapy. It has developed a validated platform using expanded allogenic adipose-derived stem cells (eASCs) for the treatment of autoimmune and inflammatory diseases. TiGenix currently markets a product that it is indicated for regenerating knee cartilage, and it has another three products under development in the field of health technology, an area of research with an important potential for growth.

### Araclon Biotech

This company specializes in the research and development of therapies and diagnostic methods for neurodegenerative diseases, principally Alzheimer’s disease (AD). Its activities currently focus on two lines of research: early diagnosis of AD, for which it has developed blood diagnostic kits (ABTest), and treatment of the disease through immunotherapy, in particular by developing a series of patented vaccines.

Araclon Biotech does not currently have any products at market, although its ABtest is available to the scientific community for use in research studies. Araclon Biotech was founded in 2004 as a spin-off from the University of Zaragoza.

### Progenika Biopharma

This company specializes in the development of technology for personalized medicine. It focuses on the design and manufacture of in vitro genome-based tests for the diagnosis and prognosis of diseases, and to predict and monitor the response to pharmacological treatment. It has also developed its own technology for the production of molecular-based diagnostic and prognostic tests, and is an international leader in this field. In particular, Progenika is a global pioneer in the development of molecular biology tests for the performance of transfusion compatibility studies.

### Aradigm Corporation

An American pharmaceutical company specialized in the development and marketing of drugs delivered by inhalation for the treatment and prevention of severe respiratory disease such as cystic fibrosis (CF), and bronchiectasis (BQ) unrelated to cystic fibrosis, among others.
GLOSSARY OF TERMS

PLASMA-DERIVED PROTEINS
Are purified plasma proteins with therapeutic properties that are obtained through the fractionation of human plasma. Plasma-derived products have become essential medicines, capable of saving lives and improving the quality of life and life expectancy of patients with chronic illnesses for which there are no alternative treatments.

ALBUMIN
Is one of the most important plasma proteins, together with intravenous immunoglobulin and clotting factors.

INTRAVENTOUS IMMUNOGLOBULIN (IVIG)
Antibody-rich plasma protein, with multiple applications in the treatment of infectious diseases and immunodeficiencies.

PLASMAPHERESIS
Method developed by Dr. Grifols in 1949 and that continues to be the most widely used method in the world for the collection of plasma. The first plasmapheresis center opened in Barcelona in 1953. This process enables blood to be extracted and immediately separated into its cellular components, which are then injected back into the donor, with the plasma being retained.

APHERESIS
This consists of the extraction of a limited amount of plasma from the patient (up to 800 ml) and its replacement with albumin or intravenous immunoglobulin (IVIG).

DRUG ADMINISTRATION (FDA)
Official name of the US government agency that regulates food and medicines.

HEMOTHERAPY
Treatment of an illness using blood, blood components or their derivatives.

PARENTERAL
Intravenous administration of medicines.

PLASMA
Liquid part of the blood, consisting of a mix of a large number of proteins in solution.

INTRAVENTOUS SOLUTION
Medicine or homogeneous mixture of a substance in liquid, enabling it to be infused into the circulatory system through a needle.

PARENTERAL SOLUTION
Homogeneous mixture of a substance in liquid, enabling it to be infused into the intravenous system through a needle.