


ANNUAL REPORT **2021**

**KEDRION**  
B I O P H A R M A





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# LETTER FROM PAOLO MARCUCCI

*Dear Friends,*

Looking back at 2021, I am proud of the accomplishments we achieved.

Few of us imagined that the global Covid-19 pandemic would still be with us at the end of the year. And yet, thanks to the determination and hard work of the Kedrion people, we came through the year's significant challenges with notable successes.

The pandemic has had a profound impact on the collection of plasma, both in terms of volume and costs. The entire sector has been affected by this event, and our revenues from plasma sales have been hit.

Furthermore, since our competitors are focused on the US market, plasma derivatives prices did not fully adjust to the new plasma collection costs, with an impact on our profitability.

Still, with our strongest commitment to our patients, we maintained vital supplies and got a fair economic result.

We have also kept our eyes on the future, enhancing and increasing business possibilities throughout our areas of operations: in Turkey, where we widened and deepened our relationships with both patients and healthcare communities through a direct distribution model; in Germany, where we signed an agreement for exclusive distribution of 10% Intravenous Immunoglobulins; and in France, where we were able to enter the contract manufacturing market, to produce and distribute Immunoglobulins for French patients.

At the same time, we took an exciting major step into the future with the acquisition of the Prometic group of companies. This agreement has added a new plant in Laval, Canada, with 130 employees, a new country presence for Kedrion Biopharma and - most noteworthy - a new product, Ryplazim®, for the treatment of the rare and debilitating condition, Congenital Plasminogen Deficiency. Recently granted FDA approval, Ryplazim® is the

only therapeutic of its kind on the market.

We confirmed our determination to increase efficiency, foster sustainable growth and enhance profitability. An operational transformation project, NEXT, has been adopted, and it is already producing relevant and tangible results.

In 2021, we successfully refinanced Kedrion, with a very positive reception in the bond market. Capital earned from the refinancing process has been used to reimburse the existing debt and the bond issued in 2017, while sparing financial capacity to sustain our current business and its further development.

In 2021, the Marcucci family began discussions with global equity firm Permira for an operation on Kedrion equity and the simultaneous acquisition of a leading British biopharmaceutical company, Bio Products Laboratory (BPL). The deal is expected to be closed in 2022 subject to the

fulfillment of certain conditions, creating a new global player for plasma-derived medicines treating patients with rare and life-threatening conditions.

These results have been possible thanks to the commitment of all Kedrion people. To all of you I say *mille grazie!*

Finally, I'd like to offer my warmest thanks to CEO Val Romberg, who left Kedrion in January 2022. Val's leadership during 2021 was instrumental in our perseverance and success. We wish him the best in all his future endeavors.

Paolo Marcucci,  
Executive Chairman





# COMPANY OVERVIEW







# WHO WE ARE

Kedrion Biopharma is a dynamic and growing biopharmaceutical company, specializing in the development and production of plasma-derived products to address many serious, often rare, diseases and conditions. Our portfolio includes, among others, therapies for Hemophilia, Primary Immunodeficiencies, and Rh sensitization as well as more widely used products like Albumin. Our interest in rare diseases and conditions is confirmed by our acquisition of Prometic and its new therapy for Congenital Plasminogen Deficiency.

Our headquarters are in Tuscany, Italy, where the company was founded and grew to become a significant partner to the Italian National Health System. Today it is one of the world leaders in the production of plasma-derived products which it distributes in some one hundred countries.

Working on a vertically integrated business model, Kedrion Biopharma is engaged on all aspects of the production of its products, from plasma collection to development and manufacturing cycles to distribution. We operate collection centers in the US

and production plants in Italy, the United States, Canada and Hungary.

Kedrion's partnership with the Italian Health System has resulted in unique expertise which we offer in support of countries and systems pursuing self-sufficiency in the availability of plasma-derived therapies.

# WHAT WE STAND FOR

Our focus, above all, is on people: the people whose generous donations of plasma make our work possible; our dedicated employees, whose work carries out our mission; our healthcare partners, whose collaboration is essential to reach the people on whom all of our efforts focus, the patients our products help. We think of ourselves as providing a bridge: from donor to patient; from plasma to therapies; from despair to hope.

\*Including Castelvetro Pascoli plant (Lucca, Italy) completion impending  
\*\*Source: Marketing Research Bureau "The Worldwide Plasma Protein Market 2020"

As of December 31<sup>st</sup>, 2021

Headquarters in Italy with subsidiaries in Europe, North and Latin America, and Asia

2021 turnover: 660.4 million Euro

6\* manufacturing plants in 4 countries

Annual growth rate since 2014: 5.1%

29 plasma collection centers worldwide

People in the world: more than 2,700

5<sup>th</sup> world player in the field of plasma-derived products and 1<sup>st</sup> in Italy in terms of production from Italian donor plasma\*\*

BioSC, the first GLP certified laboratory in Italy for pathogen safety

Partner in the self-sufficiency program in Italy

11 voluntary standards and certifications in manufacturing, human resources, environment

Commercial presence in more than 100 countries



# OUR VALUES

Founded as a family business with deep roots in the hills of Tuscany, Italy, Kedrion Biopharma was built on a firm foundation of shared and assumed values. In 2021, we made these manifest, declaring and describing a set of standards and principles

by which we can measure our actions and the actions of each member of our Kedrion family.

These values are **Caring, Integrity, Teamwork, Reliability, Excellence and Respect.**

**WE** ARE KEDRION  
**LIVE** THESE **VALUES**



CARING  
INTEGRITY  
TEAMWORK  
RELIABILITY  
EXCELLENCE  
RESPECT





Our guiding inspiration is the generosity of our donors, the dedication of our healthcare and academic partners and - most centrally - the perseverance of our patients and their families. Our behavior needs to reflect empathy, the effort to understand and share the



feelings of others. We keep in mind the people whose fear and suffering our work helps to ease. We remember the thousands whose generous donations allow us to do our work. We extend a helping hand or an understanding consideration to our fellow team members.



All of our actions and decisions are guided by clear ethical principles, including honesty and transparency. We strive to be open and honest in all of our interactions with fellow workers, with outside agencies, with clients and customers, and of course, with our patients. We



endeavor always to be forthright in our assessments and candid about our mistakes.



We recognize that our work at its most fundamental is the product of a team. Kedrion people work as one team adopting behavior that encourages trust and contribution. Teamwork requires a mutually supportive group in which all members contribute according to their



skills and talents while helping others contribute according to theirs. While individual effort is recognized and rewarded, it is understood that no one works alone.



We assume responsibility for our actions and are always accountable for the timely, successful outcomes those actions produce. Reliability is a necessary quality for the success of any business, but it is equally important for productive teamwork and

satisfying relationships between co-workers and stakeholder partners. It is evidenced in consistently meeting deadlines and goals, being available when needed, and anticipating expectations.



We strive to excel in every aspect of our business and approach every challenge with a determination to succeed. We challenge the status quo, encouraging our people to develop their skills, while learning from failures. Excellence is a moving target;

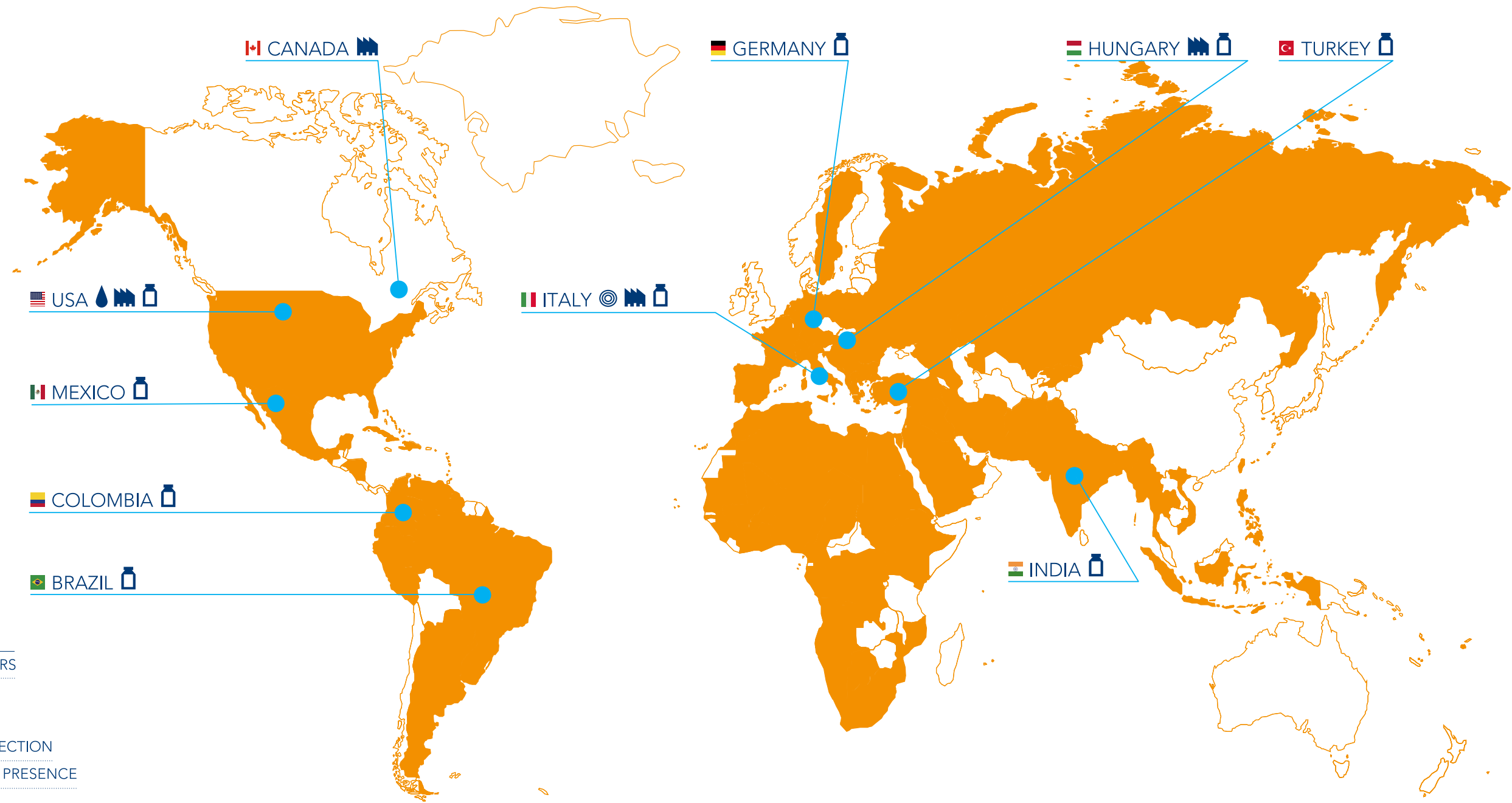
it is reached only in its pursuit. "Good enough" is the enemy of excellence.



We value trusted and enduring relationships with donors, patients, health care providers, colleagues and communities. We value diversity and proactively foster an inclusive work environment, where each person is respected and feels inspired to contribute. We seek out the best in others, assuming

and expecting to find it; we appreciate our commonalities and celebrate our differences. Treating people fairly - as you would want to be treated - is at the core of ethical behavior. We cannot respect ourselves unless we respect others; we will not respect others if we do not respect ourselves.

# OUR WORLD



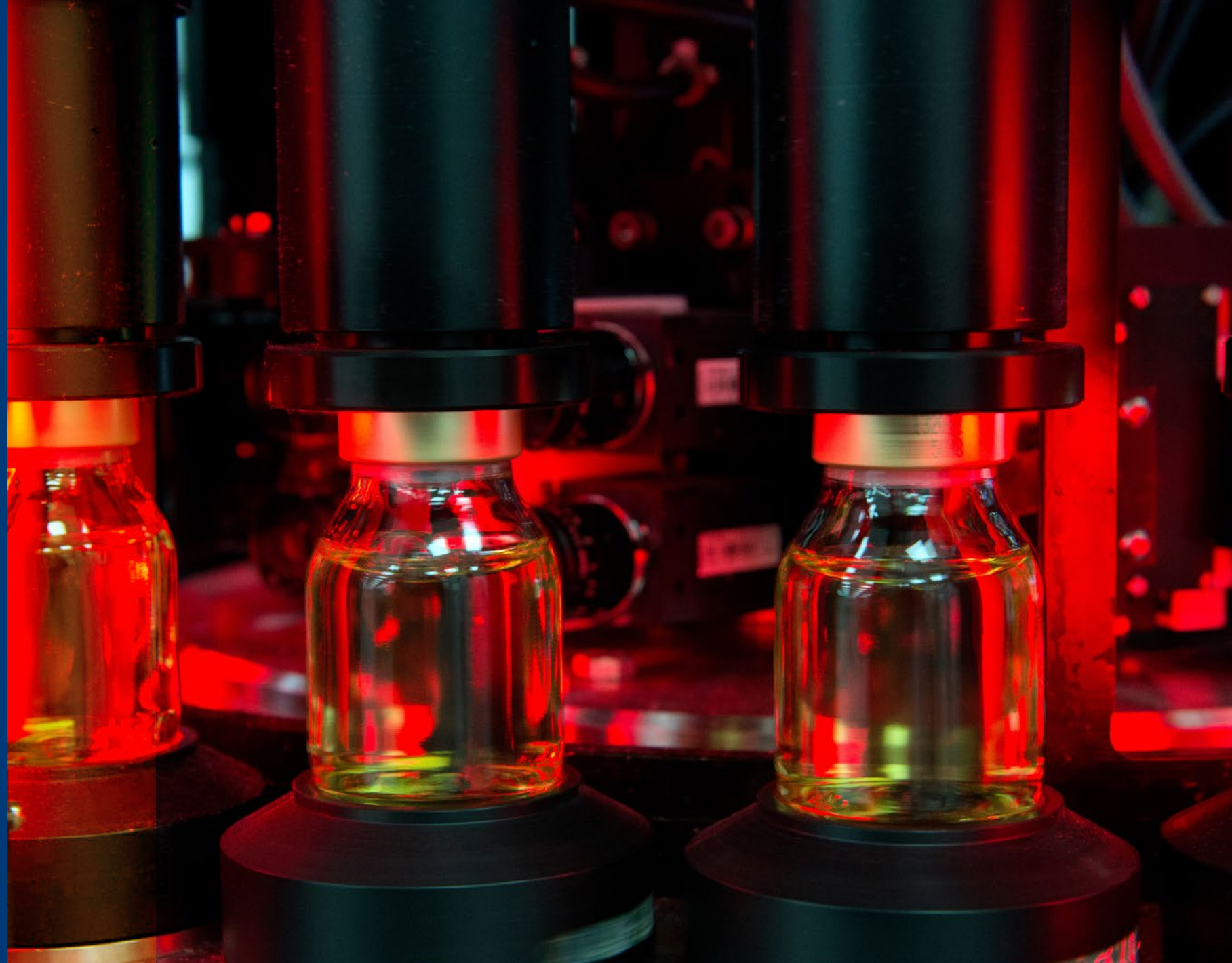
MAP LEGEND

- 📍 HEADQUARTERS
- 🏭 PRODUCTION
- 📦 DISTRIBUTION
- 💧 PLASMA COLLECTION
- 🟠 COMMERCIAL PRESENCE

As of March 2022



# WHAT WE OFFER







# PRODUCTS

## 1 RARE DISEASES

### IMMUNOLOGY / NEUROLOGY

Ig VENA / HUMAGLOBIN Liquid /  
KEDRIGAMMA / VENITAL\*  
Standard i.v. Immunoglobulin 5%

GAMMAKED\*\*\*  
Standard i.v. Immunoglobulin 10%

OPTIGLOBIN\*\*  
Standard i.v. Immunoglobulin 10%

NAXIGLO / KEYCUTE\*  
Standard s.c. Immunoglobulin

### HEMATOLOGY / HEMOPHILIA

RYPLAZIM\*\*\*  
Plasma-derived human Plasminogen

EMOCLOT / HUMACLOT /  
PLASMACLOT / EMOWIL / KLOTT\* /  
KOÂTE\*\*\*  
Factor VIII concentrate (with Von  
Willebrand Factor)

NUWIQ\*\*  
Recombinant Factor VIII

WILFACTIN\*\*  
Von Willebrand Factor concentrate

AIMAFIX / KEDRIFIX /  
HUMAFACOR-9 / IXED\*  
Factor IX concentrate

MONOFERRIC\*\*  
Iron replacement for intravenous  
infusion

EMOSINT  
DDAVP Desmopressin

## 2 MOTHER AND CHILD HEALTH

RhoGAM / IMMUNORHO / KeYrho /  
MICRhoGAM  
Anti-D i.m. Immunoglobulin

IMMUNOHBs 180 IU  
Anti-Hepatitis B i.m.  
Immunoglobulin

## 3 CRITICAL CARE AND TRANSPLANTATION

UMAN ALBUMIN / UMAN SERUM /  
HUMAN ALBUMIN / KEDRIALB /  
ALBITAL\* / KEDBUMIN\*\*\* /  
ALBUKED\*\*\* / ALBUMINA LFB\*\*  
Human Albumin solution

KEDRAB\*\*\*  
Human Rabies Immunoglobulin

VENBIG / KEYVENB / VEBIKED  
Anti-Hepatitis B i.v.  
Immunoglobulin

IMMUNOHBs / UMAN BIG /  
KEDHBs\*  
Anti-Hepatitis B i.m.  
Immunoglobulin

TETANUS GAMMA / TETIG  
Anti-Tetanus i.m. Immunoglobulin

MONOFERRIC\*\*  
Iron replacement for intravenous  
infusion

UMAN COMPLEX / KEDCOM\*  
PRONATIV\*\*  
Prothrombin Complex concentrate

AT III KEDRION / ATKED\*  
Antithrombin concentrate

KOLFIB / SILKETAL\*  
Fibrin sealant

K FLEBO  
Potassium aspartate

## 4 TRANSFUSION MEDICINE

CERUS INTERCEPT\*\*  
Plasma and platelets pathogen  
inactivation system

PLASMASAFE / PLASMAGRADE\*  
Pharmaceutical grade plasma

# SERVICES

## 1 PLASMA PROCESSING FOR NATIONAL SELF-SUFFICIENCY PROGRAMS (ITALY AND ABROAD)

## 2 TECHNOLOGY TRANSFER

## 3 VIRUS AND PRION CLEARANCE STUDIES (BioSC)

\*Products for the Italian Self-Sufficiency Program \*\*Products in license \*\*\*Products only available for the US market  
As of March 2022



# OUR 2021





# BRIDGING TURBULENT WATERS

2021 was a year of durability and determination. The global Covid-19 pandemic was no longer an event, but had become background. We accommodated to the continuing threat, but did not bend to it.

On an individual level were the trials of remote work; of restricted personal contact with co-workers, partners, clients and patients; of ever-present concern for family and friends. Kedrion continued and instituted safety measures commensurate with the evolving levels of threat and local policies.

On a corporate business level, the dominant and prevailing challenge was a precipitous decline

in plasma donations. This was a phenomenon experienced across the sector, across the world and similarly affected whole blood donations as well.

Our primary concern – as always – has been for our patients. Lower levels of plasma could have meant lower levels of derived therapies. We stepped up our recruitment of donors and ensured that they would find not only a welcoming environment in our collection centers, but one in which they could feel safe in the pandemic.

Ensuring absolute maximization and efficiency of our Plasma-to-Product processes we

also sought alternative sources of plasma and prioritized most-needed products.

While we stood firmly against these existential challenges, we kept our eyes on the future as well, concluding agreements that strengthen our position in the sector and widen our evolving ability to bring life-enhancing treatments to more patients in need.

To look forward and to expand in the face of fundamental shortages and revenue challenges demands a different way of thinking about identifying opportunity: Business Development. As **Director of Business Development, Gioacchino De Giorgi** describes it:

“

Based on the development and valuation of existing assets like production facilities, sales force, raw materials, experience and expertise, Business Development is an agile way of growing the business more quickly. And though it can lead to an acquisition (such as Prometic) it does not require the level of commitment of resources normally required for M&A.

## Our Business Development Department successfully identified several opportunities for growth:

■ The acquisition of the Prometic group of companies of Laval, Québec (Canada), including a recently FDA-approved therapy for Congenital Plasminogen Deficiency. An entire chapter of this Annual Report is dedicated to this relevant deal.

■ An agreement with Prothya Biosolutions of the Netherlands to exploit our existing sales force to distribute their 10% Intravenous Immunoglobulin in Germany, significantly increasing availability of a product in short supply.

■ Further increasing the availability of Immunoglobulin, Kedrion is completing a partnership with Laboratoire Français du Fractionnement et des Biotechnologies

(LFB) to fractionate their plasma in our Gödöllő, Hungary plant to produce Immunoglobulins for distribution in France.

■ A developing agreement with Denmark’s Pharmacosmos Group to distribute in Italy their novel intravenous iron-based therapy for patients suffering from Iron Deficiency Anemia (an estimated 5% of the female population in Italy).





# THE *NEXT* STEP ACROSS THE KEDRION BRIDGE

When CEO Val Romberg came onboard in late 2020, he announced a determination to maximize operational efficiency, enhance administrative response and communication and emphasize the values the company has observed or assumed without explicitly articulating. Employing both self-reflection as well as external consultation,

a bold program addressing these goals was approved by the Kedrion board in January.

The initiative, dubbed NEXT, grew out of the work of a consultancy agency, who first conducted a series of organizational surveys beginning in late 2020. The responses resulted in the identification of operational strengths as

well as areas of potential improvement.

The NEXT program is extremely broad, touching all levels and all activities of the company, from specific operational models to increase efficiencies to cultural models designed to enhance a sense of community and responsibility.

# NEWS AND NOTEWORTHY ALONG THE BRIDGE

## KIDCARES10 STUDY

KIDCARES10 is an important clinical study in the development of a treatment for Primary Immunodeficiency (PI) in children. A significant step forward was taken in March with the enrollment of the first subject in the Phase III trial of a 10% Intravenous Immunoglobulin (IVIG) for pediatric patients 2 – 17 years of age. PI is a rare group of disorders in which a part of the body's immune system is missing or does not function properly, leaving the person with this condition more susceptible to disease and infection.

More than 300 forms of PI have been identified, ranging from mild to severe. Immunoglobulin contains antibody proteins used by the immune system to fight infection. PI is a rare disease affecting some 250,000 people in the United States. The open-label, prospective, multi-center study will assess the efficacy, safety, and pharmacokinetics of KIG10, a 10% Intravenous Immunoglobulin (IVIG).



“

Many pediatricians who see patients diagnosed with Primary Immunodeficiency share a common goal, which is to gain an even broader understanding of the efficacy and safety of administering Immunoglobulin treatment to children affected by this condition. For this reason, today's news about the first patient being enrolled in KIDCARES10 is certainly welcome and exciting.

**Prof. Chiara Azzari, Azienda Ospedaliero-Universitaria Ospedale Pediatrico Meyer, Dipartimento Assistenza Integrata (DAI) di Pediatria Internistica. (Principal Investigator)**

And then, in July, the next big step: the first patient in the trial was treated in Italy. Eventual results of the KIDCARES10 study will be submitted to the US Food and Drug Administration (FDA).

“

The number of patients who require treatment for Primary Immunodeficiency continues to grow as this rare and serious medical condition becomes more and more well recognized and diagnosed by healthcare professionals. Data produced by the KIDCARES10 study will be extremely important in advancing an even deeper understanding of Primary Immunodeficiency in children. We are certainly pleased and proud to be participating in this important trial.

**Prof. Claudio Pignata, Professore Ordinario di Pediatria (Treating physician at the KIDCARES10 clinical site where the first patient has been treated)**



## RH&LIFE

Another Kedrion study enlisted its first subject in March. The “Rh&Life” clinical trial assesses the efficacy, pharmacokinetics and safety of an Anti-D Immunoglobulin in the prevention of Hemolytic Disease of the Fetus and Newborn (HDFN), or Rh Disease. Eventually, 200 subjects will take part from five countries.

HDFN can occur when a woman with Rh negative blood carries an Rh positive fetus. The Anti-D Immunoglobulin treatment prevents her body from creating dangerous levels of antibodies that can attack the fetus. Consequences of HDFN range from Jaundice and Anemia to brain damage and death. Effective preventative treatment has been known and available for fifty years. Yet some 200,000 babies are affected – damaged or killed

– by HDFN worldwide every year, because of lack of awareness or lack of access to the drug.

Kedrion is dedicated to making Anti-D Immunoglobulin available everywhere and has offered it in its portfolio in many countries for many years. The present study is part of these efforts to extend that availability.



## FDA EXTENDED KEDRAB'S INDICATIONS

The US Food and Drug Administration (FDA) approved a new label for KEDRAB, the Human Rabies Immune Globulin (HRIG), produced by our Israeli partner Kamada Ltd. and marketed in the US by Kedrion Biopharma in June. The FDA extended KEDRAB's indication to include individuals of all ages including pediatric patients. This made

KEDRAB the first and only HRIG available in the US to have been studied for efficacy and safety in children.

Rabies is a life-threatening disease, but it is fully preventable if treated on time. It impacts approximately 40,000 people in the US each year according to the World Health Organization.

## A GERMAN BRIDGE

Taking advantage of our robust sales organization, Kedrion Biopharma completed an agreement in July with Prothya Biosolutions of the Netherlands for three-year exclusive distribution of their 10% Intravenous Immunoglobulin (Optiglobin®) in Germany.

## A STRONGER BRIDGE TO TURKEY

Kedrion Biopharma is establishing a more robust and direct presence in Turkey. The decision was announced in October at a reception hosted by the Italian Ambassador to Turkey, His Excellency Massimo Gaiani at the Italian Embassy in Ankara.

Kedrion Betaphar, our Turkish subsidiary, announced its intention to offer an enlarged, direct portfolio of products. This will allow us to better serve patients

suffering from serious and rare conditions, while contributing the country's economy in a more tangible way.



Increasing our presence in Turkey means having the possibility to support Turkish patients more closely. This is an honor but also a big responsibility towards patients communities.  
**Riza Ommaty, Kedrion Betaphar CEO**



I am very glad that an Italian company has decided to make an important investment in Turkey in the strategical health sector. We are particularly proud also because the know-how provided by Kedrion will help patients in Turkey suffering from rare diseases.  
**His Excellency Massimo Gaiani, Ambassador to Turkey**





## A BRIDGE TO FRANCE

Kedrion Biopharma has signed a contract manufacturing agreement with LFB pharmaceutical group of France to increase the availability of Immunoglobulin, a plasma-derived medicine, for patients in that country. Under the agreement, Kedrion will fractionate in its Gödöllő, Hungary plant LFB plasma collected in France by the Etablissement Français du Sang. The resulting Immunoglobulins will then be imported and distributed to hospitals in France by LFB.



I am delighted with this partnership with Kedrion, which will enable us to meet the growing needs of the French market for Immunoglobulins, drugs that are in great demand in France and around the world.  
**Denis Delval, LFB Chairman and CEO**



I welcome the cooperation agreement with LFB as it provides a solution for patients in France. Kedrion shares LFB's values and its raison d'être, which is to provide products and therapies to patients with serious and often rare diseases.  
**Paolo Marcucci, Executive Chairman of Kedrion**

## A BRIDGE OF IRON: FROM DENMARK TO ITALY

We ended the year with a bold step into an expanding market by signing a 10-year agreement with Danish company Pharmacosmos to become exclusive distributor in Italy of their novel iron-based therapy for patients suffering from severe Iron Deficiency Anemia. The preparation, Monoffer-ic®, is administered intravenously.



This agreement will allow us to expand our commitment beyond that of rare diseases, redefining and consolidating our efforts to support a new community of patients affected by a disease that is very common among the population on a global scale.  
**Paolo Marcucci, Executive Chairman of Kedrion**



We are making our medical and commercial know-how available to this new community of patients due to the fact that Iron Deficiency Anemia is still under-diagnosed and under-treated.  
**Gioacchino De Giorgi, Kedrion Corporate Business Development Director**

## DEVELOPING LEADERS

The Kedrion Management Development Program (KMDP) was inaugurated in 2017, to support managers in developing best practices and management tools within the company's Leadership Model. Leaders from our subsidiaries around the world work together, in live (as pandemic protocols allow) and virtual classrooms learning more about leadership, creative thinking, and performance excellence. The fifth edition of the popular program commenced in April.



KMDP went far beyond my expectations. It is a program that enhances relationships with colleagues from different departments and cultures, encouraging networking of peers within the organizations. KMPD is a very complete program with excellent trainers, requiring a solid commitment from our side! A very appreciated opportunity!  
**Joana Silvério Marques, Sales Manager Portugal**

More than 80 candidates from all functions and geographies have participated in the five editions of the course. During 2021, participants who successfully attended the first three editions of the KMDP joined an advanced program called K-2025, which extended into 2022. The curriculum is devoted to the topic of "Growth vs. Fixed Mindset".



# BUILDING BRIDGES TO THE FUTURE



Perhaps the highlight of the year, and indeed a highlight of the company's history, was the acquisition of the Prometic group of companies of Laval, Québec, Canada.

When Kedrion announced the final agreement in its acquisition of Prometic in October, it represented the final step in a long journey of negotiations. And with that step the company added 130 new employees, a new plant, two new collection centers, a new product and a physical footprint in a new country.

It was a logical and mutually beneficial fit. The two companies

have been in discussions for some time regarding the development of therapies for the treatment of Congenital Plasminogen Deficiency, a rare disorder that results in the growth of "woody" lesions on any of the body's mucous membranes. Plasminogen is a protein, mainly produced by the liver and circulated in plasma, that helps regulate the body's blood-clotting process. Without it - or in inadequate concentrations - growths can occur anywhere, but primarily on the eye lids. This manifestation is known as Ligneous Conjunctivitis and usually appears in infancy. In its most severe development,

it can lead to blindness. Plasminogen Deficiency can also affect other areas with mucous membranes, including the mouth, the ear drums, the respiratory, gastrointestinal and female reproductive tracts, and - less commonly - the central nervous system. It can become life-threatening. Prometic had been researching a systemic treatment for Plasminogen Deficiency, while Kedrion has been working on an eyedrop therapy focused on Ligneous Conjunctivitis. The union of the two companies is further complementary in that Prometic has concentrated on

innovative Plasminogen isolation techniques and research, while Kedrion brings large-scale production experience. Arguably the most exciting aspect of this deal is that Prometic had finally achieved an effective treatment for Congenital Plasminogen Deficiency with Ryplazim® (plasminogen, human-tvmh), which received FDA approval in June 2021. Kedrion is offering this therapy in the US, beginning in 2022.

“

I would like us all to think of the patient and the impact on the quality of life that this new product will represent for the community of patients affected by Congenital Plasminogen Deficiency.  
**Paolo Marcucci, Kedrion Executive Chairman**

“

Finding ways to help people with rare conditions like Congenital Plasminogen Deficiency is a primary motivation for our work at Kedrion.  
**Roberto Crea, Kedrion Global Medical Affairs Director**

“

With this new drug Kedrion is showing our eagerness to grow. I think that this enthusiasm can be contagious to all the organization.  
**Gioacchino De Giorgi, Kedrion Corporate Business Development Director**



# CONGENITAL PLASMINOGEN DEFICIENCY



## THE PATIENT JOURNEY

### GRAHAM

When Rebecca and Ryan Bialas's son, Graham, was six weeks old, they noticed a growth under his left eyelid. Both Becca and Ryan are physicians and they were not alarmed, nor were their pediatrician or ophthalmologist. Their pediatrician suggested it was probably a blocked tear duct. Still no worries. But when it did not get better, they eventually took Graham to see an ophthalmologist, who thought it might be from an adenovirus infection and recommended surgically removing the lesion.

Patient and caregiver testimonials are presented for illustrative purposes only. Course of disease and results may vary.

Rebecca



Unfortunately, the growth came back as soon as it was taken off and it came back more quickly and larger. And this happened a couple of times.

We weren't really sure what was going on. We were doing what the ophthalmologist was suggesting, but it wasn't going very well. We were getting more and more worried and our son, Graham, his eye, it just looked very red. He had light sensitivity and he had a lot of tearing, and this went on for about five or six months before we just felt like we had to get a second opinion.

During this time, we'd been doing research ourselves and there's not a very long list of things that can cause this kind of a growth in a little baby under their eyelid. But one of the things that came up was this very rare diagnosis called Ligneous Conjunctivitis. We now know it is a symptom of Plasminogen Deficiency. So, we got an appointment for a second opinion where we had done some of our medical training and we came with this idea of this diagnosis and talked to the doctor about it.

And in fact, that's what it turned out to be. So, all in all we had about a six month journey from symptom onset to diagnosis. It was an extremely emotional time and it was very scary. We felt very lonely. And then when we got the diagnosis, it was also very scary because it is so rare that we really didn't know what to do with this information. And it was just this, you know, whole new world that we felt like we had to venture into without a lot of knowledge.

Ryan



And, you know, going from your pediatrician or pediatric ophthalmologist telling you that your child has just pink eye or a bad case of conjunctivitis to going down the road that they have this ultra-rare medical condition that is not just going to affect their eyes, but all kinds of other organs. And that can be life threatening. And we don't have a treatment for, it was the most terrifying thought for parents; it was horrible. I've had to make many diagnoses in my medical career, and this was the most terrifying one that I've ever had to deal with.



### SARAH

For the parents of Sarah Bein, this agonizing time of searching for answers was very much longer: 20 years between symptoms in infancy and diagnosis. And Sarah's symptoms were even more severe than Graham's (and her brother, Zach, suffered from the same condition). Her father, Marshall, also a physician, and her mother, Dawn, were at a loss.

Marshall



I'm a doctor, but this is a rare disease with no known cause. And we went through many, many different kinds of treatments. We found that it was extremely exacerbated during any time of colds. Whenever they had colds or flu, these membranes would explode on their eyes, requiring more surgeries. We tried all sorts of different kinds of antibiotics. We tried steroids, Cyclosporin. There were just so many things we tried, none of which were successful. And so yes, it was difficult. It's impossible to describe how difficult it was.



Sarah’s symptoms went far beyond her eyes.

Sarah



*I don’t really remember a time where I felt like a normal child, ever since I can remember my experience was really very much clouded by discomfort and fear. I knew something was wrong with me because I was completely different from my friends. And I was very acutely aware of that. Until I was eight years old, my symptoms were primarily in my eyes. Although I also had terrible stomach pain. I remember waking up, screaming in stomach agony. And of course, now we know I was having, um, ulcerative gastritis tiny little erosive lesions in my entire GI tract. So that was also going on when I was very little, but we didn’t associate that to the disease until much later down the line. I was in pain all the time because I had these thick lesions in my eyes.*

*They were always dripping. Sometimes it was daily where they would be trying to debulk them and cut them back. But of course, you know, they would just grow, grow right back. I remember lots of different eye drops and treatments and just a very scary, scary way to grow up. Everywhere I went, I was afraid to be seen. I did a lot of hiding behind my mom. So that was my experience, until about eight.*

*And that’s when that was a real turning point for our family. We went on a trip to visit my grandparents, and I just remember coughing and coughing and coughing. And I had never experienced anything like this before. I couldn’t really breathe, and I couldn’t stop coughing. We didn’t know what was going on. And, I can remember clear as day: it was the middle of the night and I was coughing and I heard this pop sound. And then this whooshing of air and I went into the bathroom, and I turned on the light and my whole face and neck was just puffed up like a balloon.*

*I was in the ICU for a couple weeks and they had no idea what was going on. Other than that I had popped a hole in the lining of my lung. And so all the air was escaping.*

*It was at that point that they saw over 90% of my trachea was occluded, but they didn’t know why or what. And that was the beginning of a whole new phase of this for our family, because now we didn’t know what was wrong and we did know this was no longer a disease of the eyes. And I remember thinking, what’s going to happen to me. I didn’t think I would live into my teens, let alone where I am now.*

As the years went by Sarah’s symptoms just got worse.

*By the time that I received treatment in the clinical trial, I had lesions in every place I possibly could: my eyes, my nasopharynx, my nose, my gums. I had lost a couple of my back teeth, because when the gum lesions just sit there for all those decades, the chronic inflammation erodes*

*the bone tissue. I had lesions in my vocal cords for many years, my trachea. By the time I received treatment, my right lung was completely collapsed and full of disease. I had a very large ulcer in my stomach. I had disease in my uterus and my fallopian tubes, and I had two big lesions, one in each kidney.*

As Rebecca and Ryan continued their research, trying to learn as much as they could about Graham’s condition and any possible therapies, they inevitably came across Sarah and her family, for this challenging world is thankfully quite small. Learning Sarah’s story was both terrifying and hopeful. Despite all her trials, she had become a psychiatrist.

Rebecca



*Sarah and her family have been a real inspiration to us. I mean, look what Sarah has gotten through. Sarah’s so brave and accomplished. And despite all of the challenges that she has had in her life, she has achieved so much.*

*She gave us hope that even if there was never a treatment that Graham could have some real attainable dreams in his life that he could hopefully accomplish, like Sarah has accomplished despite all of her challenges. So for us, talking to Sarah, it was scary and sad, but we took a lot of inspiration from Sarah too.*

By the time help came, Sarah had suffered for 37 years, endured more than 100 surgeries and was near death several times. Graham’s young life was just getting started and his parents were fearful for his future. And then...

## A BREAKTHROUGH

By 2015, Sarah and her parents had made contact with Dr. Amy Shapiro, a Pediatric Hematologist-Oncologist at the Indiana Hemophilia and Thrombosis Center (IHTC). Dr. Shapiro brought hope to the Bein’s and eventually to the Bialas’s. Working with Prometic, she was designing a study to determine the effectiveness and safety of a promising Plasminogen replacement therapy infusing the Plasminogen protein intravenously. Sarah was enrolled in the study.

But Sarah almost did not make it through.

Sarah



*Amy’s assistant called me on a Thursday, saying we’re ready for you for phase one. And I was truly on a plane Friday night. My first infusion was pretty remarkable: all kinds of things happened to my body that we weren’t prepared to see happen. And then I went home with so much relief.*

*Unfortunately, between phase one and phase two, I got even more sick. I really wasn’t sure I was going to make it to phase two. I think what happened after phase one was that my body started to heal but couldn’t finish healing. So, then the disease grew back with such a vengeance that then my lung really got far worse in those five months. I was completely dependent on a nebulizer treatment four or five times a day just to keep breathing, clearing all of my lung secretions, because my right side was so collapsed*

*and filled with membranes. At that point I was needing surgery every two to three months to keep me going.*

*I remember the night the call came; we were waiting and it really was down to the wire. Amy and her team were doing everything they could. So much red tape for these clinical trials. She got approval to go ahead at like six at night. I remember boarding the plane and just feeling like, okay, if I could just get on the other side and get to Amy, that I would be okay.*

*Nothing could have prepared me for what happened when we started phase two. Before you do an infusion, you have to do a physical exam. So, I remember vividly her examining my lungs. And at that point I could only just sort of cobble a little breath together and it was crackling and mucus-y and awful.*

*I have a picture of her giving me that infusion that night. And it was truly within fifteen minutes that I could take a full breath. I remember saying to*



her, “Amy, I can breathe. I’m breathing!” And she didn’t believe me. I said, “Get behind me, take a listen. I can breathe. I took a full breath, and she went, “Oh, oh my God!” And sure enough, it’s like the lesions just melted off.

And I turned pink! You know, when I came in, my lips and my skin were a little bit blue and I wanted to look and see, because she was saying, “You’re pink, you’re pink!” And I looked and you know, I just really felt like I was being brought back to life and in those first few days, I shed lesions from all everywhere. It was just a complete metamorphosis. So that was my first infusion, and I brought my nebulizer with me to Indiana and I threw it away. I never needed it. I didn’t need it after my first infusion. I chucked it.

In the meantime, Rebecca and Ryan had learned about Dr. Shapiro through Sarah. After visiting the researcher in Indianapolis, she recommended fresh frozen plasma (FFP) eyedrops, which contain a small amount of Plasminogen.

Rebecca



We dropped his eyes every two hours, and it slowed the growth, but it didn’t stop it. So these lesions continued to grow. And there were a few times where he had to have what we call debulking procedures, where we weren’t taking off the whole lesion and causing a lot of trauma. We were just taking off the part that was getting really big, that was obstructing his vision or preventing his eyelids from closing all the way, or potentially scratching his cornea.

Every two hours. For more than two years.

Eventually, they were able to enroll Graham in a trial for Kedrion’s Plasminogen eyedrops. Still every two hours, but the results were significantly better. They stopped the growth and were shrinking it slowly over time. Unfortunately, relief was short-lived. Graham developed some hoarseness and it was determined that he was growing lesions on his vocal cords and in his trachea. If they continued to

grow, they could potentially be life threatening.

It was Graham’s turn to try the infusion.

Rebecca



We were staying in a hotel in Indianapolis, and he had his infusion and they observed him for a while. And then we went back to the hotel for the evening. We were just playing with Legos on the floor. And I remember listening to him talk to me and thinking, you know, he sounds normal. He doesn’t sound hoarse anymore. And I texted Amy Shapiro, “Maybe I’m just being optimistic, but I think he sounds normal!” I mean, his vocal cord lesions responded immediately, just as Sarah described. It was - is - really as miraculous a treatment as we could ever have hoped for.

## RELIEF. GRATITUDE. ACROSS THE BRIDGE.

Ryan



When this diagnosis was made, I didn’t know if Graham was going to survive or how long his life was going to go. We met Sarah and I was like, Graham is going to be able to do whatever he wants. And we met Amy and our, my hopes, improved even more. And then when we found this replacement therapy and it worked just like a miracle for him, it was life changing. So I’m just so thankful that it, it exists. And so thankful that folks at Kedrion have taken up this cause and are doing all the wonderful things that they’re doing. I can’t put into words how thankful I am that this is happening.

Rebecca



To everyone who works for and with Kedrion on behalf of my family, on behalf of the Plasminogen Deficiency Foundation, just the biggest thank that we can offer. This treatment has given us hope that we can move forward with a future for our children and other patients with this disorder. What you do matters when you come to work each day, what you do is making a difference, and we see it and we thank you for it.

Marshall



It’s really impossible to communicate the depth of our gratitude and appreciation to the Kedrion family. As two parents who’ve suffered to this extent for 20 years before even the diagnosis was made and then waiting for the treatment... just untold gratitude and appreciation.

Sarah’s mother, Dawn, expressed her gratitude most succinctly:



How would I begin to say thank you? I’m overwhelmed. I won the lottery. Can you imagine? Thank you for letting me win the lottery!

We are extremely proud and grateful to be able to supply this breakthrough therapy, developed by the intuitive insight and determined hard work of the people of Prometic.





## SPREADING THE WORD.

When Rebecca and Ryan were at the point where they could breathe a sigh of relief, they didn't simply relax. Rebecca: "We felt that we had, at that point, the knowledge and the time to put together a nonprofit foundation with the primary goal being to basically spread the word. I would say the first step in anything like this is education. So educating doctors to be aware that this diagnosis exists, helping people to understand how to diagnose it and what to do, but also what not to do."

Thus was born the Plasminogen Deficiency Foundation.

"We want to help patients to get a diagnosis more quickly with less trauma and bring them to treatment, now that there is a treatment available, as soon as possible".

The Foundation board includes Rebecca and Ryan as well as Sarah Bein and Dr. Amy Shapiro. The Foundation website, [Plasminogendeficiency.org](https://plasminogendeficiency.org), offers "as much information as we can to help people who want to learn about this disease and find it in easily digestible, plain English. We've accomplished a lot in the short time that we have been together and we have great ambition to do even more in the name of serving patients and helping people to get the care that they need".



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## AND IN ITALY...

The development of effective treatments for Congenital Plasminogen Deficiency make education about the condition critical. Rare diseases are often missed in diagnosis precisely because they are so rare. And Plasminogen Deficiency is described as "Ultra-Rare". Educating caregivers of all kinds – ophthalmologists, surgeons, pediatricians, nurses, etc. – as well as pharmacists, researchers, biologists, etc., might lead to a dramatic expansion of relief for people suffering from un- or mis-diagnosed conditions.

To this end, in 2021, Kedrion supported an educational seminar on "Congenital Plasminogen Deficiency: Ligneous Conjunctivitis" with an unconditional grant. The virtual event, organized by the Italian Association of Ophthalmologists (AIMO) in cooperation with the Italian Federation of Rare Diseases (UNIAMO), allowed a broad sharing of knowledge of Ligneous Conjunctivitis among clinicians and healthcare professionals. It promoted additional research as well as enhanced relationships between patient associations and other stakeholders.

Patient and caregiver testimonials are presented for illustrative purposes only. Course of disease and results may vary.



# OUR NEW CANADIAN FAMILY



Acquiring a company is more than simply adding buildings, offices, production facilities and products to our list of assets. Most profound – and arguably most important – are the people. And of course, we don't acquire them; we welcome them into our family.

The employees of Prometic bring a proud tradition of working hard to help others and an optimistic enthusiasm for their new community.

"We welcome 130 amazing new colleagues based in our new plant in Laval, Canada," proclaimed Kedrion Executive Chairman, Paolo Marcucci "Bienvenu!"



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Why do I like to work here?  
For the adventure! And the great opportunity to develop a new product and put it on the market.

**Chantale Boisvert**



I'd like to thank the team at Kedrion for putting us in contact and pairing us with the wonderful Global QA team. We have an extraordinary, transparent, honest relationship with them, and we know we can count on them during the transition.

**Josée Leblanc**



The reason I love working for the Laval facility is the people, and the teamwork.

**Joanne Iuticone**



The reason why I am proud to work at Prometic is because every day I come in to work I have a meaning.

**Kathleen Gauthier**



It's an inspiration to just continue to work hard and get the product to more patients and have no interruptions. It's a connection between humans, real life and science; and it's just incredible!

**Maryse Laliberté**



I love being part of Kedrion's family because it's not just about working in a company but about changing and transforming lives. Thank you Kedrion group for believing in Prometic, in our people and in our product.

**Claudia Hernández Landaeta**



It is great to see how people from different parts of the world share the same vision and is dedicated to this noble mission of saving lives. This truly creates a family environment and provides meaning for all we do. I'm actually enjoying more working every day!

**Maria Rodríguez**



# OUR DONORS

## WHERE THE BRIDGE BEGINS

It is self-evident that our mission to help patients with serious and rare conditions starts with and depends upon a reliable and consistent supply of blood plasma. That supply is in thanks to the

generous donations of donors – in the US through our 30 collection centers and in Italy through the Italian National Health System. The pandemic has had especially profound implications for donors: any

close setting, much less such an intimate one as blood/plasma donation, is disquieting, and the mere logistics of getting to and from a collection point has often been significantly complicated.



“

I continued donating plasma during the pandemic because KEDPLASMA kept the center clean and always made me feel safe donating. The compensation I earned also helped me through a crisis. I will continue to donate at KEDPLASMA.

**Nikatto Durggin, Mobile, AL (USA)**

“

During the pandemic, I lost friends and family members to Covid-19, and many people were laid off at my job. Donating plasma helped me feel more secure if anything were to happen with my job. I also have friends and family with autoimmune diseases who benefit from plasma donations.

**Faith Norris, Altoona, PA (USA)**

“

Working through the height of the pandemic was challenging. We as a team worked together by promoting and implementing safety precautions. Donors who came in to donate and witnessed our precautions felt more at ease and continued to come back and donate.

**Tiffany Coleman, Mobile, AL (USA) employee**

“

I've been donating and working during the entire pandemic. My mother donated blood and plasma until she passed. I do not donate for the funds; I donate to help save lives. I understand how people were scared but I wanted to do my part in helping others. When coming to KEDPLASMA during the pandemic, they made sure everything was clean, staff wore masks and were always positive when I donated. They made me feel safe and that is the reasons why I continue to donate.

**Joseph Kaulsky, Bradenton, FL (USA)**

“

A lot of people were scared and going through rough times during the pandemic. Since I've started, we have made sure to support each other by assisting with covering shifts when they would be out sick or dealing with family members who were affected by the pandemic. When it comes to the donors, we ensured their safety by wearing our masks and making sure all areas were cleaned between donations.

**Zya Mitchell, Bradenton, FL (USA) employee since May 2021**

The good news is that donations leveled and began increasing in July and did so every month through the end of the year, so the future looks very promising.

KEDPLASMA took notable action against the decrease when it adopted a new, more efficient, more “donor-friendly” collection system. The Persona® System calculates collection volume for each donor based not simply on body-weight, as in the past, but on “a novel, personalized percent plasma nomogram based on body mass index and hematocrit (volume percentage of red cells in the blood), enabling a more tailored collection target using individual donor characteristics.” This individualized system increases efficiency, enhancing overall collection volumes while reducing potential impact on the donor.

Of course, the pandemic was addressed with safety protocols as well. It is a fundamental commitment of KEDPLASMA to make the donation experience as safe and as comfortable as possible.

As part of the acquisition of Prometic, Kedrion gained a new collection center in Amherst, New York. The Amherst center is now the second KEDPLASMA center in the Buffalo, New York area. Its growth pattern was significantly impacted by both Covid-19 and the sale of the Prometic business, but KEDPLASMA Managing Director, Helen Nasser reports that collection numbers have steadily risen and the center has very promising potential. It is anticipated that we will be adding several new, internally developed centers in 2022.



# ITALIAN DONORS

Plasma donation in Italy was similarly challenged in the face of the pandemic. In solidarity with Italy's National Blood System, the donor associations and the donors, we were happy to renew our support when Italy hosted the World Blood Donor Day, which had been postponed in 2020.



Kedrion will continue to stand by the Italian National Health System, defending and supporting the goal of self-sufficiency in plasma-derived products by increasing plasma collection.  
**Chiara Montingelli Marcucci,**  
**Marketing Manager, Italian Contract Manufacturing**

We continued in 2021 our dedication to partnering with the Associazione Volontari Italiani del Sangue (AVIS), the Association of Voluntary Italian Blood Donors, the major Italian charitable organization for blood donation. For the seventh year, we supported the National Training School organized by AVIS with the Fondazione Campus di Lucca. The school seeks to increase the level of awareness among upcoming generations of the donor community about the management of non-profit organizations, the ethics of giving and the various models of blood systems in Europe.





# OUR PATIENTS AND THE BRIDGES WE OFFER THEM

In a world faced with a pandemic as well as environmental pressures that directly affect the global health system, it is often patients and caregivers who face the greatest challenges. This has made it all the more compelling that we re-commit to our patient-centered mission every day: in every therapeutic area in every country we continued to build bridges to a better life for our patients.

## RARE DISEASES IMMUNOLOGY / NEUROLOGY

### Immunology

■ In 2021, the Association for Primary Immunodeficiencies (AIP) celebrated its first thirty years of activity in Italy. On the occasion of this anniversary, AIP awarded Kedrion a plaque in recognition of its strong and lasting commitment to the Association and to patients in over twenty years of collaboration.

■ In the United States, in addition to supporting the Annual Conference of the Immunoglobulin National Society (IgNS) held in Las Vegas this fall, we reaffirmed our support for the American Immu-

nodeficiency Foundation by participating in the 2021 IDF Annual Meeting and the IDF Education Forum, a virtual initiative aimed at promoting awareness of this rare disease group among healthcare professionals, patients and caregivers who are involved in the treatment pathway.

■ At the Hungarian Association of Allergology and Clinical Immunology Congress held in June in the city of Kecskemét, we supported a scientific symposium on biological therapies in patients with Systemic Lupus Erythematosus (SLE).

■ We extended our commitment in the field of Immunology to Turkey, where we promoted a webinar on Primary Immunodeficiencies for the local medical community, encouraging the exchange of knowledge and experi-

ence among participants. We also participated in the remotely held 7<sup>th</sup> Turkish Clinical Immunology Congress, where we supported a satellite symposium on the topic.

■ In 2021, we continued our partnership with the International Patients Organization for Primary Immunodeficiencies (IPOPI) through an unconditional grant for the development and launch of “4ID”, a new mobile application developed by IPOPI to help pa-

tients with Primary or Secondary Immunodeficiency around the world to more easily monitor their health status.

### Neurology

■ As part of its continuing commitment to the medical and scientific community involved in the neurological field, Kedrion was a Gold Sponsor in the Eleventh Annual Meeting of the Italian As-

sociation for the Study of the Peripheral Nervous System (ASNP), held in the autumn. We supported a scientific symposium that took a multidisciplinary approach to Peripheral Neuropathies induced by chemotherapeutic drugs.

■ In the United States, a long partnership with the GBS/CIPD International Foundation was evidenced in our support for the “Walk & Roll” events and by our

participation in the May awareness campaign promoting wider knowledge of Peripheral Nervous System disorders and research in the field.

■ To promote continuous updating of the latest research and developments in the field, we supported the third edition of the Neuroimmunology Academy in Vienna for specialists from countries in the DACH area (Germany, Austria, and Swiss) held under the auspices of the Evangelical Hospital of Vienna, Austria.

■ We supported several initiatives in Hungary, including a round table dedicated to Immu-

noglobulin-based therapies in the treatment of disorders of the peripheral nervous system, which took place in the city of Szeged.

■ And in Budapest, at the Congress of Pediatric Neurology, we supported a scientific symposium that addressed a number of topics, including Multisystemic Inflammatory Syndrome (MIS-C), which mainly affects children, and the general use of Immunoglobulins in this therapeutic area.

■ In Van, Turkey, we organized a medical-scientific meeting on the diagnosis and treatment of CIDP.





# HEMATOLOGY / HEMOPHILIA

■ “Words in Hemophilia: Towards Patient Engagement”, a project started in 2020, by the Engage-Minds HUB Research Center of the Catholic University of the Sacred Heart of Milan, continued through 2021, with unconditional support from Kedrion. A conclusory document defines key principles aimed at improving adherence to prophylaxis treatment through positive and effective communication between doctor and patient.

■ We supported a number of initiatives with the goal of stimulating medical-scientific discussion around therapeutic advances pertaining to Hemophilia and other congenital hemorrhagic diseases in Italy. These included a lecture on prophylaxis in patients with Von Willebrand Disease at the 2021 Annual Conference of the Italian Association of Hemophilia Centers (AICE) in Rome.

■ At the European level, in addition to supporting the 2021 Conference of the European Haemophilia Consortium (EHC), we participated in the Annual Meeting of the German, Austrian and Swiss Society of Haematology and Oncology, held in Berlin.

■ The pandemic did not prevent us from participating in “Gears for Good,” a bicycle race held annually by the American Hemo-

philia Federation to raise funds for patients and families suffering from coagulation disorders.

■ We participated in several major national and international conferences in Turkey, including the 12th Eurasian Congress of Hematology-Oncology (EHOC) held in Istanbul, and the 18th International Congress of

Hemophilia held in Cyprus. On both occasions, we supported a scientific symposium dedicated to explaining the current and future roles of Factor VIII-based replacement therapy in the treatment of Hemophilia A.

■ In Latin America, in addition to supporting a scientific symposium dedicated to the

personalization of prophylaxis in Hemophilia on the occasion of the International Congress of the CLATH Group (Grupo Cooperativo Latinoamericano de Hemostasia y Trombosis), our efforts were mainly focused in Colombia, where we supported a number of medical-scientific webinars for local clinicians.



We have continued to support the Hemophilia community in Colombia, cooperating with patient associations and the medical-scientific sector to encourage and improve knowledge and training of those living with and treating this disease. The pandemic has been especially challenging to those suffering from a rare disorder. They have faced new and unprecedented challenges affecting all aspects of their treatment, from diagnosis to management.

As **Doctor Lida Milena Araujo Cabrera, a pediatric hematology-oncologist at the Club Noel di Cali Pediatric Clinic in Colombia** recalls, “During the pandemic, due to the preventive isolation measures, the management of hemophilic patient care underwent drastic changes and had to be administered virtually, and given the impossibility of carrying out regular checks of the joints, diagnosis of the overall clinical picture was made even more complex. Even if this did not lead to problems accessing treatment, there were nonetheless delays and a decline in the diagnosis of new cases of Hemophilia and Von Willebrand disease.”

The emotional effects of the pandemic led to further complications managing these bleeding disorders. Dr. Araujo Cabrera: “I remember the case of one boy

who had been brought up by his grandmother, who died during the pandemic. This left the boy in a deep state of depression, which resulted in his missing his Factor-based treatment. To avoid the risk of the boy abandoning his treatment altogether, with the obvious consequences, we had to intervene with visits in person and sessions with the support of a psychologist.”

Throughout the pandemic and everywhere we operate, we are proud of our commitment to maintain the highest level of dialogue and information exchange with and within the Hemophilia community, including patients, caregivers and advocates. In Colombia, Dr. Araujo Cabrera notes, “Kedrion proved its commitment to training the medical community by resorting to the use of digital technology and, at the same time, by encouraging participation in scientific studies and subsequent publication in industry magazines at national and international levels. It is important on the one hand to continue to support the continuous training of physicians and the world of research, primarily through publication of scientific articles; on the other, it is equally important to educate patients to take care of their own joints and encourage them to practice sport responsibly.”



# MOTHER AND CHILD HEALTH

■ In 2020, we launched the Mother and Child Health campaign to raise awareness among pregnant women, healthcare professionals and the general public about two diseases that still pose a serious health threat around the world: Hemolytic Disease of the Fetus and Newborn (HDFN) and vertical (mother-to-child) transmission of Hepatitis B. Currently, both of

these serious and debilitating diseases are easily preventable by screening all expectant mothers for high-risk pregnancies and by administering proper prophylaxis. But in many countries, access to these therapies is still scarce or non-existent. We initially focused our efforts on Asia, the Middle East and Africa; in 2021, we extended the campaign to Latin America, where the number of registered cases is still very high due to a general lack of awareness. We focused first on

Colombia, where we supported a medical-scientific webinar organized by the Colombian Federation of Obstetrics and Gynecology (Federación Colombiana de Obstetricia y Ginecología). ■ Of course, the Mother and Child Health campaign continued outreach activities in Africa, the Middle East and Asia. For example, in Pakistan, we supported a remote medical-scientific meeting for clinicians.



# CRITICAL CARE AND TRANSPLANTATION

■ In Italy, we renewed our commitment alongside Epatteam - an educational healthcare networking project entirely dedicated to liver transplantation and supported by Kedrion since its launch in 2017 - by supporting several initiatives, among which was the event entitled "Face-to-Face Meetings on Liver Transplantation: Comparing Opinions" held in September at the Renaissance Tuscany Il Ciocco Resort & Spa Hotel, in Barga in the province of Lucca. This event brought together the top Italian experts in the field for a discussion on the main challenges and the most current issues in this therapeutic area. ■ As part of Epatteam, during 2021, we also provided an uncon-

ditional support to the Epatteam Young Academy, a new educational initiative which was held as a series of virtual meetings for young specialists in the field of liver transplantation and hepatology.

“

My most sincere thanks to Kedrion for supporting this in-person event, because only by meeting side by side - after almost eighteen months of only meeting remotely - can we really remember and appreciate how important it is to exchange opinions and experiences in person and how many initiatives can arise from this type of direct and spontaneous interaction. **Dr. Stefano Fagioli,** Director U.S.C. Gastroenterology and Transplant Hepatology Unit at the Papa Giovanni XXIII Hospital in Bergamo, Italy

# TRANSFUSION MEDICINE

■ We continued our commitment to encourage the transfusion community in Italy to reflect on the process of viral inactivation of blood components and especially platelet concentrates. For example, we supported a lecture entitled "Pathogen Inactivation with Psoralens. Why are Clinics Important?" at the National Congress of the Italian Society of Hemapheresis and Cellular Manipulation (SIDEM) in Rimini. Another example was our support for the "Outbreak

Management One Year Later. How are the Regions Organizing Themselves?" round table during the 2nd Virtual Conference on Transfusion Medicine of the Italian Society of Transfusion Medicine and Immunohematology (SIMTI). ■ We also supported a number of scientific lectures in Italy on the topic of viral inactivation during two educational meetings organized by SIMTI - one of which was held in collaboration with SIDEM. ■ Our commitment to the field of transfusion is global, of course. In the United States, we participated in the Annual Conference of the National Infusion Center Association (NICA).





# OUR SUPPORT TO COMMUNITIES

The pandemic has encouraged us all to be more mindful of the needs of others, while at the same time making it often more difficult to reach out. It has been a fundamental basis of Kedrion's mission to support and give back to the people and communities with whom we work.

In Italy this has meant working with important non-profit organizations like:

- The Robert F. Kennedy Foundation of Italy, where we supported a fundraiser for human rights advocacy in Milan
- The Alessandria and Asti division of the Italian Association against Leukemia, Lymphoma and Myeloma (AIL), supporting their activities aimed at improving services and social-health assistance for leukemia patients.

Supporting initiatives and projects aimed at advancing scientific research and improving the training of the medical community, is a continuing commitment, especially when it comes to younger generations. Each year,

in collaboration with the Carlo Erba Foundation of Milan, we offer two scholarships in the name of Guelfo Marcucci, the founder of Kedrion, to young scientists for original research in Non-Onco-logical Hematology. This year's Guelfo Marcucci Awards went to Giulia Ceglie of the University of Rome Tor Vergata and Maria Teresa Pagliari, IRCCS Ca' Granda Polyclinic of Milan. Also in collaboration with the Carlo Erba Foundation as well as Fondazione Campus di Lucca, we initiated the Fabrizio Fabrizzi Awards, two scholarships young scholars who have distinguished themselves with research in the field of plasma and plasma-derived drugs. This first edition of the awards, which was also supported by the Plasma Protein



Therapeutics Association (PPTA) were given to Giovanna De Simone of the University of Roma Tre and Alan Zanardi from San Raffaele University of Milan. In addition, we supported a Master Degree at the University of Tor Vergata in medical-scientific education and we confirmed our support to PharmaMark, the Master's Degree in Pharmaceutical Marketing at the "PIN - University Center, City of Prato.

Responding to pressing international needs, Kedrion cooperated with the National Blood Centre (CNS) and a number of Italian Regions supporting donations of Factor VIII for the treatment of Hemophilia to Albania. We also provided logistical support for the delivery to Palestine of various plasma-derived drugs made available by the Emilia-Romagna Region.

The pandemic did not stop us from continuing our "Kedrion Cares" program in the United States, practicing social responsibility by supporting various local initiatives such as:

- The Seasons of Giving Campaign organized by Feeding America;
- The Heart Health Awareness Campaign;

- The Backpack Program promoted as part of the Back to School Project;
- The Adopt a Family for the Holiday Campaign.

KEDPLASMA employees also teamed up with donors to support Thanksgiving food drives in various communities associated with our collection centers.

In Hungary, as well, Kedrion was committed to good citizenship, supporting such activities as:

- Medicopter Alapítvány (an organization for air rescue during health emergencies)
- Gödöllő Fire Department (part of the National Directorate General for Disaster Management)
- Gödöllő Idősek Otthona (a nursing home run by the Municipality of Gödöllő)
- The Santa Barbara Hospital Foundation, Department of Pediatrics.

We continued our commitment to environmental protection and sustainability with our support of Treedom, a web-based platform promoting the planting of trees (to date, more than 3,000,000) in developing countries such as Kenya, Madagascar, Tanzania and Ecuador.



# THE PEOPLE OF KEDRION: THOSE WHO BUILD AND MAINTAIN OUR BRIDGE

Kedrion Biopharma is proud and fortunate to have a community of employees who faced the challenges of the pandemic with unwavering commitment to our mission to serve the needs of our patients. We salute them and their dedication with respect and gratitude.

## MARCO GUERRINI

Regulatory Affairs Manager  
Castelvecchio Pascoli, Italy

2021 was a very busy, and often very frustrating, year. There were days, weeks when balancing work activities and life management during the pandemic had become very complicated, and while smart working was an excellent tool that allowed us to work safely, it also meant that we had to re-adapt our “office” habits due, first and foremost, to the loss of human contact. The People Management Journey (a course offered by Scuola Kedrion) alternated between on-site and remote

attendance. The course was invigorating; it allowed us to share our personal difficulties with our colleagues and to share the actions we took to address these situations. The sharing, the awareness that you are not alone, and knowing that your colleagues are having the same difficulties, was very motivating.

## ROSARIO SANNINO

EHS Manager  
Sant’Antimo plant, Italy

During this year, I felt like I was immersed in an improvised theatrical performance, in

which my family, colleagues and friends asked me to play different roles without a script. I was asked to play a virologist and give information about the “numbers.” I was asked to play a safety manager and provide procedures to safeguard the health of the workers. Then I was asked to play a friendly service desk worker and to reassure people who were extremely worried. Then an entertainer, for children who didn’t know what to do at home (I was among those who sang on the balcony). And then I had to play a cook, but when I played this role, my family prayed even harder that it would all end soon! This play, despite everything, convinced me that being united (as a business and as a family) and being focused on the same goal leads to winning all of life’s battles, including a pandemic.

## NICOLA ROVAI

Senior Clinical Trial Manager  
Castelvecchio Pascoli, Italy

My experience at Kedrion started right at the beginning of the pandemic. So, I immediately began working remotely without the necessary in-person “knowledge” of colleagues that would have allowed me to establish connections and relationships very quickly. Nevertheless, I found that the people I met were very adaptable, and this enabled us to work very well together. I really enjoyed my experience

with Scuola Kedrion in late 2021. It allowed me to get to know many colleagues personally, some of whom I had only met via Webex. It was definitely inspiring.

## SCOTT BECKER

Maintenance Manager  
Melville plant, USA

Melville is a 24/7 facility and many of our workers, including our maintenance team, are essential workers. Working at home is not possible: we must keep the plant running so we can produce the products patients need.

When Covid-19 restrictions continued in 2021, the maintenance team worked round the clock to keep things safe for the other essential personnel in the plant. People worked together to make sure shifts were covered, doing overtime and working longer hours. I’ve been at the facility for 24 years and am proud to be part of Kedrion.

## KATHERINE SCHEID

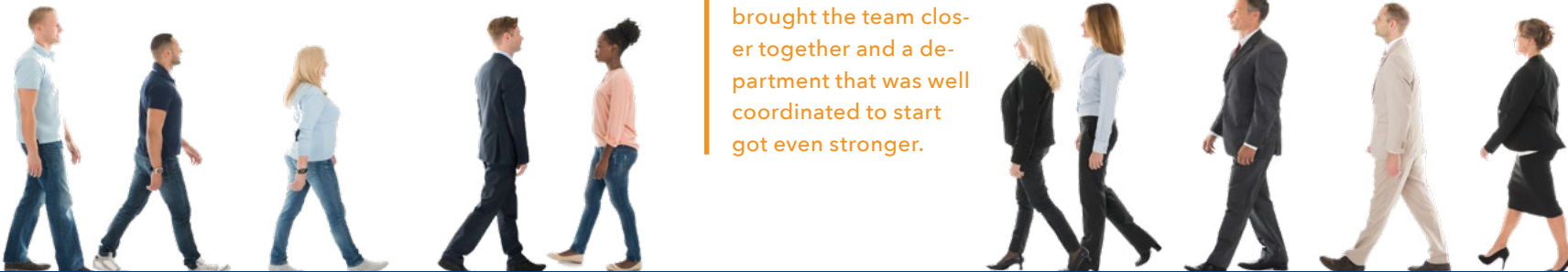
Validation Specialist  
Melville plant, USA

In 2021, we lost and gained several team members, including a manager, but the team came together to divide up the work and everyone was willing to lend a hand. These challenges brought the team closer together and a department that was well coordinated to start got even stronger.

## TERESA JONES

Sr. Hospital Specialty Manager  
Fort Lee offices, USA - home based

By 2021, Covid-19 fatigue set in and people were losing interest in remote meetings. We had to find a way to bring something more meaningful to the customer at the hospital or clinic, something that would benefit the patient. We found that focusing on events like National Pharmacy Week and Laboratory Professionals Week and working with groups like the National Nurses Society, we could provide value added by doing an in-service while recognizing their work.





# JACKIE REICK

Regional Sales Director  
Field, USA

In 2021 access started to open up in some states and we were able to get into some hospitals, working with pharmacy groups and emergency departments. Access varied from state to state so we still had to depend on virtual meetings in many cases. This type of contact is harder for some people than others, and I saw teams work together to help each other over challenges.

# AND IN HUNGARY

A clear indication that people are not merely navigating the challenges of difficult times like the pandemic, but actually thriving in them is the evidence that they are thinking about and planning for the future. A program in our Gödöllő plant encourages and rewards ideas that can lead to increased efficiencies in their work - an exercise self-evidently about the future. Viktor Gál, Thawing Supervisor at our Gödöllő plant, had his idea - to replace wasteful disposable protective suits with reusable cloth ones - before the pandemic but pursued its adoption right through it.

“

I submitted the original idea back in 2018. As a person working in the field, I also experienced how uncomfortable and how much waste it is to have to put on a new outfit every time you get in and out, which is done in the trash after about 30 seconds anyway. I think I'm environmentally conscious as much as possible.  
We dare to change the things because not only the company but also, we employees win at good ideas!  
**Viktor Gál, Thawing Supervisor, Gödöllő plant, Hungary**

Beáta Tóth is Project Coordinator at our facility in Gödöllő. When she realized that certain expensive testing procedures were being done needlessly on excipients (non-active ingredients), she acted to bring about change.

“

At that time I was leader of the microbiological control group where these tests were normally being carried out. It was closed at this time so we had to involve an external laboratory which resulted in significant additional cost.  
I made a risk assessment ending this testing and we followed the tasks required for the change in the change control process. When the result of the risk assessment was accepted, it became certain for me that it was feasible and from then on there was no question of introducing change. I am grateful to those who helped make the idea a reality. I'm sure there are a lot of similar ideas waiting to be implemented in a lot of areas, we just need to take some time to rethink our processes, in addition to our daily routine.  
**Beáta Tóth, Project Coordinator, Gödöllő plant, Hungary**





# ECONOMIC AND FINANCIAL INDICATORS





# SIGNIFICANT EVENTS OF THE FINANCIAL YEAR

## INTRODUCTION

The year ended December 31, 2021 generated a turnover for the Kedrion Group of 660.4 million Euro (697.2 million Euro in 2020), down 5.3% from the previous year due to the negative impacts of the Covid-19 pandemic, both in terms of reduced hospital treatments and reduced plasma availability. Despite these difficulties, which have affected the entire plasma-derivatives sector, the Group has consolidated its international positioning through an integrated business model that has enabled it to achieve turnover in around 100 countries, with an export share of 83.3% in 2021. The United States remains the leading market with a 43.3% share of turnover, followed by the countries of the European Union with 32.4% (with Italy at 16.7%) and the Rest of the World with 24.7%.

EBITDA amounted to 99 million Euro, with an increase in profitability from 13.8% during the previous year to 15.0% in 2021, boosted by the proceeds from the Ryplazim® product deal, despite the negative effects of the

Covid-19 pandemic, which impacted sales and non-recurring costs (within which 35.6 million Euro of Covid-19-related costs were recorded).

Adjusted EBITDA (calculated excluding the impact of non-recurring items) amounted to 139.0 million Euro, reaching 21.0% as a percentage of sales compared to 23.0% in 2020.

Finally, Net Income for the year was 13.8 million Euro, up from 6.0 million Euro in 2020 due to the growth in profitability and the improvement in financial management, with exchange rate differences having a positive impact on the result for the period of 10.8 million Euro (compared to a negative impact of 30.9 million Euro recorded in 2020).

## ACQUISITION OF RYPLAZIM®

In October 2021, Kedrion completed the last of a series of acquisitions related to the Prometic division, dedicated to the development and production of the product Ryplazim®, from the Canadian company Liminal Bio-Sciences.

This deal took place in several "business combinations" which began in May with the acquisition of the two companies, Prometic Plasma Resources US (PPR USA) and Prometic Plasma Resources Canada (PPR CAD), owners of two FDA-approved plasma collection centers, located in Amherst, New York (USA) and Winnipeg, Manitoba (Canada), respectively, and the exclusive option to acquire the rights to the drug and the manufacturing facility in Canada where it is produced, subject to the seller obtaining FDA regulatory approval for Ryplazim®. The Amherst center was fully integrated into KEDPLASMA's network of centers through the merger of PPR USA, which took place at the end of July 2021, while the Winnipeg center was sold to Grifols at the end of 2021, as it was not considered to be a strategic part of the Group's development plans.

Following FDA approval on June 4, 2021, Kedrion exercised the option in July by acquiring the Canadian company Prometic BioProduction Inc, owner of the Ryplazim® production facility and, in October, by acquiring the

US company Prometic BioTherapeutics Inc., owner of the FDA commercial license (Biological License), the orphan drug designation and intellectual property on the purification process and technology.

Ryplazim® is a plasma-derived Human Plasminogen, indicated for adult and pediatric patients for the treatment of clinical symptoms associated with Congenital Plasminogen Deficiency. This is the first approved therapy for this extremely rare disease, which can lead to blindness, respiratory failure and other serious complications.

The product was launched commercially with first sales taking place in January 2022 and is currently in the process of being approved for reimbursement by US patient insurers. At the same time, the manufacturing facility has started producing the first commercial batches and a gradual increase in production capacity is planned.

In addition to the product, Kedrion has acquired the intellectual property of a state-of-the-art pu-

rification technology, which could lead to further developments on other plasma proteins and has significantly consolidated its presence in the North American market, having, for the first time, a controlled company on the Canadian territory.

## COVID-19: EFFECTS AND MEASURES TAKEN

The Covid-19 pandemic, which went on in 2021 with new variants, continued to have a significant impact on the world economy, although to a gradually decreasing extent. Travel restrictions and quarantine measures continued, as did severe restrictions on hospital access and treatment not related to the pandemic emergency. Businesses continued to experience significant reductions in revenues and supply difficulties, although the economy withstood the impact, due in part to the financial support measures for individuals and businesses implemented by the various governments. The economy began to show important signs of recovery in the second half of the year, demonstrating its resilience and adaptation to





the containment measures, which were progressively loosened as a result of the vaccination campaign launched at the beginning of 2021 and the vaccination “passports” which were issued as a result.

The pandemic has also had significant and ongoing effects on the worldwide plasma-derivatives market and on Kedrion’s performance. In particular, the lock-down measures (“stay-at-home orders”) and the economic subsidy program have had a combined effect on the number and frequency of donations, especially for certain regular groups of donors such as students, contributing to an increase in the cost per liter of plasma collected, both due to the increase in the “donor-fees” paid to donors, and due to the greater influence of the fixed costs of the centers compared to the lower volumes collected. The closure of the US-Mexico border for all Mexican donors residing in border areas also impacted plasma collection in centers near the border. Donation collection trends rebounded in the middle of 2021, finally returning to pre-Covid-19 monthly levels toward the end of 2021.

On the product side, sales of Antirabies Hyperimmune Immunglobulins (KEDRAB®) on the US

market were again significantly impacted, following reduced exposure to infection due to the travel ban. Sales of Factor VIII were also impacted because the effects of the pandemic led to more home-based treatment. Finally, it should be noted that higher costs were incurred for safety and prevention measures (sanitization, protective devices, etc.) designed to ensure the continuity of production at the plants. In addition to this, the reduced availability of collected plasma, although sufficient to supply the production facilities, has negatively affected sales of third-party plasma, as described below, and has incentivized the search for foreign plasma contract manufacturing contracts. In November 2021, an agreement was signed with the French company LFB to fractionate over 100,000 liters of plasma collected as part of the self-sufficiency program in France, in order to produce 5% Intravenous Immunoglobulins under our Humaglobulin® brand produced in Gödöllő, Hungary, the processing of which began in December. Moreover, at the end of December, Kedrion S.p.A. won a tender for 250,000 liters of Polish plasma, a tender that provides that 75% of the Immunoglobulins produced from that plasma will be made available to the Polish market, which is starting to pur-

sue a policy of self-sufficiency similar to that of other European countries.

The pandemic was an opportunity for Kedrion and the Group to rethink their working methods, by promoting a progressive return to the workplace, in compliance with the law, together with extended and flexible forms of “smart working.”

**RHOGAM®” AND “KIG10” STRATEGIC PROJECTS**

The US plant in Melville, in addition to continuing to ramp up fractionated volumes, which reached around 700,000 liters in 2021, continued its filling and packaging activities for the RhoGAM® product, while waiting for the completion of the bulk technology transfer that will lead to the full internalization of the production cycle in 2022, according to the project timelines revised in response to the integration requests received from the FDA in 2020 with reference to our regulatory dossier (PAS). Project activities continued during the year in accordance with the plan, and PPQ batch productions are currently underway.

The increase in production at the Melville plant, for both the fractionation plant and the new RhoGAM® filling and packaging

line, led to a further significant improvement in the income statement for the year, primarily due to a reduction in unabsorbed plant costs, and also resulted in an increase in margins on product sales to the American market.

The income statement for the year includes non-recurring costs caused by the lengthening of the time required for FDA approval of the new RhoGAM® line, which forced the subsidiary Kedrion Biopharma Inc. to extend the contract with the current supplier of the finished product until the end of 2023 in return for payment of an “extension fee,” in order to avoid the risk of product discontinuity. It also did not allow absorption of the costs of the production structure that the subsidiary has already set up in accordance with previous plans. These events therefore led to non-recurring costs for the year, amounting to 9.0 million Euro.

During the year, the validation procedure for the production process continued at the new plant for the purification of the investigational product Klg10 (10% Immunoglobulin) using the chromatographic method in Castelvechchio Pascoli (Lucca, Italy). Clinical trials were also continued in preparation for the commercial authorization of the new product. During the year, activities relating

to the clinical trial for the PID (Primary Immunodeficiencies) indication on an adult population in the United States (the so-called “CARES10” trial) were completed and the final report for the study was obtained, in which no significant reactions were recorded. In addition, in April 2021, the enrollment and treatment of pediatric patients within the PID pediatric study in Italy, Hungary, Slovakia, Russia and Portugal (the so-called “KIDCARES10” study) was begun for the purpose of registering this indication in the United States and Europe.

Currently, production for clinical trials is carried out in the Gödöllő plant (the purification phase) and the completion of the technological transfer to the industrial plant in Castelvechchio Pascoli is underway. The validation activities have continued as planned, and in the coming months, batches of PPQ will be produced in Castelvechchio Pascoli in preparation for the regulatory approval expected to be received in the United States in 2024.

Project costs charged to the year that have not yet been balanced in production and related revenues amount to 2.0 million Euro, while total investments in 2021 amount to 23.1 million Euro.

**OTHER STRATEGIC TRANSFORMATION INITIATIVES**

For Kedrion, the 2021 was also a year of intense changes and planning efforts included in the “NEXT” program, launched in 2020 to improve the Group’s profitability and competitive position. The program, which was supported by qualified external consultants and an internal working group, has continued a series of initiatives to improve performance, efficiency and procurement excellence that had already been launched in the previous two years, particularly in the Operations, Commercial and G&A areas of the “plasma-derivatives” segment, including initiatives to increase yield and capacity and initiatives to restructure and simplify the company. Among these initiatives, it is worth mentioning the merger by incorporation of the subsidiaries Kedrion International GmbH (Austria) and Kedrion Portugal Lda (Portugal) into Kedrion Biopharma GmbH (Germany), which took place on June 11, 2021 with retroactive accounting effect as of January 1, 2021, and the simultaneous opening of commercial branches of the German subsidiary in Austria, Portugal and Poland in order to simplify the Group’s structure and therefore to consolidate operations and streamline local administrative costs.



**NEW BOND AND PARTIAL REPURCHASE OF EXISTING BOND**

In 2021, Kedrion S.p.A. completed the process of refinancing its existing debt.

This process resulted in the issuance of a new bond amounting to 410 million Euro with an issue price of 100%, maturing on May 15, 2026 and listed in the Euronext Dublin Official List. Interest on this new bond is payable half-yearly with an annual coupon of 3.375%.

The proceeds from the issuance of this new bond have been allocated to (i) the repayment of indebtedness under the Company's existing credit facilities, (ii) the financing of the 150 million Euro purchase of the Existing Securities pursuant to the tender offer announced by the Company on April 23, 2021 and (iii) the payment of related fees and expenses.

Along with this bond issue, Kedrion S.p.A. has also entered into a new loan agreement amounting to 240 million Euro.

The proceeds of this credit line will be used to refinance part of the Existing Bonds and to support any working capital requirements.

**DISPOSALS AND PURCHASES/ START-UP OF COMPANY-OWNED COLLECTION CENTERS**

During the course of the year, the business segment saw the sale of seven plasma collection centers in America and the center in Canada to the Grifols company, as well as the purchase during the year of five centers in the United States and the start-up of other centers, for a total of 29 company-owned centers at the end of the year, compared to 27 centers at the end of the previous year. In addition, three centers (Lincoln North, Springfield and Urbana) were opened and developed internally during the year and are now working to bring donations and collection levels up to capacity.

The sale of the assets of the seven US collection centers and one Canadian center, and the resulting transfer of all the risks and benefits connected with these centers, made an important contribution to the result for the period, recording an amount of around 24.7 million Euro among other income (last year the sale of the Hungarian centers led to the recognition of income of around 15.5 million Euro).

**REVENUES**

Revenues from the production and marketing of plasma-derived products segment as of December 31, 2021 amounted to 596 million Euro (+90.2% of the total) with a growth of 2.8%. The increase in the relative weight of this segment from 83.2% to 90.2% of the total is partly due to the decline in sales in the plasma segment due to the reduced availability of plasma caused by the Covid-19 pandemic, and above all, due to the excellent performance of certain products.

First among all products in order of importance were Standard Immunoglobulin, mainly due to the increase in average prices brought about by focusing on the most profitable sales markets, and Albumin, due to the price-volume mix, followed by Factor IX and Antirabies Immunoglobulin which managed to grow despite the reduced mobility caused by the continuation of the pandemic throughout 2021.

Within the segment, the US plasma-derivatives market maintained its strategic importance with 41% of total turnover with 12% growth. Europe had the highest growth rate, +29.6%, due to the performance of markets that are increasingly important for the Group (Germany, Austria,

Portugal and France), while Italy, as better detailed in the geographical breakdown of revenues, is declining due to lower volumes of plasma processed for the Italian National Health System.

The Rest of the World, with 26% of the total, took second place in terms of importance in the segment and registered a growth of 3%.

In addition to the production and sale of plasma derivatives, and the contract manufacturing service segment for the Italian Healthcare System, the contract manufacturing service segment for certain foreign countries is being consolidated. The contracts for these services were signed in 2021 and generated revenues during the year of 4.6 million Euro, the strategic effects of which in terms of revenues and plasma availability will be seen in subsequent years.

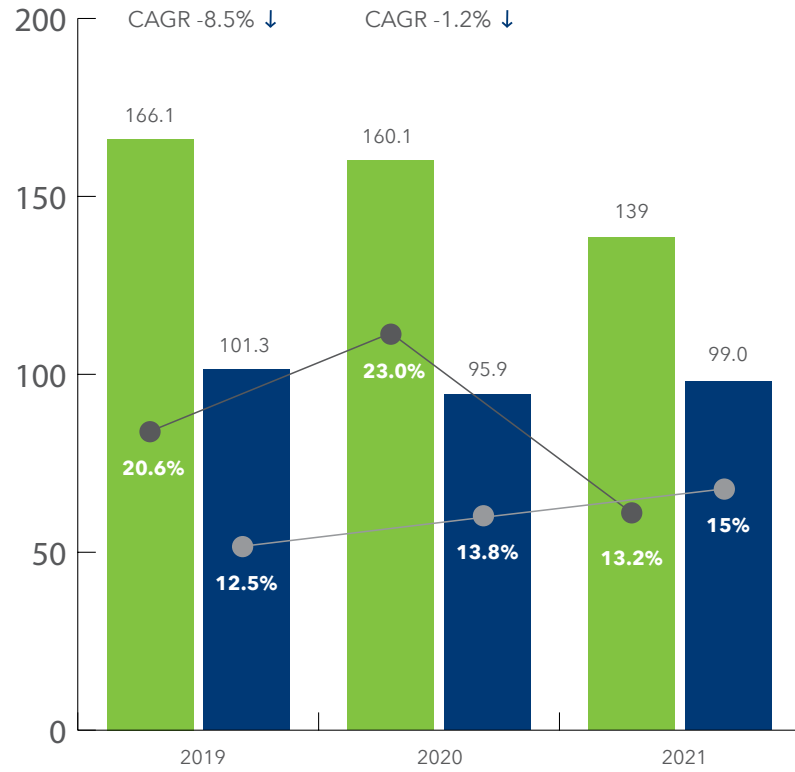
Revenues from the plasma collection and marketing segment as of December 31, 2021 amounted to 47.0 million Euro, a decrease of 50.2% from the previous year. This reduction is due to lower availability of US plasma related to a further decline in collection (-10% from 2020 due to the pandemic) and lower purchases of plasma from suppliers.





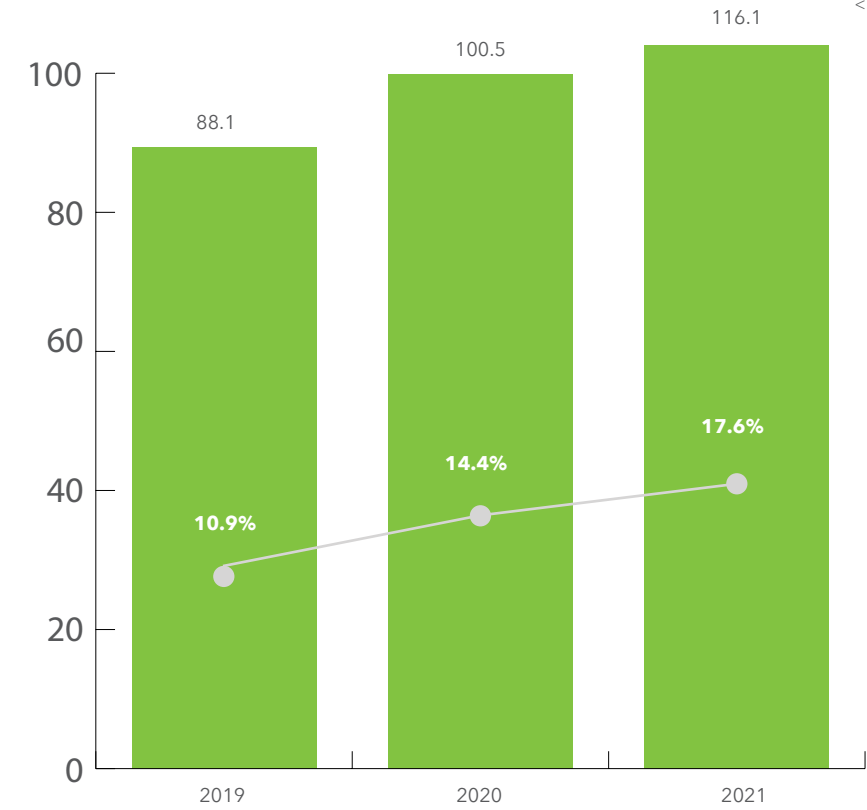
### ADJUSTED EBITDA (€ MLN) AND REPORTED EBITDA (€ MLN)

- ADJUSTED EBITDA
- REPORTED EBITDA
- % ADJUSTED EBITDA/  
REVENUES
- % REPORTED EBITDA/  
REVENUES



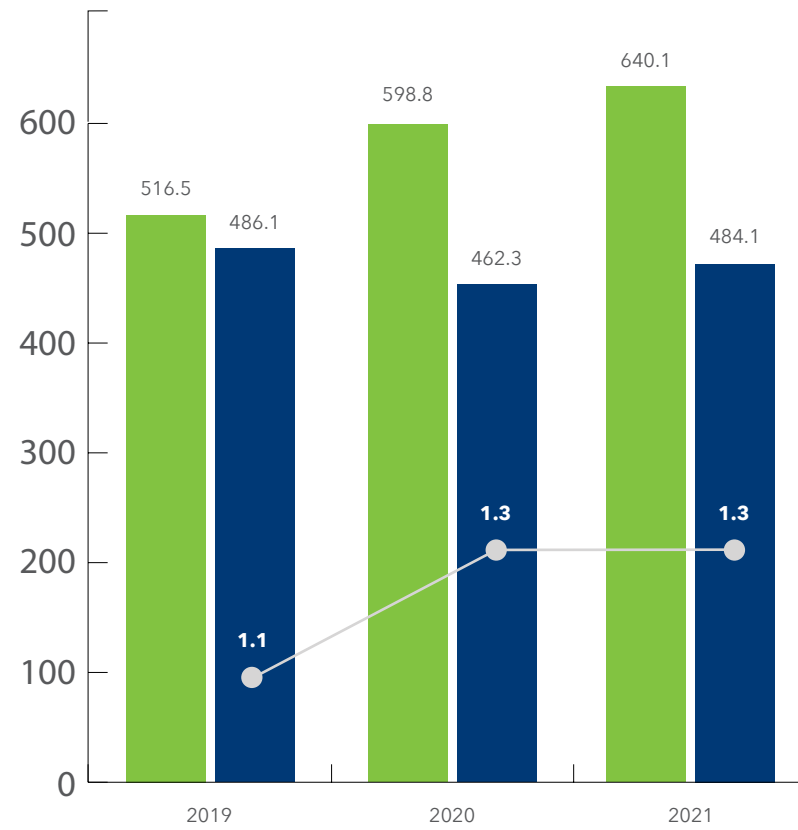
### GROSS CAPEX INVESTMENTS (€ MLN)

- % OF REVENUES



### NET FINANCIAL POSITION (NFP\*) AND NET EQUITY (€ MLN)

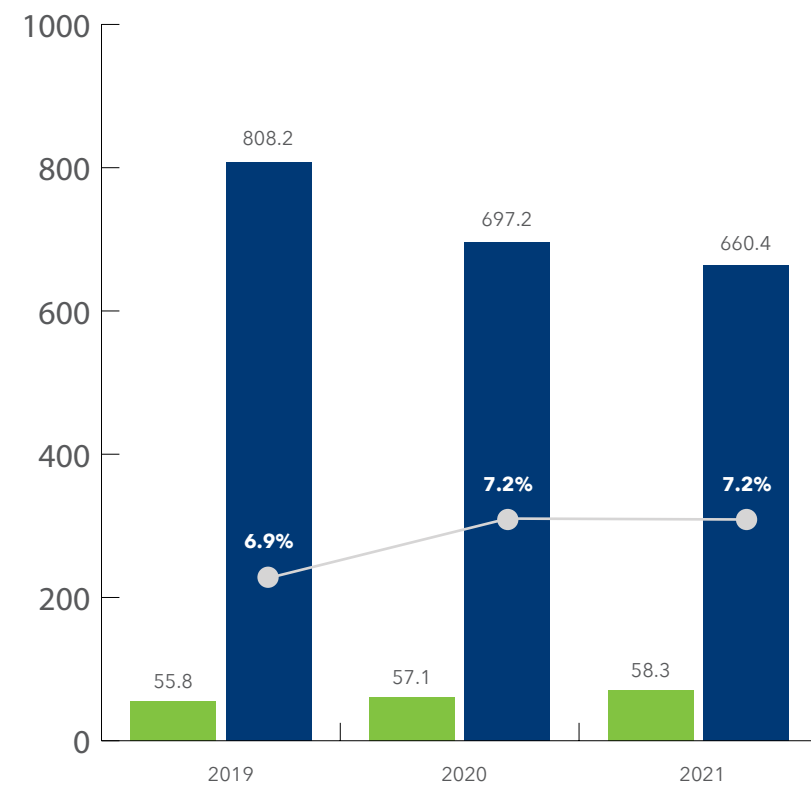
- NET FINANCIAL POSITION (NFP)
- NET EQUITY (€ MLN)
- NFP/NET EQUITY



\*NFP included the impact of IFRS16 of about 112.2 MLN

### R&D TOTAL EXPENDITURE AND INVESTMENTS (€ MLN)

- R&D
- REVENUES
- %







**THE UNITED STATES**

Plasma sales in this market slowed down slightly by -2.1% in 2021, as a result of the reduction in volumes available for sale. Plasma-derivatives led the growth with +12.2% in Euro (+16.3% in USD) of sales compared to the previous year. Standard Immunoglobulin remains the main driver of growth (+18.8%), followed by Albumin (+16.2%) and Anti-rabies Immunoglobulin which, despite the impact of reduced mobility due to Covid-19, recorded an increase in sales (+4%). Factor VIII and Anti-D Immunoglobulin experienced a decrease in sales volumes linked to the reduction in inventories by distributors and the decrease in hospital treatments, although this was partially offset by the increase in prices of Factor VIII as a result of the new sales strategy.

**ITALY**

The Italian market as of December 31, 2021 decreased by 26.6% compared to the previous year with a turnover of 110.1 million Euro, corresponding to 16.7% of total revenues, achieved through the sale of finished products on the commercial market and the contract manufacturing service for the Italian National Health System. The decrease compared to the previous year was mainly due to the decrease in the volume of contract manufacturing work for the Italian National Health System, which was partially offset by the start of foreign contract manufacturing.

**EUROPEAN UNION**

Revenues in other countries of the European Union amounted to 103.6 million Euro at December 31, 2021, or 15.7% of total revenues, an increase of 5.1% compared to 2020. Plasma sales to European customers fell sharply to 3.9 million Euro compared with 20.4 million Euro in the previous year due to lower product availability for sale. The lower sales of plasma were fully offset by the growth of plasma-derivatives (+29.6%) which was mainly driven by higher volumes of Standard Immunoglobulin (placed at increasing prices in this geographical area as well) and Albumin. Of particular note was the growth in the main markets (Germany, Austria, Poland, Portugal, France and Greece) which, by growing by a total of 10%, accounted for 90% of the segment's turnover.

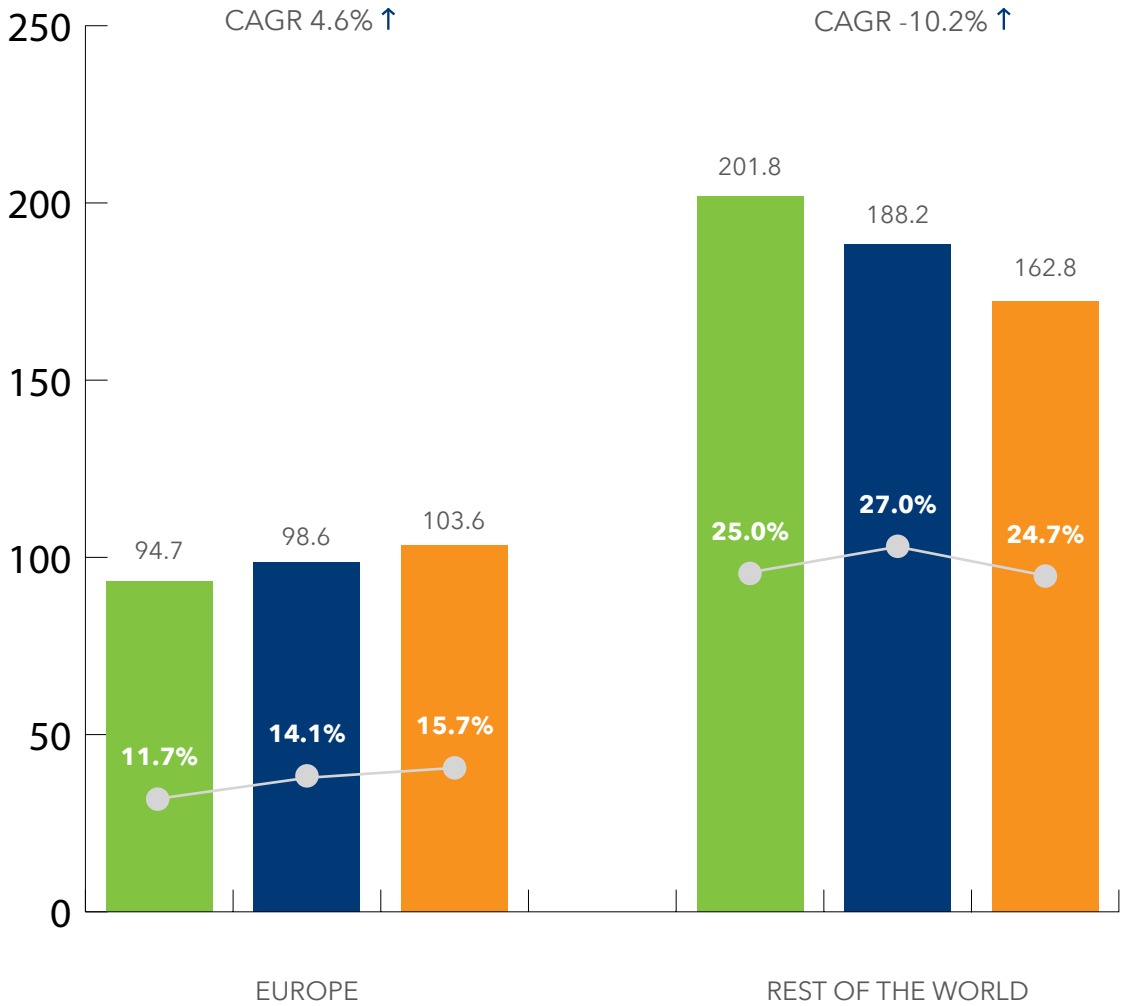
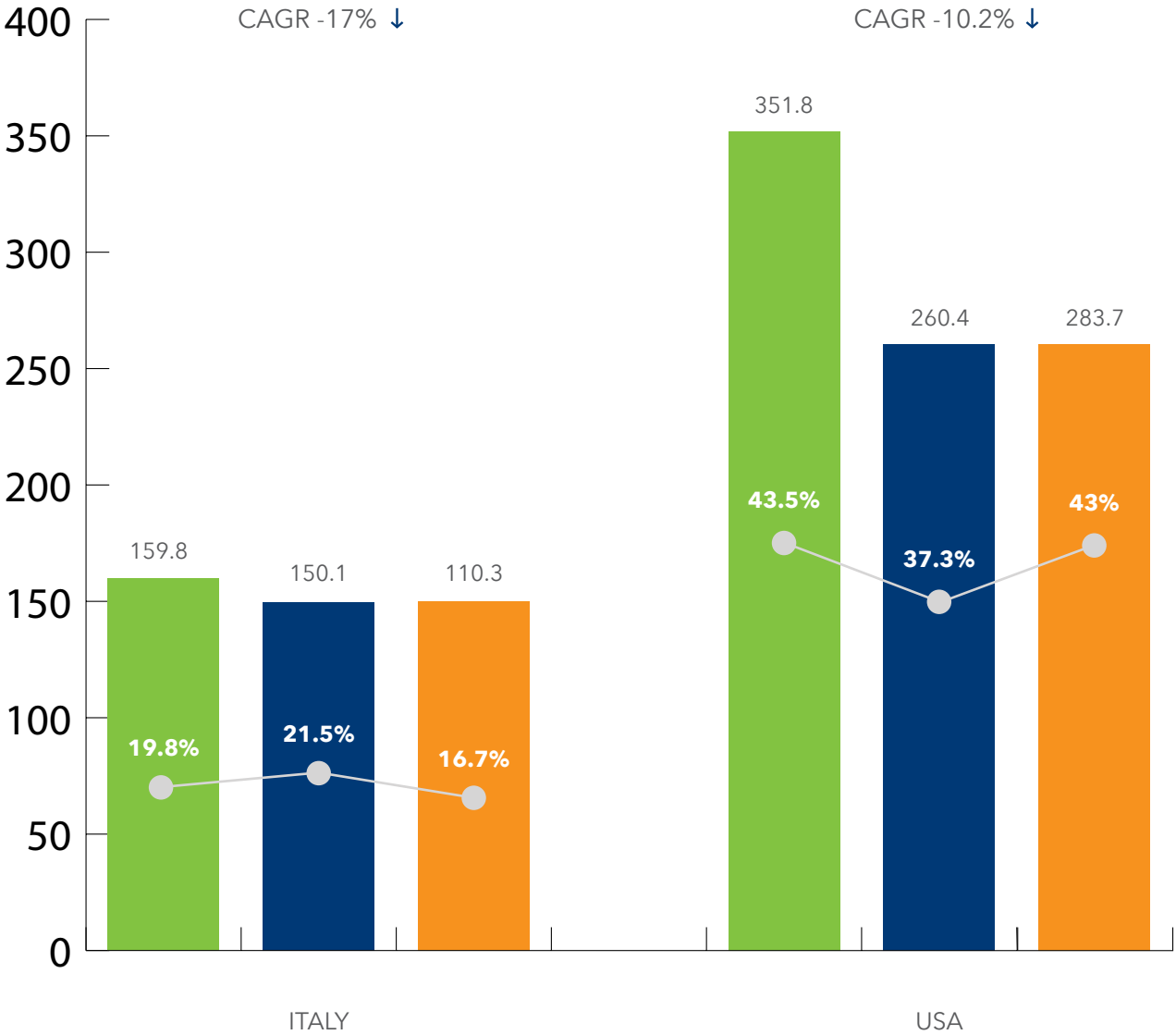
**THE REST OF THE WORLD**

Revenues for this geographic area as of December 31, 2021 amounted to 162.9 million Euro and represented 24.7% of total revenues despite a 13.4% decrease compared to 2020 due to lower plasma sales. The main markets served in the plasma-derivatives segment, which grew by 3.1% due to Standard Immunoglobulin, Albumin and Factor IX, are Mexico and Turkey.



**DISTRIBUTION OF SALES  
BY GEOGRAPHIC AREAS (€ MLN)**

2019 ■  
2020 ■  
2021 ■  
% ●





# FINANCIAL STATEMENTS

| CONSOLIDATED STATEMENT<br>OF FINANCIAL POSITION (In thousands of Euro) | 12/31/21                   |
|--|----------------------------|
| <strong>NON CURRENT ASSETS</strong>                                    |                            |
| Property, plant and equipment  | 322,150                    |
| Investment property  | 1,465                      |
| Goodwill   | 269,889                    |
| Right of use   | 106,476                    |
| Intangible fixed assets with a finite useful life                      | 162,133                    |
| Investments in other companies   | 20                         |
| Other non current financial assets                                     | 6,455                      |
| Deferred tax assets  | 10,009                     |
| Income tax receivables   | 1,783                      |
| Other non-current assets   | 945                        |
| <strong>TOTAL NON CURRENT ASSETS</strong>                              | <strong>881,325</strong>   |
| <strong>CURRENT ASSETS</strong>  |                            |
| Inventories  | 266,438                    |
| Trade receivables  | 133,354                    |
| Contractual assets   | 33,896                     |
| Income tax receivables   | 9,503                      |
| Other current assets   | 29,062                     |
| Other financial current assets   | 1,016                      |
| Cash and cash equivalents  | 134,200                    |
| <strong>TOTAL CURRENT ASSETS</strong>                                  | <strong>607,469</strong>   |
| <strong>TOTAL ASSETS</strong>  | <strong>1,488,794</strong> |

| CONSOLIDATED STATEMENT<br>OF FINANCIAL POSITION (In thousands of Euro)                | 12/31/21                   |
|---|----------------------------|
| <strong>SHAREHOLDERS' EQUITY</strong>   |                            |
| <strong>GROUP SHAREHOLDERS' EQUITY</strong>   |                            |
| Share capital   | 60,454                     |
| Reserves  | 409,332                    |
| Net profit attributable to the Group  | 13,823                     |
| <strong>TOTAL GROUP SHAREHOLDERS' EQUITY</strong>                                     | <strong>483,609</strong>   |
| <strong>SHAREHOLDERS' EQUITY ATTRIBUTABLE TO NON-CONTROLLING INTERESTS</strong>       |                            |
| Capital and reserves of non-controlling interests                                     | 2,737                      |
| Net profit attributable to non-controlling interests                                  | (2,210)                    |
| <strong>TOTAL SHAREHOLDERS' EQUITY ATTRIBUTABLE TO NON-CONTROLLING INTERESTS</strong> | <strong>527</strong>       |
| <strong>TOTAL SHAREHOLDERS' EQUITY</strong>   | <strong>484,136</strong>   |
| <strong>NON CURRENT LIABILITIES</strong>  |                            |
| Medium-/long-term loans   | 519,481                    |
| Payables to banks and other lenders   | 0                          |
| Provisions for risks and charges  | 778                        |
| Liabilities for employee benefits   | 3,707                      |
| Other non current liabilities   | 2,999                      |
| <strong>TOTAL NON CURRENT LIABILITIES</strong>  | <strong>526,965</strong>   |
| <strong>CURRENT LIABILITIES</strong>  |                            |
| Payables to banks and other lenders   | 50,052                     |
| Current portion of medium/long-term loans   | 212,241                    |
| Provisions for risks and charges  | 16,444                     |
| Trade payables  | 148,157                    |
| Contractual liabilities   | 6,253                      |
| Income tax payables   | 4,097                      |
| Other current liabilities   | 40,449                     |
| <strong>TOTAL CURRENT LIABILITIES</strong>  | <strong>477,693</strong>   |
| <strong>TOTAL LIABILITIES</strong>  | <strong>1,004,658</strong> |
| <strong>TOTAL SHAREHOLDERS' EQUITY AND LIABILITIES</strong>                           | <strong>1,488,794</strong> |



| STATEMENT OF PROFIT OR LOSS FOR THE YEAR (in thousands of Euro) | 12/31/21       |
|---|----------------|
| Revenue   | 660,384        |
| Cost of sales   | 516,380        |
| <b>Gross margin</b>   | <b>144,004</b> |
| Other income  | 103,820        |
| General and administrative expenses                             | 98,949         |
| Sales and marketing expenses                                    | 50,305         |
| Research and development expenses                               | 40,157         |
| Other operating costs   | 8,355          |
| <b>Operating Profit</b>   | <b>50,058</b>  |
| Financial expenses  | 61,573         |
| Financial income  | 31,410         |
| <b>Profit before taxes</b>                                      | <b>19,895</b>  |
| Income taxes  | 8,282          |
| <b>Net profit for the period</b>                                | <b>11,613</b>  |
| <b>of which:</b>  |                |
| <b>Net profit attributable to the Group</b>                     | <b>13,823</b>  |
| <b>Net profit attributable to non-controlling interests</b>     | <b>(2,210)</b> |

| CONSOLIDATED CASH FLOW STATEMENT (In thousands of Euro)                         | 12/31/21       |
|---|----------------|
| Net cash flow generated by operating activities (A)                             | 74,205         |
| Net cash flow absorbed by investment activities (B)                             | (53,311)       |
| Net cash flow absorbed by financing activities (C)                              | 13,172         |
| <b>Total net cash generated/(absorbed) flow D=(A+B+C)</b>                       | <b>34,066</b>  |
| Cash and cash equivalents opening balance (E)                                   | 100,584        |
| Net effect of conversion of foreign currencies on cash and cash equivalents (F) | (464)          |
| <b>Cash and cash equivalents closing balance G=(D+E+F)</b>                      | <b>100,584</b> |



## KEDRION SPA CORPORATE HEADQUARTERS

### REGISTERED OFFICE

Loc. Ai Conti, Castelveccchio Pascoli  
55051 Barga, Lucca (Italy)

### KEDRION SPA

Loc. Il Ciocco, Castelveccchio Pascoli  
55051 Barga, Lucca (Italy)  
Tel: +39 0583 767100  
Fax: +39 02 57763789  
E-Mail: [info@kedrion.com](mailto:info@kedrion.com)  
Website: [kedrion.com](http://kedrion.com)

### KEDRION BIOPHARMA INC.

400 Kelby Street, 11th Floor, Suite 1200,  
Fort Lee, New Jersey - 07024 USA

Tel: +01 (201) 242 8900  
Fax: +01 (201) 242 8913  
E-Mail: [us\\_contactus@kedrion.com](mailto:us_contactus@kedrion.com)

### PROMETIC BIOPRODUCTION INC.

531 Boul. Des Prairies, Bldg 15,  
Laval, Québec H7V 1B7

Tel: +01.450.781.4474  
Fax: +01.450.781.4474  
Email: [s.larabee@prometic.com](mailto:s.larabee@prometic.com)

### PROMETIC BIOTHERAPEUTICS INC.

400 Kelby Street, 11th Floor, Suite 1200, Fort Lee,  
New Jersey - 07024 USA

Tel: +01 (201) 242-8900  
Fax: +01 (201) 242-8913  
Email: [m.mackay@kedrion.com](mailto:m.mackay@kedrion.com)

### HUMAN BIOPLAZMA KFT.

Táncsics Mihály út 80.  
H-2100 Gödöllő (Hungary)

Tel: +36 (28) 532200  
Fax: +36 (28) 532201  
E-Mail: [reception@kedrion.com](mailto:reception@kedrion.com)

### KEDRION BIOPHARMA GMBH

Bahnhofstrasse 96  
82166 Gräfelfing, BY (Germany)

Tel: +49 (89) 7167715-0  
Fax: +49 (89) 7167715-98  
E-Mail: [info.de@kedrion.com](mailto:info.de@kedrion.com)

### KEDRION MEXICANA SA DE CV

Torre de los Parques Insurgentes Sur 1196,  
9° Piso Col. Tlacoquemécatl Del Valle  
Deleg. Benito Juárez CP 03200 Ciudad de  
México

E-Mail: [info@kedrion.com](mailto:info@kedrion.com)

### KEDRION BRASIL DISTRIBUIDORA DE PRODUTOS HOSPITALARES LTDA

Rua Desvio Bucarest s/n, Qd. 255, Lt. 11, Jd.  
Novo Mundo 74.703-100 Goiânia,  
Estado de Goiás (Brazil)

Tel: +55 (62) 32069044  
E-Mail: [info@kedrion.com](mailto:info@kedrion.com)

### KEDRION DE COLOMBIA SAS

Avenida Calle 26, No. 69D-91 Oficina 509  
Centro Empresarial Arrecife Bogotá D.C.  
Colombia

Tel: +57 19262052  
E-Mail: [j.beltran@kedrion.com](mailto:j.beltran@kedrion.com)

### KEDRION BETAPHAR BIYOFARMASÖTİK İLAÇ SANAYİ VE TİCARET ANONİM ŞİRKETİ

Çankaya Mahallesi Cemal Nadir Sokak No:18/1  
Çankaya/Ankara (Address code: 2705837017)

Tel: +903 124191527  
E-Mail: [info@kedrionbetaphar.com.tr](mailto:info@kedrionbetaphar.com.tr)

### KEDRION BIOPHARMA INDIA PRIVATE LIMITED

House No. R-265C, Ground Floor Greater Kailash  
Part-I, New Delhi 110048 (India)

Tel: +91 (124) 4069391/92  
Fax: +91 (124) 2567301  
E-Mail: [info@kedrion.com](mailto:info@kedrion.com)

### KEDPLASMA LLC

400 Kelby Street, 11th Floor, Suite 1200, Fort Lee,  
New Jersey - 07024 USA

Tel: +01 (201) 242-8900  
Fax: +01 (201) 242-8913  
E-Mail: [contactus@kedplasmausa.com](mailto:contactus@kedplasmausa.com)

# CONTACTS



# CREDITS

Photographs by  
Christian Sinibaldi  
with the contribution of  
Elisabetta Gianasi  
(page 4, 5, 7, 26, 41)









# KEDRION

B I O P H A R M A

**KEDRION SPA**

Loc. Ai Conti, Castelvechio Pascoli, 55051 Barga, Lucca (Italy)  
Tel: +39 0583 767100 | Fax: +39 02 57763789 | E-Mail: [info@kedrion.com](mailto:info@kedrion.com)  
Website: [kedrion.com](http://kedrion.com)