

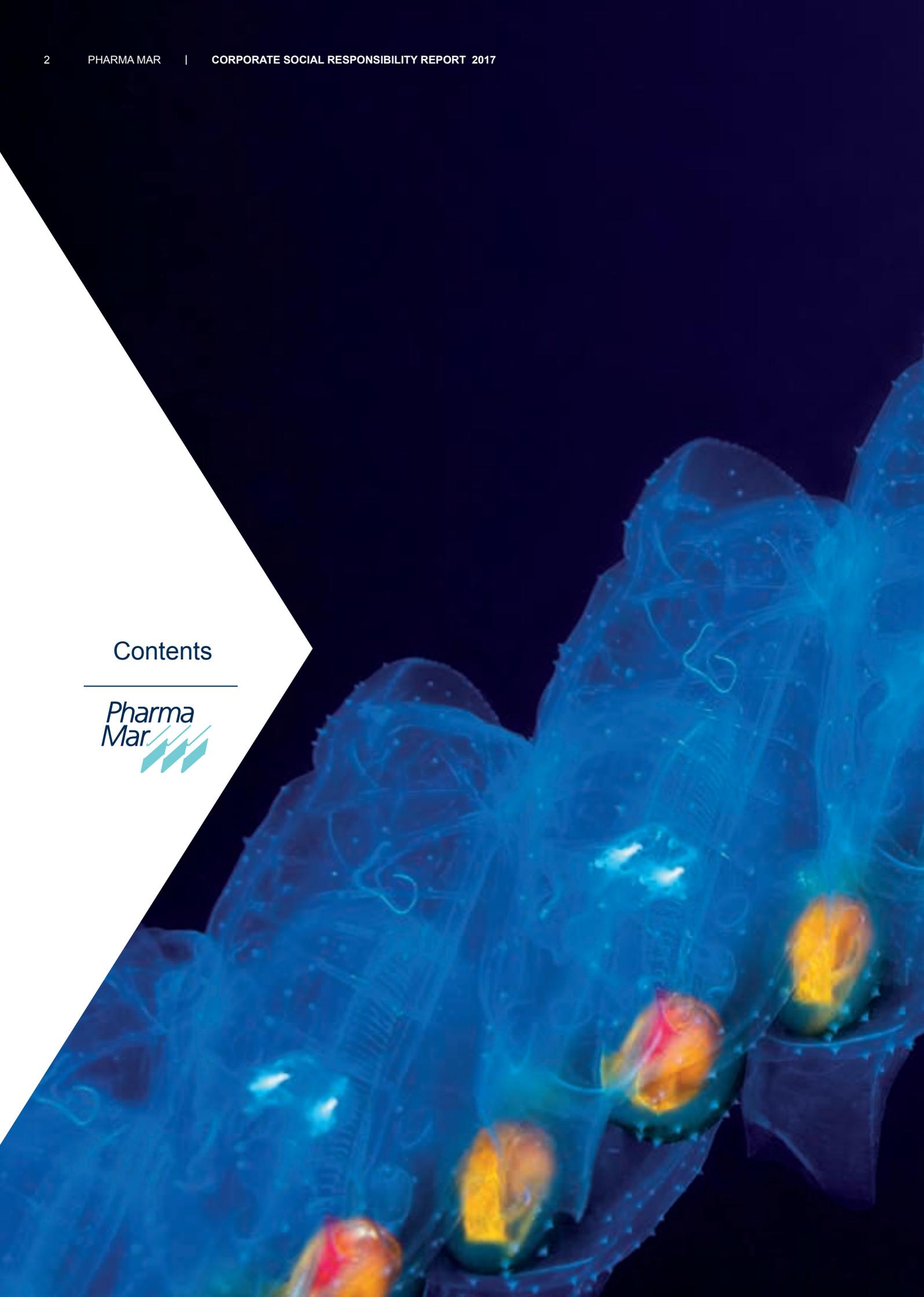
# CORPORATE SOCIAL RESPONSIBILITY REPORT

2017



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## Group Description

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# 1. Group Description

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A group of companies founded in 1939,  
comprising:

**PharmaMar:** the world leader in the discovery of anti-tumour drugs of marine origin. Its drug Yondelis<sup>®</sup>, is approved in 78 countries

**Genómica:** the first privately-owned laboratory in Spain to be accredited by ENAC to perform DNA-based identification

**Sylentis:** dedicated to the search for innovative drugs using RNA interference, a technology rewarded with the Nobel Prize for Medicine

**Xylazel:** manufactures and markets wood and metal protection products under the Xylazel and Oxirite brands

**Zelnova Zeltia:** owner of the Casa Jardín, Kill-Paff, Coopermatic, Baldosinin and Hechicera brands and the company Copyr

## THE GROUP TODAY



### OTHER BUSINESSES

#### Biopharmaceutical



#### Consumer Chemicals



The Pharma Mar Group focuses mainly on oncology. The other businesses are in the Biopharmaceutical and Consumer Chemicals areas. The Group is made up of the following companies:

**PHARMAMAR, S.A.** is a company inspired by the sea to discover molecules with anti-tumour activity. Its commitment to patients and to research has made PharmaMar a **world leader** in this field.

PharmaMar currently has **one approved drug on the market: Yondelis®**, for treating soft tissue sarcoma and relapsed ovarian cancer. It also has a solid product pipeline. One-third of all patents on drugs of marine origin and a similar proportion of academic papers on the subject are the result of the PharmaMar's research. PharmaMar currently has the world's largest collection of marine organisms: 200,000 samples of macro- and micro-organisms that are constantly being added to. From the original marine sample, PharmaMar synthesises the active compound so as to have a source of the molecule without affecting the seas or relying on natural sources. Founded in 1986, the company is based in the Madrid region.

**GENOMICA, S.A.U.** was founded in 1990 and was the first private company in Spain to provide **molecular diagnostic** services. The company has two lines of business: it develops and markets *in vitro* molecular diagnostic kits based on the Clinical Arrays platform. Genómica is also a leader in DNA analysis, and it was the first laboratory in Spain to be accredited by ENAC (Spain's national accreditation agency) for this type of test. The company is based in the Madrid region.

**SYLENTIS S.A.U.** was incorporated in 2006. This company seeks innovative therapeutic agents based on **interference RNA** (RNAi), a new technology whose discoverers were awarded the Nobel Prize for Medicine in 2006. Focused primarily on treatments for ophthalmology, it has two compounds in clinical trials for glaucoma and dry eye syndrome. Sylentis is based in the Madrid region.

**XYLAZEL, S.A.** manufactures and markets paint and varnish, and is specialised in wood decoration and treatment products of all types. It caters to the DIY, professional and industrial segments. It also produces metal protection products, such as rust-proof enamels. Its wood protection products include **Xylazel Fondo**, **Xylazel Plus**, **Xylazel aceites de teca** (teak oils), **Xylazel carcomas** (woodworm treatment), while its metal protection products include **Oxirite**. The company was founded in 1975 and is headquartered in Galicia.

**ZELNOVA ZELTIA, S.A.** produces and commercialises chemical products for household and industrial use, such as insecticides, air fresheners, cleaners and disinfectants. It has leading brands such as **Casa Jardín**, **Kill-Paff**,

**ZZ Paff**, **Bio-Kill**, **Coopermatic**, **Baldosinin** and **Hechicera**. Zelnova Zeltia has been using ozone-friendly propellants for over 20 years. It has also pioneered, in Spain, the use of electric mosquito killers that do not use refill tablets, and the first electric air freshener (based on the Kill Paff system). It was founded in 1991 and is headquartered in Galicia.

**COPYR, S.p.A.** was founded in 1962 and is headquartered in Milan. It was acquired by Zelnova Zeltia in 2006. Copyr has continued with its main activity of **manufacturing and selling automatic aerosol dispensers** under its Copymatic brand. Copyr also produces products for ecological farming.



## HISTORY

### 1939

Zeltia was founded as a spin-off from the Miguel Servet laboratory in Vigo.

Zeltia obtained one of the first slow-release insulins in the world, from abattoir by-products. Sulphamide was synthesised in the Porriño laboratories.

Zeltia began manufacturing products such as rye ergot alkaloids and digitalis extracts, tapping into the region's medicinal flora.

### 1942

Zeltia explored new avenues, manufacturing agricultural products and insecticides. The ZZ brand became leader in terms of market share.

### 1945

Antibióticos, S.A. was founded, and soon became a major domestic company and exporter. Zeltia owned a stake in Antibióticos until 1985.

### 1950's

Zeltia expanded its product range and entered into scientific and commercial alliances with foreign companies such as Imperial Chemical Industries (ICI) and Cooper McDougall & Robertson Limited.

### 1960's

Zeltia joined forces with UK companies to set up three new ventures: Zeltia Agraria (later ICI-Zeltia), to address problems in agriculture; ICI Farma, to develop and manufacture pharmaceuticals; and Cooper Zeltia, to manufacture insecticides and veterinary products.

### 1980's

Antibióticos and ICI Farma were divested.

### 1963

Zeltia was listed on the Madrid Stock Exchange, in the open outcry market.

### 1975

Zeltia formed an alliance in Spain with German company Desowag Bayer Holzschutz to produce and market wood decoration and protection products, as a result of which Xylazel was founded.

## HISTORY

### 1990's

The Zeltia Group stabilised in the current configuration, through the definition of the two main business areas in which it currently operates: Biopharmaceuticals and Consumer Chemicals.

### 1990

PharmaGen was founded to focus on molecular diagnostics and forensic research; it was renamed Genómica in 2002.

### 1991

Zelnova was spun off from Cooper Zeltia.

### 1986

PharmaMar, a world pioneer in the development of anti-tumour drugs of marine origin, was founded.

### 1998

Zeltia shares were listed in the electronic market of the four Spanish stock exchange.

### 2003

Zelnova acquired leading household cleaning brands, such as "Hechicera", "Bonacera" and "Baldosinin", from Spanish company Thomil.

### 2006

Zeltia founded biopharmaceutical company Sylentis to seek innovative therapeutical agents based on interference RNA (RNAi).

Zelnova bought Italian company Copyr, the principal supplier of automatic aerosols for the hospitality business in its domestic market.

### 2007

Yondelis®, a PharmaMar drug, was approved by the European regulator for treating soft tissue sarcoma, and was the first Spanish anti-tumour drug approved in Europe.

### 2009

Yondelis®, was approved by the European regulator to treat relapsed ovarian cancer.

### 2014

The Group celebrated its 75th anniversary: A long, sound track-record that stands out among Spanish biopharmaceutical companies.

### 2015

PharmaMar absorbed Zeltia in a reverse merger, and the group was renamed "Pharma Mar Group".

Zelnova, S.A. became Zelnova Zeltia, S.A. in order to maintain the "Zeltia" name, which is backed by 75 years of history.

Yondelis® was approved by the US and Japanese regulators for the treatment of soft tissue sarcoma. Yondelis® is currently approved for sale in 78 countries.

### 2017

Following the incorporation of a subsidiary of Genómica in Brazil, the Group is now present in France, Germany, Switzerland, Italy, the United Kingdom, Austria, Belgium, Sweden, the United States, China and Brazil.

Corporate  
Governance



## 2. Corporate Governance

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Pharma Mar is the Spanish company that invests the largest percentage of revenues in R&D: 42%

Pharma Mar also ranks first in Spain in terms of R&D expenditure per employee: €106,276 per employee

Pharma Mar ranks second in the Spanish pharmaceutical industry in total absolute expenditure on R&D

A Code of Conduct is applicable to all employees and executives

Satisfactory outcomes of audits on data protection with respect to both patients and customers

Ethical care standards applied in trials with volunteers and in animal models

PharmaMar is rated Excellent within the Profarma Plan

## Management Structure

José María Fernández Sousa-Faro is the Executive Chairman of Pharma Mar.

The members of senior management are as follows:

María Luisa de Francia Caballero	CFO
Belén Sopesén Veramendi	Head of Market Research
Luis Mora Capitán	Managing Director of the Oncology Business Unit
Sebastián Cuenca Miranda	General Secretary and Secretary of the Board of Directors
José Luis Moreno Martínez-Losa	Head of Investor Relations and Capital Markets
Juan Carlos Villalón Gómez	Internal Auditor

For profiles of the members of Group's senior management, see the corporate website: [www.pharmamar.com](http://www.pharmamar.com).

## Board of Directors

The Board of Directors is the company's organ of administration and is vested with all powers that are legally non-delegable and those reserved for

the Board of Directors by the Board's own terms of reference.

The Board of Directors comprises the following members:

Name of director	Representative	Office	Category
José María Fernández Sousa-Faro	N/A	Chairman	Executive director
Pedro Fernández Puentes	N/A	Vice-Chairman	Executive director
Ana Palacio Vallelersundi	N/A	Director	Independent director
ROSP CORUNNA PARTICIPACIONES EMPRESARIALES, S.L.	José Francisco Leyte Verdejo	Director	Proprietary director
JEFPO, S.L.	José Félix Pérez-Orive Carceller	Director	Other external director
Jaime Zurita Sáenz de Navarrete	N/A	Director	Independent director
Carlos Solchaga Catalán	N/A	Director	Independent director
EDUARDO SERRA Y ASOCIADOS, S.L.	Eduardo Serra Rexach	Director	Independent director
Montserrat Andrade Detrell	N/A	Director	Proprietary director

The Board Secretary (not a director) is Sebastián Cuenca Miranda

## CORPORATE GOVERNANCE AND ETHICAL MANAGEMENT POLICY

### Code of Conduct

The Board of Directors of Pharma Mar approved a Code of Conduct for the entire group, which entered into force on 1 February 2016. The Code of Conduct is applicable to the members of the Board of Directors, senior management and, generally, to all employees and executives of the companies that form part of the Pharma Mar Group, without exception.

The purpose of the Code of Conduct is to formalise the principles and values that should guide the conduct of all people forming part of companies in the Pharma Mar Group, among themselves and in their relationships with customers, partners, suppliers and, generally, all those people and institutions, whether public or private, with which they interact in the course of their work.

### Data protection

It is Group policy to comply scrupulously with the law with regard to the confidentiality of the data gathered in our activities and research. The principal companies in this connection are PharmaMar, Genómica and Sylentis. Patient and client personal data is afforded special protection, as is the personal data collected in the course of each company's ordinary activities: information about employees, suppliers, external scientists, labour representatives, etc.

All the information gathered about participants in clinical trials is handled in confidence and protected appropriately. To this end, measures aimed at guaranteeing anonymity and providing special protection are taken at clinical centres, and agreements are reached with contract research organisations (CROs) to process the data in accordance with the law. Accordingly, all the measures required by law to protect the integrity and confidentiality of the data have been implemented, and security is guaranteed in data capture, storage, processing and transmission.

To date, all the files reported to the Data Protection Agency and required under the Organic Law on the Protection of Personal Data have passed regular independent audits. The company also updates its technology and processes constantly to adapt to new requirements.

In Genómica, special measures are in place for data from genetic analyses:

- ▶ The files requiring protection are registered with the Data Protection Agency.
- ▶ The position of Security Manager was created and is held by Amaya Gorostiza, head of the forensic area.
- ▶ ENAC (*Entidad Nacional de Acreditación*) audits the forensic genetics department, including data treatment, once per year.

### Ethics in Clinical and Pre-clinical trials

All **clinical trials with volunteers** conducted by PharmaMar and Sylentis conform to the Declaration of Helsinki, national and international bioethics codes, such as the Oviedo Declaration, and Good Clinical Practices (GCP). These trials are always assessed and approved by the applicable clinical research ethics committees.

Patients sign an express consent form in order to participate in trials and they receive all applicable information about the trial in accordance with the requirements of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). That information is also assessed and approved by the clinical research committees and regulatory authorities where the trials are to be conducted.

**Trials conducted with animal models** also conform to ethical guidelines and to the recommendations of the leading scientific associations related to research with laboratory animals in the US and Europe: AALAS (American Association for Laboratory Animal

Science) and FELASA (Federation of European Laboratory Animal Science Associations). Before they commence, all trials are evaluated and approved by the corresponding animal experimentation ethics committees to guarantee the welfare and humanitarian treatment of the animals during the trial.

### **Drug promotion**

Pharma Mar has also adopted the Farmaindustria Code of Good Practices in Promoting Medicines, adapted from that of the EFPIA (European Federation of Pharmaceutical Industries and Associations), which represents the pharmaceutical industry.

### **Platform membership**

PharmaMar, Genómica and Sylentis participate in the "Nanomedicinas" Spanish Technology Platform. The goal is to promote technological development and define strategic policy, enhance public and private investment in nanomedicine, identify priority areas, promote innovation in nanobiotechnology for developing new drugs, and raise public awareness of this field. Genómica belongs to the ASEBIO biotechnology markets platform.



## DISTINCTIONS

The Pharma Mar Group has received numerous awards and distinctions down through the years, evidencing the Company's decades-long

commitment to research, development and innovation. The most recent awards are:

▶ Mr José María Fernández Sousa-Faro, Chairman of Pharma Mar, was named "Pharma industry entrepreneur of the year" by *El Economista* newspaper in 2016.

▶ That same year, *El Economista* ranked Pharma Mar third among the top pharmaceutical companies of the year.

▶ Award for business transparency ("IBEX medium and small cap" category) to Zeltia from the *Asociación Española de Contabilidad y Administración de Empresas (AECA)*.

▶ Recognition by ASEBIO of Zeltia as a founding member, coinciding with the platform's 15th anniversary.

▶ 2015 Award for Chemical Enterprise Excellence granted to Zeltia by the Official Association of Chemists of Galicia.

▶ BONUS diploma awarded by *Fraternidad Muprespa* to Pharma Mar in recognition of its commitment to reducing workplace accidents.

▶ "Safest company in Galicia" award to Xylazel (in the category of undertakings with under 250 employees) from *Asociación Gallega de Organismos de Control Autorizados (ASGOCA)*.

▶ *El Economista* readers voted Pharma Mar "Pharmaceutical company of the year" in the newspaper's special edition featuring the best companies of 2015.

Trabectedin, the main ingredient in Yondelis®, is the subject of a chapter in the book "Molecules that changed the world", by prestigious researchers

K.C. Nicolaou and Tamsyn Montagnon. The book highlights 40 natural products which have had a major impact on our daily lives.

**Pharma Mar is the highest-ranking Spanish company in terms of R&D investment according to the Industrial R&D Investment Scoreboard, drawn up by the European Commission's Joint Research Centre (JRC), since it spends 42% of revenues on R&D (32.8% in 2016):** that is almost triple the amount spent by the next Spanish company in the list (16.6% of revenues); the average among Spanish companies is 5.5%. **Furthermore, the Group also ranks first in Spain in terms of R&D expenditure per employee: whereas Spanish companies invested an average of €14,800 in 2017, Pharma Mar invested €106,276 per employee.**

In 2017, the company ranked #298 (up from #321 in 2016) in terms of private investment in R&D in the European Union, and **#2 among Spanish pharmaceutical companies in terms of total R&D spending.** Pharma Mar ranked #1,164 among the world's companies that spent the most on R&D in 2017, up from #1,221 in 2016 <sup>1</sup>.

PharmaMar was granted the category of Excellent within Group A ("Companies with significant research activity and their own production plant or R&D facility") in the latest edition of the Spanish government's Profarma Plan, the same result as in the previous fourteen editions. This designation is granted by the Ministry to companies that come closest to meeting the goals in terms of R&D expenditure, investment in production, and the ratio of R&D

expenditure to revenues, among others. The ranking for 2017 is currently being evaluated.

With regard to institutional matters, Carmen Eibe Guijarro, Director of Pharma Mar's Project Coordination Department, was re-elected Second Vice-Chairman of the Spanish Association of Biotechnology Companies (ASEBIO) and has represented that association on the Board of Europabio since 2014.

<sup>1</sup> Source: The 2017 EU Industrial R&D Investment Scoreboard.



Commitment  
to R&D



### 3. Commitment to R&D

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4 new projects financed by CDTI in  
2017

PharmaMar participated in an IMI  
project

Group spending on R&D in 2017: €77  
million

Despite the continuing efforts of the scientific community, there are still diseases for which there is no effective remedy, including some types of cancer, and eye pain. Responding to this reality, the Pharma Mar Group has made a firm commitment to advance in researching drugs in the areas of oncology (PharmaMar) and ophthalmology (Sylentis).

The Pharma Mar Group's tireless research efforts were recognised in 2017 by the concession of support by a number of public agencies: Spain's Centro de Desarrollo Tecnológico Industrial (CDTI) gave two new subsidies to PharmaMar, and two to Sylentis for an individual project.



Internationally, PharmaMar and Sylentis are participating in projects under the EU's framework programme. In 2017, PharmaMar achieved approval from the European Commission for a project in the Innovative Medicines Initiative (IMI). As in previous years, the Group tracked the new Horizon 2020 programme closely with a view to optimising the participation by Group companies in innovative collaboration projects between European countries.

The Pharma Mar Group spent €77 million on R&D in 2017.



5 molecules undergoing clinical trials.

3 national projects financed by the Spanish Ministry of Economy, Industry & Competitiveness (MEIC), the State Research Agency (SRA) and the ERDF.

3 international projects funded by the European Union.

3 products designated as orphan drugs.

## Research and development

PharmaMar explores the sea's ecosystems as a source of new chemical substances with anti-tumour activity. Identifying new marine products with biological properties that differ from existing drugs is an essential route to finding molecules with novel action mechanisms that may improve cancer treatment. PharmaMar currently has five molecules in various phases of clinical development.

There is also a move towards personalised medicine based not just on the tumour's histological characteristics but also on molecular criteria, which will allow a more rational treatment of patients in the future. Consequently, the current goal is for the treatment to be administered only to patients with tumours with a defined molecular characteristic (e.g. the presence of a target which the antitumour compound attacks), as they would theoretically benefit most from the treatment. PharmaMar is working to identify such patients by applying pharmacogenomic techniques in its trials.

Among the numerous research and development projects being conducted by PharmaMar, the following public-private partnerships financed by the Spanish Ministry of Economy, Industry & Competitiveness (MEIC), the State Research

Agency and the European Regional Development Fund (ERDF) are particularly noteworthy:



- ▶ **DESPOL** consortium: comprising PharmaMar (consortium leader) with the University of Oviedo and Spain's National Research Council (CSIC). The goal is to induce expression in marine bacteria of "silenced" genes that regulate the expression of certain biosynthetic routes. This enhances the likelihood of identifying new medicines from these bacteria.
- ▶ **INMUNOTOP** consortium: PharmaMar heads this consortium, with the University of Seville, the University of La Coruña and the Autonomous University of Madrid. The goal of the project is to discover new drug candidates in oncology based on the topoisomerase system and regulation of the immune response.
- ▶ **UNDERLIPIDS** consortium: comprises PharmaMar (consortium leader), the University of the Basque Country and the Institute of Material Science of Barcelona, which is part of the CSIC. The project is to develop a scalable, economically competitive formula for subcutaneous administration of a cytotoxin in solution or suspension.

PharmaMar is also involved in three joint projects under the European Union framework programme: Those projects are

**“BLUEPHARMTRAIN:**

Co-Cultivation of Sponge Cells & Microorganisms”, **“INMARE:** Industrial Applications of Marine Enzymes: Innovative screening and expression platforms to discover and use the functional protein diversity from the sea”

and, more recently, **“ITCC-P4:**

ITCC Pediatric Preclinical

POC Platform”. The latter project is part of the “Innovative Medicines Initiative” (IMI-2) and seeks animal models for studying paediatric cancer, in cooperation with large pharmaceutical companies.



## Researching new pharmaceutical forms

The latest progress with pharmaceutical technology offers promising tools for dealing with the stability problem posed by some pharmaceuticals. These approaches can improve the compounds' solubility and tissue permeability, protect the molecules from chemical degradation, selectively direct the cytotoxic drugs towards tumour cells, or modify their toxicological profile.

PharmaMar contributes to these new drug release systems by researching, developing and applying sophisticated new techniques, including notably: micelles of new polymers, antibody conjugated polymeric nanoparticles, nanoparticle-stabilised nanocapsules, solid nanodispersions obtained using supercritical fluid techniques, and alternative routes for administering insoluble drugs, such as subcutaneously.

This research has developed and performed pre-clinical evaluations of new nanosystems designed specifically to address the problems posed by PharmaMar's novel molecules and unleash their full potential.

## Clinical trials

PharmaMar is conducting clinical trials on Yondelis<sup>®</sup>, which has already been authorised for sale, and also on Aplidin<sup>®</sup>, Zepsyre<sup>®</sup>, PM184 and PM14, which have not yet been authorised for sale. PharmaMar currently has the following molecules undergoing clinical trials:

▶ **Yondelis<sup>®</sup> (trabectedin):** A number of post-authorisation trials are under way which seek to optimise the drug's clinical use in the two indications for which it has marketing authorisation: soft tissue sarcoma, and platinum-sensitive ovarian cancer (in combination with pegylated liposomal doxorubicin—PLD).

▶ **Aplidin<sup>®</sup> (plitidepsin):**

### ▶ **Multiple Myeloma**

A Marketing Authorisation Application (MAA) for plitidepsin to treat multiple myeloma was filed with the European Medicines Agency (EMA) in September 2016. After the Committee for Medicinal Products for Human Use (CHMP) issued a negative opinion in December 2017, PharmaMar applied for a review on 14 February and the outcome is expected in the first half of 2018.

In order to position plitidepsin in an earlier stage of treatment for multiple myeloma, enrolment continues in the combination trial with bortezomib and dexamethasone, and enrolment has commenced in a trial to assess a quadruple combination.

### ▶ **Lymphoma**

The registration trial with plitidepsin as monotherapy in patients with angioimmunoblastic T-cell lymphoma continues recruiting.

▶ **Zepsyre<sup>®</sup> (lurbinectedin):**

### ▶ **Platinum-resistant ovarian cancer**

CORAIL pivotal Phase III trial with lurbinectedin as monotherapy vs. topotecan or PLD.

▶ **Small-cell lung cancer**

The ATLANTIS Phase III registration trial that compares the activity and safety of the combination of lurbinectedin plus doxorubicin with topotecan or CAV (cyclophosphamide, adriamycin and vincristine) for treating patients who have relapsed after a first round of platinum treatment.

Recruitment is ongoing. The Independent Data Monitoring Committee (IDMC) conducted an interim safety data analysis in November, after which it recommended continuing the trial without change.

▶ **Combination trials**

Recruitment concluded for the combinations with doxorubicin, cisplatin, capecitabine and paclitaxel with or without bevacizumab. The latter two trials produced promising preliminary results in a range of cancer types; consequently, the next stages of development are currently being assessed. Recruitment continues on schedule for the Phase I trial in combination with irinotecan.

▶ **Basket trial in advanced solid tumours**

Recruitment continues for a Phase II trial with lurbinectedin as monotherapy in selected indications: small cell lung cancer, neuroendocrine tumours, carcinoma of the head and neck, germ cell cancer, endometrial cancer, bile duct cancer, cancer of unknown primary, Ewing sarcoma, and breast cancer with BRCA 1/2 mutation.

▶ **Phase I trial in Japan**

This important trial, designed to ascertain the dosage for lurbinectedin in Japanese patients in order to continue with clinical development in that country, is still in the active enrolment phase.

▶ **Phase I mass balance trial**

Six patients have been recruited for this trial, which will provide full information on the pharmaceutical profile of lurbinectedin and its metabolites, and their transformation and elimination pathways.

▶ **PM184:**

▶ **The Phase I** dose escalation trial assessing the combination of PM184 with gemcitabine continues recruitment on schedule. Recruitment is being focused on the non-small cell lung cancer, breast cancer and head and neck cancer cohorts.

▶ **The first stage of the Phase II** trial with PM184 in hormone-receptor positive advanced breast cancer patients concluded, and there will not be a second stage as the necessary efficacy threshold was not attained.

A second Phase II trial in colorectal cancer will begin enrolment in the first quarter of 2018 after completing the administrative requirements in 2017.

▶ **PM14:**

▶ In September 2017, the first patient was enrolled in the clinical development programme for a new molecule: PM14. The first trial is expected to include approximately 50 patients with a confirmed diagnosis of advanced solid tumour for which there is no standard treatment available.

## Communication with patients

The Clinical Oncology Department regularly receives queries and requests from interested patients, which are answered as quickly as possible. All patient queries receive a response, explaining that they need to discuss the issue with their doctor and offering the possibility for their oncologist to contact oncologists and researchers at hospitals where PharmaMar compounds are undergoing clinical trials with a view to possible participation in a clinical trial if the patient's specific case is appropriate and complies with the protocols.

## Research into rare diseases

PharmaMar's commitment to developing drugs for treating diseases of this type is evidenced by the fact that three of its main drugs have been designated as orphan drugs by the European Commission and the FDA for soft tissue sarcoma, ovarian cancer and multiple myeloma. Additionally, two of those drugs have been granted orphan drug status in Switzerland: one for soft tissue sarcoma and ovarian cancer and the other for multiple myeloma. One of PharmaMar's products has also been designated as an orphan drug for soft tissue sarcoma in Korea and Japan.

## Quality management

PharmaMar has been authorised by the Spanish Agency for Medicines and Healthcare Products (AEMPS) to manufacture medicines for human use and investigational drugs (secondary conditioning and batch certification), and to import human use and investigational drugs. It is also registered with the Subdirectorate-General of Drug Inspection and Oversight at the AEMPS as a laboratory authorised to commercialise drugs and as a manufacturer of active ingredients for human use, including the manufacture of radiopharmaceuticals for investigative drugs.

All products produced by PharmaMar for patients' use are subject to strict quality assurance procedures in order to ensure their purity, potency, quality and safety. The Quality Assurance Department reviews the documentation on the production process so as to ensure that all pre-defined quality requirements are met.

All significant pre-clinical trials conducted by PharmaMar as part of drug development are carried out in accordance with internal procedures and systems that ensure compliance with Good Laboratory Practices (GLP).

PharmaMar's clinical trials are conducted in accordance with Good Clinical Practices (GCP) and information processing standards

and conform to the rules and guidelines of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), the FDA (Food & Drug Administration) and EMA (European Medicines Agency), as well as all local regulatory requirements in the countries where trials are carried out.

There were no incidents related to the quality of PharmaMar products in 2017.

The person in charge of this entire process is José Luis Ortega, Director of the Quality Unit in the Oncology Business Area.

## Cooperation with other bodies

PharmaMar attaches great importance to cooperation with high-level research groups at public and private schools and universities in Spain and other countries. These relationships facilitate the exchange of technical knowledge in the pursuit of science and research, thus contributing to the future of our society.

There are agreements with scientific institutions throughout the world which assist with R&D, providing the latest research in such fields as molecular biology, cellular biology, structural elucidation, action mechanisms, nanotechnology and other related disciplines, enhancing the scientific knowledge and human resources brought to bear on each project based on each group's degree of specialisation.

Bioprospection efforts are assisted by universities, centres for marine biology, and Environment and Fisheries Ministries throughout the world to enable the company to comply with global and local regulations on biodiversity while engaging in joint initiatives to expand knowledge of flora and fauna in each marine habitat.

The Clinical Department works with over 300 hospitals in Europe, the USA and Canada, Asia and Australia, where the studies required for product development during clinical trials are carried out.

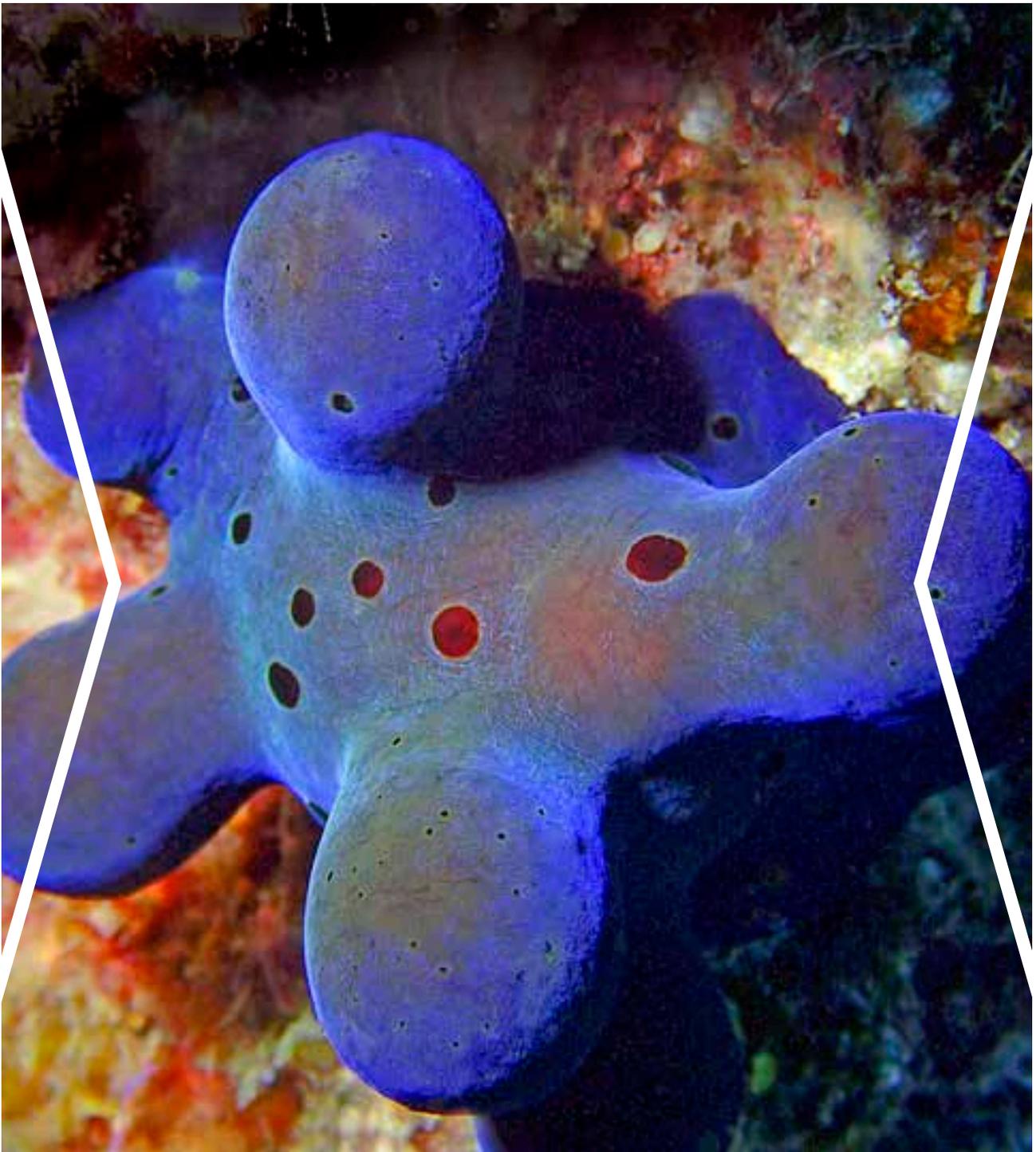
## Pharmacovigilance

Pharmacovigilance is the activity that enables the pharmaceutical industry, among the various agents that use medicines, to protect patients' health through early identification, quantification and evaluation of the risks associated with its products. Through pharmacovigilance, pharmaceutical companies can continuously assess the safety profile of their drugs (both in clinical trials and those commercially available)

and ensure that the necessary preventive and/or corrective measures are taken to safeguard patients' welfare.

All PharmaMar employees receive training in pharmacovigilance in order to report any adverse effects of any of the company's products of which they become aware.

There were no pharmacovigilance-related incidents with any PharmaMar products in 2017.





2 molecules undergoing clinical trials.

2 national projects funded by the MEIC, SRA and ERDF.

2 international projects funded by the European Union.

“Madrid Excelente” award from the Madrid Regional Government.

## Research and development

Sylentis focuses its research on drugs obtained using interference RNA (RNAi) technology. The importance of this novel technique is evidenced by the fact that its discoverers, Andrew Fire and Craig Mello, were awarded the Nobel Prize for Medicine in 2006. RNAi has revolutionised biology by making it possible to design and develop drugs from a totally new perspective.

It can be used to selectively silence genes through post-transcriptional degradation of the messenger RNA that leads to the corresponding protein or enzyme. Accordingly, the technique acts on specific enzymes involved in pathologies and enables them to be regulated through the rational design of drugs that can silence the expression of the gene that codes for the enzyme or protein.

The RNAi mechanism of action also prolongs the drug's action over time and provides for safer and more effective treatments which are also perfectly compatible with the eye surface and have no systemic effects.

Sylentis is pursuing several lines of research:

- ▶ **Ocular:** glaucoma, dry eye syndrome, retinal alterations, ocular allergies and other diseases of the eye.

- ▶ **Inflammatory:** inflammatory bowel diseases (Crohn's disease and ulcerous colitis).

- ▶ **Central nervous system:** cerebral ischaemia, neurodegenerative diseases and dementia.

- ▶ **Basic research:** formulation and chemical modification of molecular structures to increase stability and efficacy in models *in vivo*.

- ▶ **Formulation of RNAi products** for oral administration.

In the last two years, Sylentis has been working on a new line of research into innovative drugs for treating diseases of the retina. In 2017, the company developed drugs for treating age-related macular degeneration which are applied topically to the eye instead of via intravitreal injection, the standard form of administration in treating this pathology. The goal is to develop products with a novel action mechanism that enhance patients' quality of life.

Alnylam Pharmaceuticals has granted Sylentis an option to licence the intellectual property of InterfeRx™ for the development and commercialisation of RNAi therapeutics.



Among the numerous research and development projects being conducted by Sylentis, the following public-private partnerships financed by the Spanish Ministry of Economy, Industry & Competitiveness, the State Research Agency and the European Regional Development Fund (ERDF) are particularly noteworthy:

▶ **SEKEYE** consortium: Sylentis heads this consortium, whose members are the University of Santiago de Compostela, the University of Oviedo and the University of Valladolid. The project seeks alternatives to existing commercial solutions for treating dry eye syndrome and the associated eye pain.

▶ **GLAUKUS** consortium: headed by Sylentis, this consortium includes the University of Santiago de Compostela, Madrid Complutense University and the University of the Basque Country. The project aims to develop personalised treatments for glaucoma, focusing particularly on children and the elderly.

Sylentis is also participating in two cooperation projects under the European Union framework programme: “**NANOPILOT**: A Pilot Plant for the Production of Polymer-based Nanopharmaceuticals in Compliance with GMP” and “**NABBA**: Design and Development of Advanced Nanomedicines to Overcome Biological Barriers and to Treat Severe Diseases”.



## Clinical trials

Sylentis is one of only four companies in the world with RNAi-based products undergoing clinical trials and it is the first company in Spain to develop a product based on this technology.

The company's most-advanced compound, SYL1001 (tivanisiran), is for treating ocular pain associated with dry eye syndrome. The Phase I and II trials produced satisfactory results in terms of both safety and efficacy and the drug is currently undergoing Phase III development.

The company's second-most advanced compound is SYL040012 (bamosiran), for treating elevated intraocular pressure and glaucoma. Phase I and II trials demonstrated excellent tolerance to the drug, as well as statistically significant efficacy of one of the evaluated doses. Based on the results, the next steps with this compound are currently being considered.

## Quality research

Sylentis obtained the "Madrid Excelente" distinction. Madrid Excelente is a mark granted by the Madrid Regional Government in recognition of companies' quality and excellence, with a view to fostering competitiveness. The mark does not refer to a specific product or service but is based on an analysis of the company's overall quality. It is given to companies that are committed to innovation and continuous improvement, social responsibility, satisfying people, and contributing actively to the region's economic and social development.

The Spanish Agency for Medicines and Healthcare Products (AEMPS) authorised Sylentis as a pharmaceutical laboratory to manufacture research drugs. This recognition is a response to the company's hard work and to the expectation that it is generating. Inspections by the Spanish Agency for Medicines and Healthcare Products (AEMPS) for renewal of the authorisation were passed successfully.

Sylentis has implemented Good Manufacturing Practice (GMP) in its facilities. Additionally, most of the preclinical trials it performs in-house or outsources adhere to Good Laboratory Practices. Its role as promoter of clinical trials also conforms to Good Clinical Practices, as required by law, and it ensures that contract research organisations and individual researchers also comply with this requirement.

### Cooperation with other bodies

Sylentis has cooperation agreements with numerous public and private institutions in Spain and other countries so as to effectively transfer knowledge and resources and make progress

with product research and development. It works with numerous universities and research centres as well as private contract research organisations to conduct its trials.



## Customers



## 4. Customers

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The Pharma Mar Group is present in France, Germany, Switzerland, Italy, the United Kingdom, Austria, Belgium, the United States, Sweden, China and Brazil

IFS HPC certification for Zelnova Zeltia products

SEAIC seal for the Xylazel Aire Sano line of paints

New certifications for Genómica in Brazil and Korea

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The Pharma Mar Group's current customers are the users of Zelnova Zeltia-Copyr, Xylazel, Genómica and PharmaMar products and services. Our companies have a commitment to the customer in their respective areas of activity: guarantee a quality service, maintain satisfactory communications with customers, and solve their problems as efficiently as possible, all in combination with continuous improvement of our offer by developing new products.

The Group has commercial presence in France, Germany, Switzerland, Italy, the United Kingdom, Austria, Belgium, Sweden, China and Brazil, as well as a centre of activity in the

United States. These are markets with high growth potential where the Group seeks to increase its sales.



There were generally no incidents in 2017 in connection with non-compliance with the regulations on product labelling, advertising, sponsorship or customer data protection. The only incident in this regard was at PharmaMar's UK subsidiary and was related to product promotion: as a result of an anonymous complaint, this subsidiary was sanctioned

for a breach of the Association of the British Pharmaceutical Industry (ABPI) code on promotion in the context of a meeting of the *British Sarcoma Group*. In 2018, the Prescription Medicine Code of Practice Authority and PharmaMar are working together to identify and establish a plan of action to avoid breaches of this type.

## **ZELNOVA ZELTIA-COPYR**

Zelnova Zeltia-Copyr has approximately 3,400 direct customers.

It offers chemical products for household (insecticides, air fresheners, odour neutralisers, rat poison, wax, impregnators, cleaners, bathroom products, grease removers, furniture cleaners, etc.) and industrial use (hospitality industry). Copyr also has a range of products for organic farming (fertilisers, fungicides, herbicides, wound paint).

## **XYLAZEL**

Xylazel has approximately 1,300 direct customers.

Its products and services include paints, varnishes, wood and metal protectors, fillers, putty, and oils, and a technical service to handle customer queries, advice, complaints, etc.

## **GENÓMICA**

Genómica has approximately 104 direct customers.

It provides proprietary *in vitro* diagnostic kits (papillomavirus, herpes, enterovirus, viruses and bacteria causing respiratory infections, enterobacteria, micro-organisms that cause sepsis, sexually transmitted micro-organisms, and detection of mutations in the genes associated with the response to anti-tumour therapy), as well as genetic identification analysis, and technology transfer.

## **PHARMAMAR**

PharmaMar has approximately 972 customers.

Following the launch of Yondelis® in Europe, in 2007 for soft tissue sarcoma and in 2009 for ovarian cancer, the company's customers are

hospitals and clinics in Europe which are served by PharmaMar's own sales network or its sales and distribution partners.

## **Communication with customers**

Customers can obtain information through a variety of channels; the main channel is via area sales representatives and arranged visits. At an international level, sales efforts are conducted through subsidiaries or distributors.

End customers can contact the companies via their websites. They may also contact the companies by phone or e-mail to clarify queries. Contact details are given on product packages and on the company's brochures and advertising material.

In the case of the Oncology unit, contact with the customers (healthcare professionals) is conducted via the commercial structure or by telephone or e-mail. Because of this unit's high degree of specialisation, clinical queries from patients are channelled through the doctor responsible for their treatment.

## **Information for customers**

The Marketing departments generally take all necessary steps to ensure that the company responds to customer needs: information addressed to customers is drafted clearly and comprehensibly, based on consumer feedback.

Customers' opinions are very important when making decisions about any product (development, design, production, labelling, manuals and marketing) and, where necessary, product literature and labels are corrected on the basis of customer feedback.

In the Oncology unit, scientific information and promotional materials provided to healthcare professionals undergo a rigorous approval process that conforms to the regulations in the individual countries.

## **Customer satisfaction**

Our companies conduct regular surveys of customers and end consumers to gauge their satisfaction with the products. The Commercial Department analyses the data and, based on complaints and non-conformities, takes the appropriate measures to address the least positive aspects.

Any complaint or claim from a customer is registered in writing. All complaints are channelled through the Commercial Department, which refers them to the pertinent department in order for the problem to be analysed, a report issued and a solution proposed. Once the report has been drafted, it is remitted to the Commercial Department, which decides on the appropriate commercial solution to the problem raised by the customer. The Commercial Department draws up regular reports on trends in complaints and complaints handling.

The people in charge of customer relations at the various subsidiaries are: José Antonio Pérez Raya (Zelnova Zeltia), Alfredo Álvarez Álvarez (Xylazel), Antonio Sevilla and Juan Bataller (Genómica), and Juan Nogués Ortuño (PharmaMar).

## **Advertising and competitors**

Zelnova Zeltia-Copyr and Xylazel products are advertised in the media during periods of peak demand. These companies also work with customers in designing brochures, display cases, etc. to promote the products all year round. With respect to rivals, we are committed to complying with the general rules of fair trading and to avoiding any action that will be explicitly harmful to a competitor.

Since Genómica and PharmaMar produce very specialised biotechnology products, they advertise directly to customers, emphasising the benefits of their products over the competition, but without mentioning the latter. For this purpose, the company uses independent scientific studies that support its message, as well as small comparative surveys. They also advertise at scientific conferences which are attended by product advisers familiar with the industry. Competitors receive our utmost respect, and sales arguments are purely technical, enabling the customer, who is technically sophisticated, to judge which product best meets their needs and the available analytical and therapeutic options.

## **Product quality**

Appropriate control and monitoring systems are in place to ensure that only products meeting the established requirements are sold. Checks are performed from reception of raw materials through the manufacturing phase down to the final product, diagnostic test or drug.

There were no product returns or recalls in 2017 due to health or safety issues.

The people in charge of Quality at the various subsidiaries are: Mónica Mascato (Zelnova Zeltia), Roberta Coppi (Copyr), José Ramón Álvarez (Xylazel), Ascensión Hernández (Genómica) and José Luis Ortega (PharmaMar).

Zelnova Zeltia, Copyr, Xylazel and Genómica are certified to ISO 9001, audited to the latest version of the standard. Zelnova Zeltia also has the Higher Level certification under the IFS HPC standard, which was renewed in 2017.

## IFS HPC CERTIFICATION



► **Zelnova Zeltia** obtained the highest possible certification, Higher Level, under the IFS HPC standard (International Featured Standard Household and Personal Care).

IFS HPC is used to audit companies which manufacture personal care and household products and sell them to consumers under their own brand names (private label).

It is an internationally-recognised standard which ensures that IFS-certified companies deliver products that adhere

to defined specifications with a view to continuously improving product safety and quality.

Very few companies in Spain or Europe have obtained this certificate; Zelnova Zeltia's certification evidences its commitment to developing high-quality innovative products and provides a clear competitive advantage over other manufacturers.

The IFS certification is used by such large retail chains as Carrefour, Auchan, Aldi, Casino, Lidl, Leclerc, Metro, Migros, Wal-Mart and Coop.

**Xylazel**, has the following quality certifications:

- The SEAIC Seal of the Spanish Society of Allergology and Clinical Immunology, endorsing the new line of Xylazel Aire Sano paints for people with allergies and asthma.



- AITIM Quality Seal from the Technical Research Association of Woodworking Industries, for the Xylazel IMPRALIT KDS wood protector.

- ECOLABEL , for its Aire Sano product line.



- The A+ Seal from the French Ministry of Ecology, Sustainable Development, Transport and Housing for the new line of "Aire Sano" products, certifying their suitability for people with allergies and asthma.



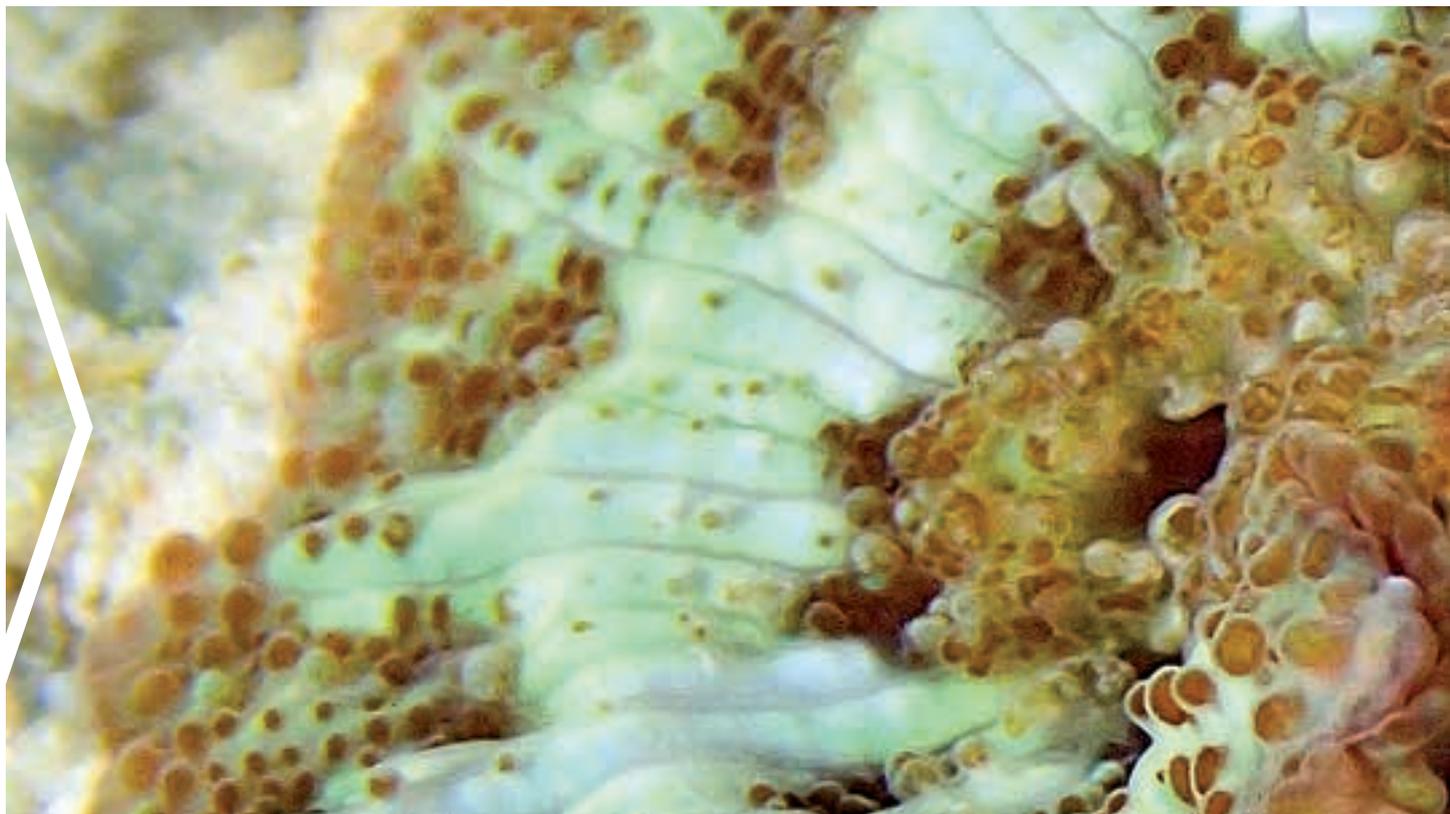
- Certification of compliance with the EN71:3 standard on toy safety, and the migration from hazardous compounds for Xylazel's Aire Sano paint for children's environments.

- ▶ Compliance with the Euroclass B-s1, d0 fire safety requirements by Xylazel Aire Sano paint for healthcare environments.
- ▶ Compliance by Xylazel Aire Sano paint for healthcare environments with the criteria under Regulation 852/2004 for food environments without direct contact with food.
- ▶ Compliance by Xylazel Aire Sano paint for healthcare environments with the criteria for resistance to certain disinfectants under the UNE-EN ISO 2812:3 standard.
- ▶ Backing from the Spanish Society of Preventive Medicine, Public Health and Hygiene for Xylazel Aire Sano paint for healthcare environments.
- ▶ Cooperation agreement with the Spanish Paediatric Association (AEP) for Xylazel Aire Sano paint for children's environments.



**Genómica** has the following quality certificates:

- ▶ EC Conformity certificate for the following products CLART® HPV, CLART® Pneumo Vir, CLART® ENTHERPEX, CLART® SeptiBac, CLART® EnteroBac, CLART® CMA, and CLART® STIs, in accordance with Directive 98/79/CE on *in vitro* diagnostic medical devices.
- ▶ ENAC accreditation for the genetic identification laboratory in accordance with ISO 17025. This accreditation has been expanded to include genetic-forensic tests with stem cells, adipocytes, cells in suspension and teeth.
- ▶ Certification (renewed) to ISO 13485:2003, i.e. its quality management system complies with the regulatory requisites of any country in the world.
- ▶ ISO 9001:2015 certification by TÜV Rheinland.
- ▶ GMP (Good Manufacturing Practices) certification in Brazil by ANVISA for the production of class III and IV *in vitro* diagnostic health products.
- ▶ Certificate that healthcare product production conforms to Korean Good Manufacturing Practices.



## New product research and development

### ZELNOVA ZELTIA-COPYR

New product development is aimed not only at rounding out the product range to meet market demands but also at complying with new legislation regarding health and environmental protection. This new legislation has drastically reduced the number of active ingredients available for use, making it necessary to develop new formulations.

Various research lines are currently under way, in fields ranging from air fresheners to insecticides, and new formulae with optimised toxicological and environmental profiles are being developed. Work is also ongoing to register new formulae in accordance with the latest legislation on biocides.

The latest research is focused on novel natural compounds as possible active ingredients.

### XYLAZEL

The company seeks to develop innovative products that comply with increasingly demanding legislation and improve both personal and environmental safety. It is working on adapting its range of wood protection products to the new regulation on the classification and sale of biocides.

In 2017, Xylazel completed registration of its entire range of wood protection products under the European Biocidal Product Regulation (BPR) and is awaiting a decision.

The company worked on the following lines in 2017:

- ▶ Development of new formulas in the Oxirite Xtrem line for satin, iron and matt finishes.
- ▶ Development of new water-based varnish and enamel paint for universal indoor and outdoor use. They include a water-based varnish that adheres to floating wood floors.
- ▶ Transition of decorative wood varnish to a water base using new resin technology.
- ▶ Development of a new water-based sealant to avoid leaching of wood tannins.
- ▶ Development of a new oil to treat indoor woodwork that is suitable for contact with food.
- ▶ Development of a new walkable fibre-reinforced waterproof paint.
- ▶ Replacement of propiconazole and tebuconazole as the main active ingredients in wood protection products with a newly developed fungicide that is less hazardous for human health and the environment.



## GENÓMICA

Genómica worked on the following lines in 2017:

- ▶ In the Microbiology area, work continues on lyophilisation of CLART® products. In particular, the CLART® PneumoVir-2 product has been successfully lyophilised, the critical issue being to obtain an enzyme capable of amplifying RNA viruses with all their functional characteristics.
- ▶ In relation to the company's Autoclart and Autoclart plus products, the CLART® Pneumovir-2 and Pneumo CLART Bacteria® detection processes have been combined into a single visualisation protocol in Autoclart. In addition, the CLART®SeptiBac product has been implemented on both platforms.

- ▶ The Oncology area is working very actively in the area of fluid phase biopsy, and Genómica's CLART® EGFR BL product, which is already on the market, has been shown to be compatible with Streck tubes. These tubes make it possible to store blood from a cancer patient for 14 days while preserving the circulating tumour DNA, and are vital for the implementation of our system in hospital logistics.

## PHARMAMAR

PharmaMar's research and development of new products is described in considerable detail in section 3 of this report, concerning the company's commitment to R&D.

## GENÓMICA AND PERSONALISED MEDICINE

- ▶ Years ago, Genómica decided to take diagnosis a step further by exploring personalised medicine. Evidence of this are the six products launched to date that detect specific mutations, the presence or absence of which allows a suitable treatment to be chosen: CLART® CMA KRAS.BRAF.PI3K and CLART® CMA NRAS.iKRAS in metastatic colorectal cancer, CLART® CMA EGFR in non-small cell lung cancer, CLART® CMA BRAF.MEK1.AKT1 in melanoma and, most recently, CLART® CMA ALK.ROS1 and CLART® CMA EGFR LB in lung cancer.

As part of its commitment to researching this area, the company has reached a cooperation agreement with *Fundación para la Excelencia y Calidad en la Oncología* (ECO), a platform comprising the heads of the medical oncology departments of the leading Spanish hospitals. This agreement is aimed at improving cancer treatment by fostering research projects and optimising clinical management in oncology.



## Suppliers



## 5. Suppliers

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The supplier selection process is objective and transparent

We require that our suppliers comply with workplace safety and environmental management standards

We support the principles of the UN Global Compact and the OECD Guidelines

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Pharma Mar Group's chemical and biopharmaceutical companies interact with a large number of suppliers who provide a broad range of products and services for our production process. As business partners, we strive to maintain solid, lasting relationships with our suppliers based on mutual benefit, contributing to the growth of the organisation.

Suppliers are selected on the basis of compliance with quality standards, reputation in the market, suitability to our needs, and an excellent price-quality ratio. That is to say, we seek suppliers that offer the best combination of quality, service and price using an objective, transparent selection process that takes account of sustainable procurement criteria. Our companies apply purchasing processes certified to ISO standards. There is no discrimination against suppliers for reasons of race, creed, nationality or gender. We use questionnaires to ensure that our services suppliers have the same anti-discrimination values with regard to their own suppliers.

Candidates must submit documentation certifying their capabilities and complete a form disclosing such information as: any quality, environmental, social responsibility and health and safety certificates they possess, as well as whether or not they have internal procedures for training, manufacturing processes and internal organisation. All this information is evaluated by a Supplier Management Committee, which issues a recommendation as to whether or not the supplier is appropriate. Approved suppliers are subject to a system of continuous improvement and scoring based on the number of quality incidents and other factors such as

fulfilment statistics; this method re-evaluates suppliers and appropriate improvement actions are identified and implemented.

We demand that our suppliers provide products and services of the required quality and that they comply with their tax obligations. Raw materials suppliers must comply with the regulation on the registration, evaluation, authorisation and restriction of chemicals. Pharma Mar Group companies reserve the right to conduct audits to verify suppliers' quality systems.

The International Standards for Phytosanitary Measures (ISPMs) set out the rules for reducing risks associated with wooden pallets in international trade. The most recent revision to the standards maintains heat treatment as the standard phytosanitary measure for these materials, recommending it as an alternative to fumigation with methyl bromide, a gas considered to deplete the ozone layer. In order to contribute to protecting the ozone layer, PharmaMar requires that its packaging suppliers have certificates and identifying marks to the effect that the wooden pallets it receives were heat treated and not fumigated with methyl bromide.

COMPANY	PHARMAMAR	GENÓMICA	SYLENTIS	XYLAZEL	ZELNOVA ZELTIA COPYR
<b>NO. OF SUPPLIERS</b>	<b>467</b>	<b>167</b>	<b>514</b>	<b>151</b>	<b>297</b>
Of which:					
Spanish	387	151	397	119	110
Rest of Europe	58	13	71	32	173
Developing countries	--	--	--	--	1
Rest of the world	22	3	46	--	13



The vast majority of our suppliers are based in Spain or elsewhere in Europe; accordingly, they are assumed to comply with labour legislation and respect human rights. We also require that suppliers comply with regulations on workplace safety and environmental management.

The Pharma Mar Group supports unconditionally the principles of the United Nations Global Compact and OECD Guidelines, and we are openly opposed to worker exploitation, child labour, discrimination in any form, and any abuse of human rights or complicity with such abuse.





## Employees



## 6. Employees

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Over 93% of the Group's employees have indefinite contracts

### Pharma Mar Equality Plan

51 interns in the Group: 3 of them were subsequently hired

Over €880,000 spent on employee training

### Employee share ownership plan

The accident rate is well below the industry average

At the end of 2017, the Pharma Mar Group, including subsidiaries outside Spain, had 727 employees.

We are proud of the loyalty and trust of the employees at our chemical companies, where the average length of service is 15 years, providing us with the invaluable experience accumulated over time. We are also very pleased that our biopharmaceutical companies have highly-qualified researchers with superb skills and knowledge. Additionally, the Group

employs a large proportion of women, including at executive level.

We would like to take the occasion of this Corporate Social Responsibility Report to publicly thank each and every one of our employees for deciding to work with the Pharma Mar Group, and express our most sincere acknowledgement of their efforts, dedication and talent. With such an exceptional team, we have full confidence in our future.

## Workforce statistics in 2017 and 2016

Chemical Companies	Xylazel		Zelnova Zeltia		COPYR	
	2017	2016	2017	2016	2017	2016
No. of employees	102	105	84	87	19	19
Average age (years)	46	47	46	46	43	42
Average length of service (years)	15	16	15	16	9	10
No. of employees from other countries	0	1	0	0	0	0
No. of employees with disabilities	3	2	2	2	0	0
<b>Breakdown by gender</b>						
% of men in total work force	64	66	64	60	47	53
% of women in total work force	36	34	36	40	53	47
% of men in management	80	100	80	83	16	16
% of women in management	20	0	20	17	0	0
<b>Academic qualifications</b>						
% Graduates & PhDs	25	24	23	19	47	47
<b>Breakdown of total work force by area</b>						
Administration	22	23	19	19	4	4
Commercial & Marketing	35	36	16	16	6	7
R&D/Quality/Control	7	6	11	12	4	3
Production & Distribution	36	38	36	38	4	4
General services	2	2	2	2		

Biopharmaceutical companies	PharmaMar				Genómica		Sylentis	
	2017		2016		2017	2016	2017	2016
	Spain	Subsidiaries	Spain	Subsidiaries	Spain and subsidiaries	Spain and subsidiaries	Spain	Spain
No. of employees	373	69	363	69	53	58	21	21
Average age (years)	44	46	43	45	41	38	37	37
Average length of service (years)	9	2	8	2	8	6	7	6
No. of employees from other countries	17	69	18	69	2	4	2	3
No. of employees with disabilities	5	0	5	1	1	1	0	0
<b>Breakdown by gender</b>								
% of men in total work force	42	36	41	35	37	36	19	28
% of women in total work force	58	64	59	65	63	64	81	72
% of men in management	67	57	67	50	40	40	5	5
% of women in management	33	43	33	50	60	60	95	95
<b>Academic qualifications</b>								
% Graduates	50	80	49	72	43	45	47	47
% PhDs	18	12	18	0	25	26	38	38
<b>Breakdown of total work force by area</b>								
Administration	59	11	53	12	7	6	2	2
Commercial & Marketing	37	48	35	57	12	15	0	0
R&D/Quality/Control/Regulatory	233	7	232	0	16	19	17	17
Production & Distribution	31	0	30	0	18	18	2	2
General services	13	0	13	0	0	0	0	0

PharmaMar subsidiaries: Germany, France, Italy, Belgium, the United Kingdom, Switzerland, Austria and the United States

Genómica subsidiaries: Sweden, China and Brazil.

The Pharma Mar Group adheres to the principles of the International Labour Organisation (ILO), the international body responsible for drawing up and overseeing international labour standards, which receives worldwide support and recognition in promoting workers' fundamental rights.

### Employment contracts, collective agreements and remuneration

Over 93% of the Group's employees have indefinite contracts. Occasionally, staff is hired on temporary contracts to cater for seasonal surges in production.

All employees are covered by the Chemical Industry General Wage Agreement, and the company generally improves on the basic conditions of the agreement, including the remuneration, on a voluntary basis.

The remuneration paid to employees generally increases year-on-year in line with the collective labour agreements. Salaries are

fair and competitive since we need to retain highly-qualified staff. There is no significant difference between wages paid to employees of either sex within the same category.

The Oncology business unit (PharmaMar) has an Equality Plan in order to promote equal work opportunities for women and men. There is a Standing Committee on Equality comprising equal numbers of representatives of the company and workers. The committee's purpose is to organise information and awareness campaigns for the workforce and to implement and monitor the Equality Plan. No complaints of discrimination were received and the Group is not aware of any incident in this connection arising in the Group companies.

In order to enhance employee commitment and motivation, many employees receive variable remuneration or a bonus based on targets agreed upon with their supervisor. Attainment of objectives is examined by the employee and supervisor, and a percentage of achievement is established which is used as the basis for establishing the employee's bonus.

The main managers with operational responsibility for labour matters are: Pedro González Blanco (Zelnova Zeltia-Copyr), Belén Sopesén Veramendi (Xylazel), Luis Rupérez (PharmaMar), Rosario Cospedal (Genómica) and Ana Isabel Jiménez (Sylentis).

## CREATING STABLE EMPLOYMENT

- ▶ The Pharma Mar Group was particularly active in creating long-term jobs in 2017. A total of **47 persons were hired on indefinite contracts by Group companies during the year**: 34 by PharmaMar, 3 by Genómica, 1 by Sylentis, 4 by Zelnova Zeltia and 5 by Xylazel.
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## PROMOTING YOUTH EMPLOYMENT

▶ We have numerous agreements with universities and educational centres to provide internships.

In 2017, the Group had 51 interns, three of whom were subsequently hired after graduating.

### Developing talent

We draw up training plans to determine employees' training needs and ensure that they receive the education they need to carry out the specific tasks entrusted to them. Training plans include both internal training using company personnel and external training (Master's degrees, courses, conferences, seminars, etc.).

At Genómica, employees give regular lectures each month about an aspect of the company's activities or another area of interest. These

activities seek to enhance general knowledge and foster interaction, initiative, teamwork, cooperation and respect.

In 2017, the Pharma Mar Group invested over €880,000 in training, 15% more than in 2016.

The table below shows the breakdown of training expenditure among the various Group companies:

	Genómica		Sylentis		PharmaMar		Zelnova Zeltia-COPYR		Xylazel	
	Hours	€	Hours	€	Hours	€	Hours	€	Hours	€
Scientific training	74	3,903	384	31,114	8,330	353,000	74	3,624		
Executive training			44	917	372	66,534	24	1,890	380	11,666
Administrative training					741	17,827	30	1,008	370	1,490
Languages	334	6,888	160	1,955	12,924	111,980	567	9,339	156	2,843
Other types of training	16	435			3,918	236,722	125	12,702	1,628	5,345

### Benefits and perks

The Group companies try, as far as possible, to help employees combine work and family life. In companies and departments where this is possible, employees are allowed to arrange their annual vacation at any time of the year, subject to taking two weeks in the summer. Companies which work a single unbroken shift allow flexitime and finish early on Fridays.

Employees receive other benefits, such as advances and bonuses for seniority. Almost 50% of employees avail themselves of a supplementary private medical plan. Employees of the chemical companies also have life and casualty insurance. Xylazel offers a pension plan and Zelnova Zeltia and Xylazel provide study grants for employees' children, an

in-house doctor and nurse, a social worker and fitted protective clothing.

Almost all Group companies have staff dining areas equipped with crockery, refrigerators, microwave cooker, etc. so that employees can bring their own food if they wish. Most employees whose working day includes a lunch break receive lunch vouchers.

Improvements are made to facilities each year in an attempt to enhance the working environment. PharmaMar and Zelnova Zeltia buildings have eliminated architectural barriers or have installed ramps at the accesses. In 2015, Genómica relocated within the Madrid region to Parque Empresarial Alvento, Europe's first green business park. Its new, larger facilities have 1,809 m<sup>2</sup> of workspace adjoining large windows and there is abundant natural light in laboratories and offices. The building is fully adapted to persons with disability and can be reached easily via public transport.

PharmaMar, Sylentis and Xylazel provide buses to carry employees between the plants and the cities of Colmenar Viejo, Tres Cantos and Vigo, respectively.

A special Christmas dinner is held at which the Chairman addresses the employees. All employees receive a Christmas hamper.

### Incentive plan

In accordance with a decision adopted by the Shareholders' Meeting, the Board of Directors executed the Employee Stock Ownership Plan under which certain Group executives and employees (excluding members of the Board of Directors) received shares of the company in 2017, free of charge, as a function of the degree of attainment of their 2016 targets. A total of 211,664 shares were distributed.

This Stock Ownership Plan has a double objective: to reward employees and executives whose performance in 2016 was satisfactory, and to incentivise beneficiaries to stay in the Group.

### Workplace health and safety

Safety at work is a necessity from both an ethical and an economic standpoint. All Group companies have workplace safety programmes, and they conduct regular evacuation drills and simulacra. All personnel receive instruction in workplace safety, the existing risks and the measures to be taken where necessary. The Group companies have passed the legally-required safety audits.

The main people in charge of Health and Safety issues are Pedro Torrens (Zelnova Zeltia), Mario Di Leva (Copyr), Alejandro Gundín (Xylazel), Andrés Sanz (PharmaMar), Verónica Ruz (Sylentis) and Ascensión Hernández (Genómica).

The following table shows the number of work-related accidents and days lost due to illness at Group companies in 2017:

	Number	Days lost
Due to illness	137	4,718
Accidents with medical leave	1687	109
Accidents without medical leave	4	---
Accidents on the way to/from work	4	27

Xylazel and Zelnova Zeltia are also exemplary when it comes to workplace safety. There is a fire-fighting team comprising six employees trained and ready to take the immediate necessary measures until the professional fire-fighters arrive. That team is equipped with fireproof suits and breathing apparatus and it conducts a drill every two weeks, while checking that all the company's firefighting systems and equipment are in good working order. All members of staff participate in regular drills using fire extinguishers with controlled real fires.

PharmaMar is certified to the OHSAS 18001 Occupational Health and Safety Management System standard by Lloyd's Register Quality Assurance; in this connection, it is a pioneer in the biotechnology sector, where few companies are certified to this standard.

Below are the accident statistics for PharmaMar and Xylazel, the Group's two largest companies:

	Xylazel	Industry	PharmaMar	Industry
<b>Incidence rate</b>				
No. of accidents with lost days per 1,000 workers	18.69	21.04	2.65	9.10
<b>Frequency rate</b>				
No. of accidents with lost days per 1,000,000 hours worked	10.67	12.01	1.52	5.20
<b>Severity rate</b>				
No. of lost days per 1,000 hours worked	0.04	0.24	0.01	0.13



## Employee health

All employees are offered an annual medical check-up; tests are subject to informed consent, and the medical data obtained is treated as confidential. The check-ups are conducted in line with the risk inherent to each employee's specific job.

Under a broad interpretation of health monitoring that goes beyond the requirements of labour legislation, the Group's medical check-up includes blood and urine analysis, a blood pressure measurement, and nutritional counselling. The larger subsidiaries also offer an eye test and other specific tests such as

PSA, electrocardiograms, etc.; they also have a company nurse to monitor employee health.

In 2017, PharmaMar undertook the following actions to promote the health of its employees:

- ▶ Free flu vaccination for employees.
- ▶ 3rd Workplace Health and Safety Week, with workshops on ergonomics and first aid.
- ▶ 1st Health Campaign to raise employees' awareness of certain illnesses and risks. The 2017 campaign focused on cholesterol, cardiovascular diseases and vasovagal syncope





## Shareholders



## 7. Shareholders

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80.000 shareholders and  
investors

€552 million market  
capitalisation

€650 million of trading in the  
share in the year

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Close to 80,000 investors have placed their trust in Pharma Mar and, in return, we have a duty to create value.

At 31 December 2017, Pharma Mar's market capitalisation was €552 million. Its shares are traded on the four Spanish stock exchanges.

## **Number of shares and share performance**

At 31 December 2017, the Company's capital stock amounted to €11,132,464.35, represented by 222,649,287 shares with a par value of €0.05 each.

Pharma Mar's shares have been listed on Spain's electronic market since 2 November 2015, after Pharma Mar shares were exchanged for shares of Zeltia, S.A. (1-for-1); Zeltia had been listed on the electronic market from 20 October 1998 to 30 October 2015.

In 2017, Pharma Mar's share price fluctuated between €2.17 and €4.19 (closing prices), ending the year at €2.48 euro.

In 2017, trading in Pharma Mar stock totalled €650 million, with an average of 805,031 shares changing hands each day; trading reached its low in August and peaked in November.

Worldwide, the financial market had one of its best years in a decade in 2017. The year appeared to mark the end of a decade marked by the deep world crisis that commenced in 2007. In this macroeconomic environment, the euro appreciated over 15% against the US dollar.

In macroeconomic terms, Spain significantly outperforms the European average. However, both the high unemployment rate, the high public deficit and the dependence on external funding mean that the Spanish economy is still viewed with a degree of uncertainty.

Nevertheless, the IBEX-35, Spain's main equities index, started the year as one of the top performers among the developed countries, appreciating by over 15%, but the trend changed in the second half of the year, mainly as a result of the resolution of Banco Popular and the uncertainty caused by the Catalan crisis.

During 2017, Pharma Mar achieved some very important clinical milestones, resulting in a 50% increase in the share price in the first half of the year. The share price reached its high for the year in May: €4.19. This was achieved after the company held an "R&D Day" in New

York at which it detailed the progress with its pipeline and ongoing and potential clinical trials. In June 2017, promising results with Zepsyre® in a Phase Ib trial in endometrial cancer were presented at the American Society of Clinical Oncology (ASCO) meeting. In September 2017, the results of the phase I/II trial with Zepsyre® in patients with small cell lung cancer were presented at the European Society of Medical Oncology (ESMO) meeting.

However, the share experienced difficulties in November 2017, when it was announced that the EMA's CHMP had issued a negative opinion as to the approval of Aplidin® for treating multiple myeloma in Europe. The political turmoil due to the Catalan situation also had an impact on the market towards the end of the year. As a result, despite a strong rally in December, Pharma Mar's share ended the year down 8%.

## **Breakdown of capital**

Pharma Mar's shares are widely held. According to disclosures to the National Securities Market Commission (CNMV) by the parties themselves, the following hold significant shareholdings: Mr José M<sup>a</sup> Fernández Sousa-Faro owns 11.08% (4.65% through Ms Montserrat Andrade Detrell), Rosp Corunna Participaciones Empresariales, S.L. owns 5%, and Mr Pedro Fernández Puentes owns 4.5% (3.87% through Safoles, S.A.).

## **Shareholders' rights**

Shares grant their legitimate holder the status of shareholder and the rights acknowledged in the law and in the Bylaws:

- ▶ The right to attend Shareholders' Meetings and to challenge decisions by the Shareholders' Meeting. An Ordinary Shareholders' Meeting is held once per year.
- ▶ The pre-emptive right to acquire new shares or convertible bonds.

- ▶ The right to share in the corporate profits and in the proceeds from its liquidation.
- ▶ The right to information.

Once notice has been given of the Ordinary Shareholders' Meeting, any shareholder may obtain, from the Company's registered offices or the office at Plaza del Descubridor Diego de Ordás 3, Madrid, the financial statements, proposed distribution of income, directors' report, auditors' report, the annual corporate governance report, any other documentation that must be made available to shareholders.

Shareholders may also request the delivery or shipment of the full text of those documents, free of charge. All that documentation is also available on the company's website, [www.pharmamar.com](http://www.pharmamar.com)

From the date of notice of the Shareholders' Meeting and up to and including the fifth day prior to the date scheduled for the Meeting at first call, shareholders may submit written

requests for reports or clarifications that they wish, or may raise any question they desire about the items on the agenda.

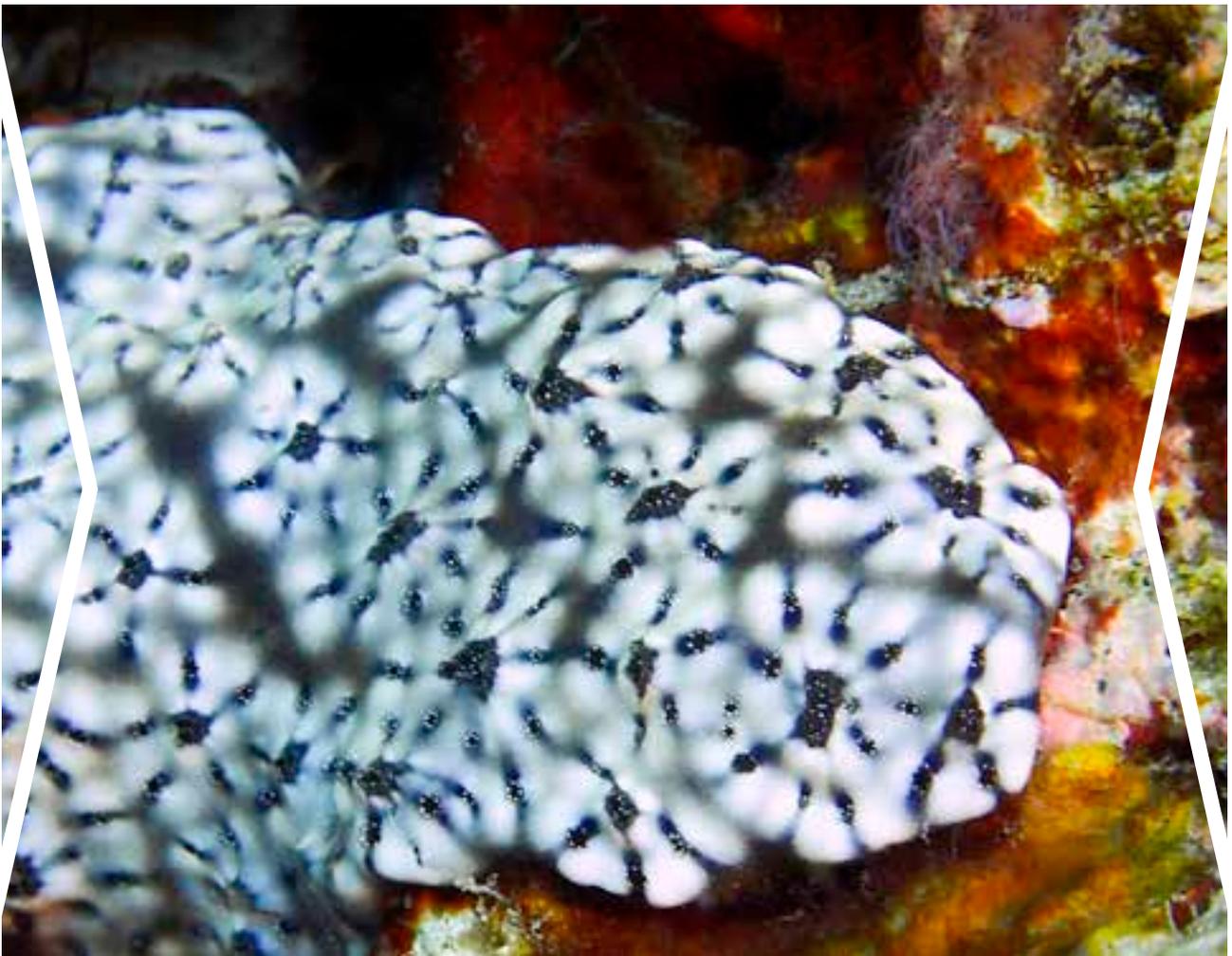
During the Shareholders' Meeting, shareholders may verbally request any information and clarification they wish about the items on the agenda.

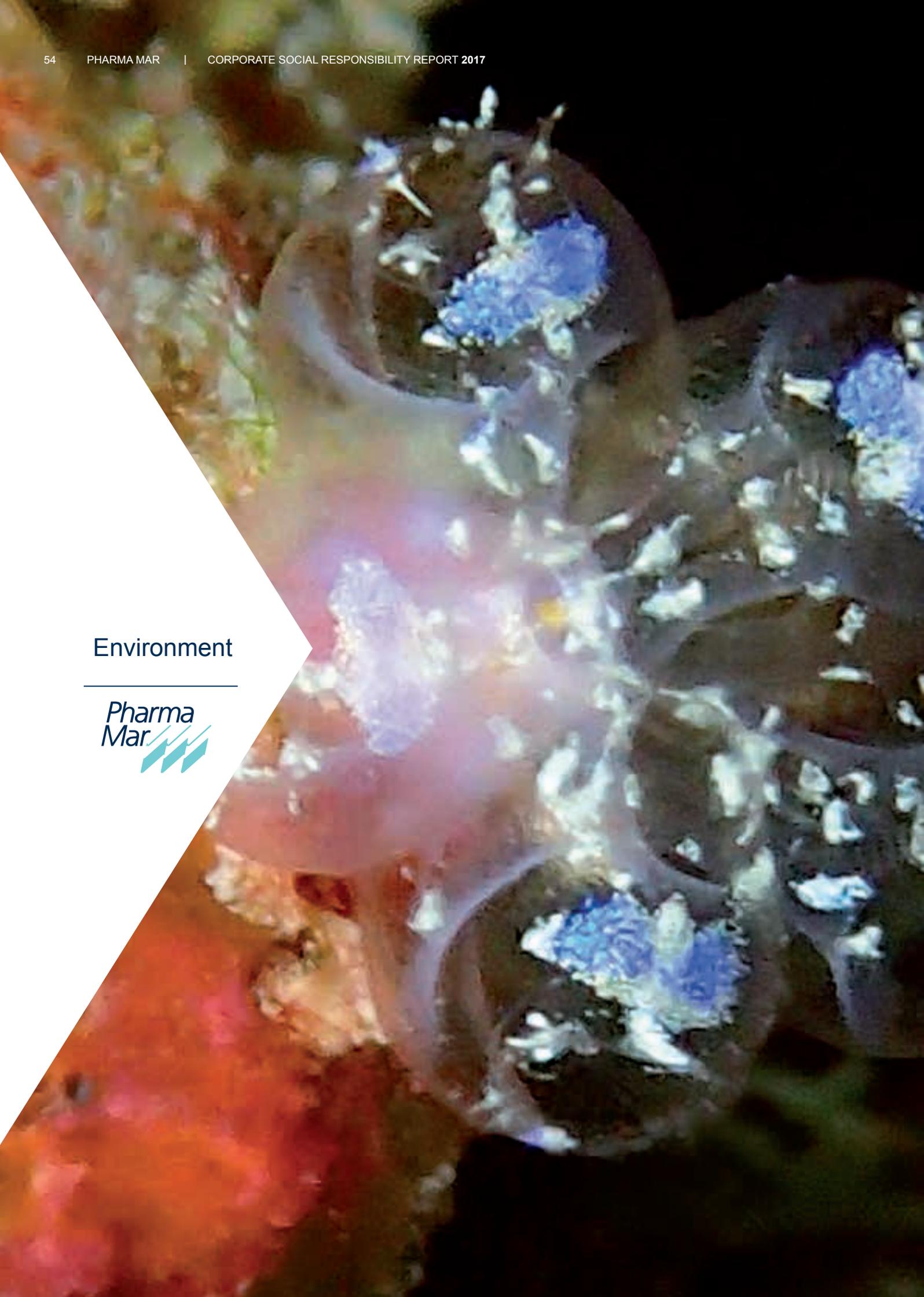
### **Communications with shareholders**

All material information about Pharma Mar is kept up to date and is available to shareholders and the general public on the company's website, [www.pharmamar.com](http://www.pharmamar.com).

The web site also has news, monographs and presentations on health-related matters.

Shareholders may also call the shareholder hotline at 902 101 900 or send an e-mail to: [investorrelations@pharmamar.com](mailto:investorrelations@pharmamar.com)



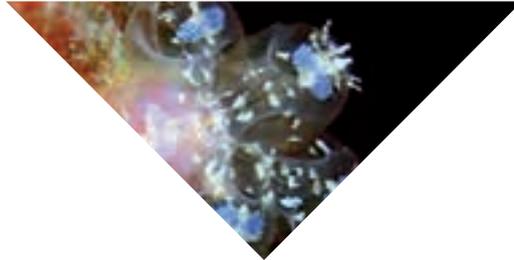


## Environment



## 8. Environment

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PharmaMar and Xylazel are certified to the ISO 14001 environmental management standard

€167,000 spent on environmental issues in 2017

Samples are collected selectively by hand

Measures to reduce electricity consumption

Upgrade of water separation networks

Our companies strive to protect the environment, not just in their activities but also in the development of products that comply with environmental regulations. As a manufacturer of wood protection and conservation products, Xylazel is ecologically responsible since, by protecting wood, it protects the forests.

PharmaMar's research work is conducted with the utmost respect for the sea; molecules of interest are synthesised. This provides the compound without having to resort to the natural

organisms that produce it. Moreover, no more than 100 grams of each marine organism are extracted. In accordance with the Convention on Biodiversity, the company defends the sustainable use of the sea's valuable resources and the equitable distribution of its findings. In this way, PharmaMar not only contributes to the development of new anti-cancer treatments from just a few grams of sample, but also furthers knowledge and conservation of local marine ecosystems.

PharmaMar and Xylazel are certified to the ISO 14001 environmental management standard. Those two companies together represent 65% of the Pharma Mar Group's revenues and 77% of its workforce.

There were no environmental incidents or sanctions at any of our companies in 2017.

Pharma Mar Group companies expended €167,000 in environmental matters in 2017.

In order to respect the environment, this Social Responsibility Report is issued in electronic format only, thus saving the paper of a print edition.

The policies of the Group's largest companies, PharmaMar, Zelnova Zeltia and Xylazel, with regard to waste are detailed below. The people in charge of the environmental policy at those companies are: Andrés Sanz, Pedro Torrens and Alejandro Gundín, respectively.

## **PHARMAMAR**

PharmaMar is certified to the ISO 14001 environmental management standard. PharmaMar is a pioneer in the biotechnology sector, where there are very few companies with this certification.

PharmaMar conforms to Article 1 of the Convention on Biodiversity, which refers to the sustainable use of natural resources to balance ecosystems, society and the global economy. There are two existing international documents whose principles are reflected in the criteria applied in sample collection: the Red List of endangered species, and CITES (Convention on International Trade in Endangered Species of Wild Fauna and Flora).

Samples of marine invertebrates are collected selectively by hand by scuba divers; no mechanical systems, such as drag nets or dredging, are used, thereby eliminating the impact on the natural environment. We also use an underwater robot with an umbilical that is operated from the surface and provides a real-time view of the seabed, allowing for the selection of sample zones and minimising human interaction with the ecosystem.

PharmaMar has implemented the following measures to control and reduce the environmental impact and increase energy efficiency:

- ▶ Calculation of the company's carbon footprint, which ranges from sea expeditions to collect marine samples through to commercial distribution of drugs.
- ▶ Development of training plans in environmental matters, which ensure that all employees are highly qualified in this area.
- ▶ Minimisation of atmospheric emissions by means of HEPA particle filters in process areas and scrubbers for gases from the laboratory fume cupboards.
- ▶ Control of hazardous waste produced at PharmaMar installations and minimisation of the impact using waste separation programmes.
- ▶ Control of process water using a purifying plant that homogenises the water and adjusts chemical parameters to ensure that discharged industrial water is within the allowed limits.
- ▶ Product storage areas are built of concrete, and drain towards the water purification system to avoid risks of chemical spills and leaks.



## SPANISH GREEN GROWTH GROUP



In 2014, **PharmaMar** joined the Spanish Green Growth Group, an association created to foster public-private cooperation in addressing environmental challenges. The goals of the Spanish Green Growth Group are as follows:

- ▶ Convey to society and government the potential for a green economic growth model for Spain.
- ▶ Work on common positions with a view to international negotiations on climate change, and combat climate change via public-private partnerships.
- ▶ Influence the development of a low carbon economy that is compatible with the goal of economic growth and job creation.

## PACT FOR THE BIOSPHERE



**The Pharma Mar Group** sees respect for and promotion of biodiversity as one of the key tenets of its business.

The Company's bioprospection efforts are assisted by universities, centres for marine research, and Environment and Fisheries Ministries throughout the world to enable the company to comply with regulations on biodiversity while sharing findings with local scientific communities.

PharmaMar has discovered hitherto unreported marine organisms on its expeditions. For example, the company discovered a new species of deep-sea sponge, *Streptomyces pharmamarensis*, which was isolated from marine sediment and characterised by PharmaMar researchers<sup>2</sup>.

As an expression of this commitment, the Pharma Mar Group has signed the Pact for Biodiversity, which aims to promote economic development that is compatible with biodiversity conservation.

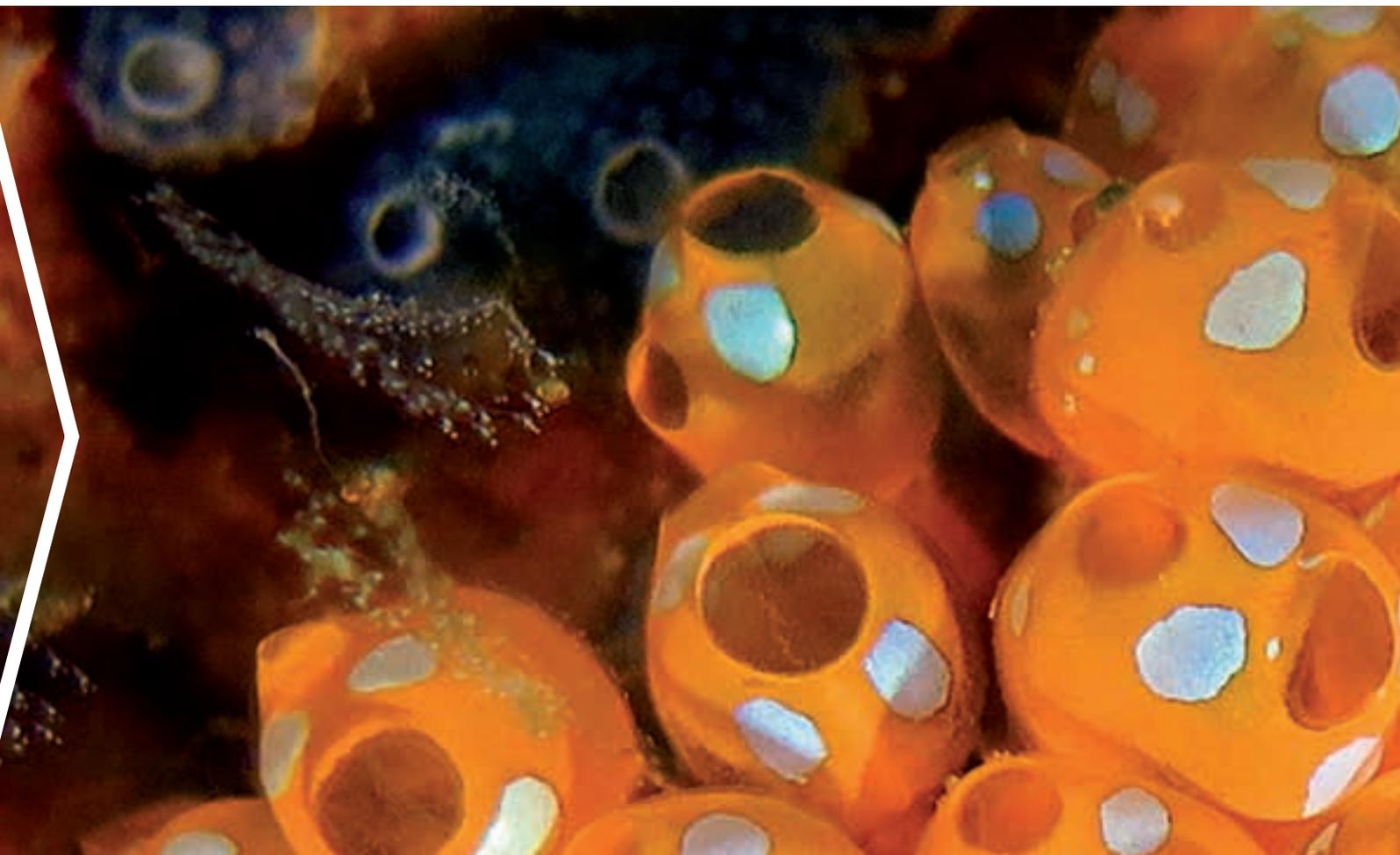
This is a formal commitment to what the Pharma Mar Group was already doing: preserving biodiversity, using components sustainably and distributing in an equitable manner the benefits deriving from the use of genetic resources.

<sup>2</sup> International Journal of Systematic and Evolutionary Microbiology (2012), 62, 1165–1170 DOI 10.1099/ijs.0.034066-0

## **ZELNOVA ZELTIA**

The company's environmental policy sets out its goal of preserving and improving the natural environment. The most significant actions in this area include:

- ▶ Waste treatment: The use of a solid waste separation centre, and a wastewater treatment plant for separating water and liquid wastes; it separates waste at source and is a member of several waste management systems, such as ECOEMBES (packaging waste), ECOELEC (electricity appliances), ECOPILAS (dry cells and batteries) and SOGARISA (Galicia industrial waste treatment and disposal centre).
- ▶ Reduction in electricity consumption: improved use of natural lighting, programming factory lines to be synchronised with the machinery start-up and shut-down and maximal use of machinery uptime.
- ▶ Regular external measurements of atmospheric emissions and liquid discharges, whose results are sent to the Galicia Regional Government Department of the Environment and the Louro river authority, respectively.
- ▶ Segregation of chemicals on the basis of danger, and installation of containments in each specific risk area.
- ▶ Water separation: process cleaning water is subjected to a specific treatment process to separate sludge from clean water (wastewater). Wastewater, sewage and storm water are channelled separately to allow for better control over discharge quality.
- ▶ The factory roof was replaced in 2017: polycarbonate sheets were installed to make use of natural light, which resulted in a reduction in electricity consumption. LED lamps were also installed in the factory and offices.



## **XYLAZEL**

Xylazel is certified to the ISO 14001:2004 environmental management standard, and is audited each year by Bureau Veritas.

In compliance with the standard, Xylazel has defined an environmental policy including a number of emergency plans to deal with potential environmental accidents:

- ▶ Regular evaluations of the consumption of raw materials and of ancillary utilities (diesel, electricity, water, paper, etc.) in manufacturing. The system also monitors emissions, discharges and waste production.
- ▶ Implementation of a new water recirculation system for firefighting in the factory, notably reducing water consumption.
- ▶ Progressive modernisation of lighting equipment by replacing conventional sodium vapour lamps with LED lamps, which consume less electricity.
- ▶ A new aspiration system was installed for removing powder produced in the factory and waste processing systems.
- ▶ Also in 2017, work commenced to upgrade all of the company's storm drains, including automatic shut-off valves for the event of an emergency.

## **RESOURCE CONSUMPTION IN 2017**

	<b>PharmaMar</b>	<b>Zelnova Zeltia</b>	<b>Xylazel</b>
Electricity (MWh)	5,102	933	559
Diesel (fuel) (l)	---	36,924	9,100
Natural gas (fuel) (l)	308,334	---	---
Water (m <sup>3</sup> )	10,650	10,000	2,674

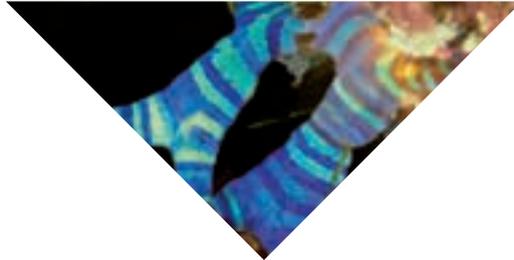


## Community Action



## 9. Community action

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Work with numerous patients' groups,  
including FEDER

Cooperation agreement between  
PharmaMar and CNIO

Sponsorship of scientific conferences  
and meetings

Mentoring to help young people find their  
first job

Blood donation drives

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Our greatest contribution to society is searching for new drugs against diseases for which there is no effective cure as yet. Activities in that area are described in detail in the section of this report that deals with patients.

We also cooperate actively with numerous initiatives to promote research, disseminate

knowledge and support education. The Pharma Mar Group's contributions in this area include:

Scholarships	€ 116,000
Donations (mainly to hospitals)	€ 53,154
Sponsorship of scientific conferences and seminars	€ 908,427
Cooperation with organizations	€ 89,280

**feder** entidad de utilidad pública  
FEDERACIÓN ESPAÑOLA DE ENFERMEDADES RARAS

**DÍA MUNDIAL DE LAS ENFERMEDADES RARAS**  
28 DE FEBRERO

**LA INVESTIGACIÓN ES NUESTRA ESPERANZA**  
#SOMOSFEDER

**INVESTIGA EN RED POR UN FUTURO LLENO DE ESPERANZA.**

El diagnóstico y tratamiento de las enfermedades raras sólo es posible gracias a la investigación de manera coordinada. Esta investigación que debe ser liberada a todos los ámbitos del proceso socioeconómico y a todos los tipos de acciones desde hoy. Porque sólo abordando en red en el presente, podremos conseguir soñar con un futuro esperanzador.

[www.enfermedades-raras.org](http://www.enfermedades-raras.org)

Logos of sponsors: Johnson & Johnson, janssen, Boehringer Ingelheim, Shire, Novartis, AstraZeneca, Roche, Pfizer, CSL Behring, Esteve, Merck, Nacel, etc.

Notable actions to **promote research and disseminate knowledge** include:

- ▶ Working with **patients' groups**, such as *Federación Española de Enfermedades Raras (FEDER)*, European Organisation for Rare Diseases (**EURORDIS**), Sarcoma Patients Euronet (**SPAEN**), European Network of Gynecological Cancer Advocacy Groups (**ENGAGE**), *Asociación de Afectados por Cáncer de Ovario (ASACO)*, *Grupo Español de Pacientes con Cáncer (GEPAC)*, Myeloma Patients Europe (**MPE**) and *Cura e Ricerca in Oncologia Ginecologica (IRIS)*.
- ▶ Specifically, PharmaMar took part in the FEDER 2017 campaign "*La investigación es nuestra esperanza*" (Research is our hope), coinciding with world Rare Disease Day. The

company works with FEDER in a number of ways:

- Donations of funds
- Employee participation in the Hope Race in March 2017. PharmaMar paid the entry fee for its employees who participated.

PharmaMar also sponsored the 8th National Race to End Women's Cancer, which supports research, education and awareness of gynaecological cancers.

- ▶ Cooperation with **medical associations**: Groups of oncologists engaged in independent research into sarcoma, ovarian cancer and other types of cancer, assisting them in pursuing their goals.



Pharma Mar Group employees took part in the Spanish Conquer Cancer Campaign's annual run



PharmaMar sponsored the Eighth National Race to End Women's Cancer, held in Washington DC in November 2017



Left to right: Carmen Vela (Spanish Government Secretary of State for R&D and Innovation), María Blasco (Director of the Spanish National Cancer Research Centre — CNIO), and José María Fernández Sousa-Faro (Chairman of the Pharma Mar Group) at the signature of the cooperation agreement between PharmaMar and CNIO

▶ **Signature of a cooperation agreement between PharmaMar and the Spanish National Cancer Research Centre (CNIO)** to characterise the anti-tumour potential of marine organisms.

▶ **Scientific publications** in a range of prestigious international journals and specialist press, in the fields of oncology, pharmacology, therapeutics and diagnosis. According to the ASEBIO report, Pharma Mar is the Spanish company with the second-largest number of publications in high-impact scientific journals.

▶ Publication of the book "**El mundo submarino de PharmaMar**" (PharmaMar's Undersea World), which contains photographs of marine organisms taken on expeditions by our marine biologists, from which the company extracts the compounds for R&D and innovation.

▶ Sponsorship of, and support for, a number of **research bodies**, including the **Spanish**

**Conquer Cancer Campaign** (in addition to regular cooperation, many PharmaMar employees participated in the annual run), and the **Mari Paz Jiménez Casado Foundation**, a non-profit organisation that helps people with sarcoma and incentivises training and scientific research.

▶ Sponsorship of, and participation and presentations at, numerous **scientific conferences and meetings**. Among the many domestic and international conferences was the 2nd International Conference on "**Soft Tissue Sarcoma: Evidence & Experience**" and the 4th "**Foro del Cáncer de Ovario**", both organised by PharmaMar.

In April 2017, Sylentis hosted a meeting of world-class ophthalmologists to agree on the approach to new pharmacological treatments for dry eye syndrome.

▶ Active participation in associations to **promote biotechnology**, such as **ASEBIO**, the Spanish Association of Bioenterprises.

- ▶ Cooperation with associations to promote the pharmaceutical industry, such as **EBE** (European Biopharmaceutical Enterprises), which represents the pharmaceutical industry in Europe.

In the area of **education**, Pharma Mar undertook the following actions:

- ▶ Agreements with numerous universities, business schools and institutes in Spain and other countries as part of a **training programme for interns** at PharmaMar, Genómica, Sylentis and Xylazel.
- ▶ Participation in **post-graduate seminars and courses** organised by universities and in Master's programmes and conferences in the fields of biomedicine and biotechnology. These courses facilitate the exchange of technical knowledge in order to promote science and research.

A good example of this is the *Blue Biotech Master* programme at Universidad Católica de Valencia San Vicente Mártir. This master's programme arose out of obtaining a European project under the "*Blue Careers in Europe*" funding round. PharmaMar assists in curriculum development and incorporating material on industrial applications into the

curriculum. Additionally, Fernando de la Calle, PharmaMar's Head of Microbiology, teaches some units and seminars on marine biodiversity.

- ▶ Cooperation with **FEUGA** (*Fundación Empresa-Universidad Gallega*). This is a not-for-profit entity specialised in transferring knowledge, innovation and technology from Galicia's universities to business and society at large.
- ▶ **Mentoring initiative**, involving Sylentis: a project to guide final-year students facing the challenge of finding a job. The project arranges rounds of contacts between these young people and mentors from various professional backgrounds, who transmit their experience and what kind of profile they look for when hiring a person, answer mentees' questions and, ultimately, help them find their first job.
- ▶ **Programme of specialised Fulbright visits** to PharmaMar's facilities. This programme focuses on outstanding US researchers with a strong international profile to give them first-hand knowledge of Spain's leading companies and institutions in the area of R&D and innovation.



Fulbright programme researchers visited PharmaMar facilities

In addition, the Group also engages in the following **activities in support of society**:

- ▶ Outsourcing of advertising materials and graphic design to sheltered **workshops for persons with disabilities**, such as Trébore, a Paideia Galiza Foundation initiative. It also works with Integral AV, a travel agency which employs persons with disabilities.
- ▶ Blood donation **drives in cooperation with** the Spanish Red Cross: PharmaMar organised two blood donation sessions in cooperation with Madrid's Transfusion Centre, in which 61 employees donated.
- ▶ **Donation of Zelnova Zeltia products to "Acompartir"**, a not-for-profit association. The association redistributes funds to NGOs that work with people at risk of social exclusion. Zelnova Zeltia also collaborates by donating plastic bottle caps and containers to BANTA (*Banco de Tapones del Bajo Miño*), which helps children with special needs.
- ▶ Collaboration with **Círculo de Confianza**, a private platform for meeting, observation and analysis which seeks to promote a better understanding of new trends and changes in economics, society and politics.

## Sello Solidario



**¡Enhorabuena!**

Felicidades porque recibir el sello es un símbolo de que habéis gestionado socialmente vuestros productos, siendo generosos y compartiendo vuestros productos con personas en exclusión social además de cuidar el medio ambiente.

**¿Cómo utilizarlo?**

Formato web/papel



Estatuilla para poner en recepción



En vuestros envases



**¿Para qué sirve?**

Os animamos a que enseñéis vuestros empleados, clientes y proveedores que sois una empresa que se preocupa por las personas y el medio ambiente.

El logo ayuda a comunicar visualmente a nuestro entorno qué hacéis con los productos invendidos (defectuosos, fin de stocks, devoluciones, excedentes, etc.)

C/ Marqués de Madrid 28014

**GRACIAS**

08679676



Zelnova Zeltia works with NGO "Acompartir"

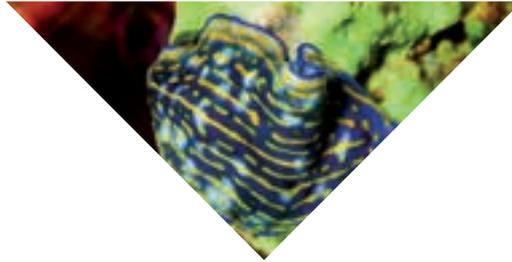


## Communities



## 10. Communities

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602 employees in the Madrid and Galicia regions

Guided visits to the company's facilities

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The Pharma Mar Group companies are established in the municipalities of Colmenar Viejo, Tres Cantos, Madrid and Porriño (Galicia). The companies contribute to the growth of their local communities by creating and maintaining stable employment, paying taxes—which fund infrastructure and government programmes—and providing a range of services. Additionally, the companies take the necessary steps to minimise the environmental impact of their activities, as detailed in the chapter on the Environment.

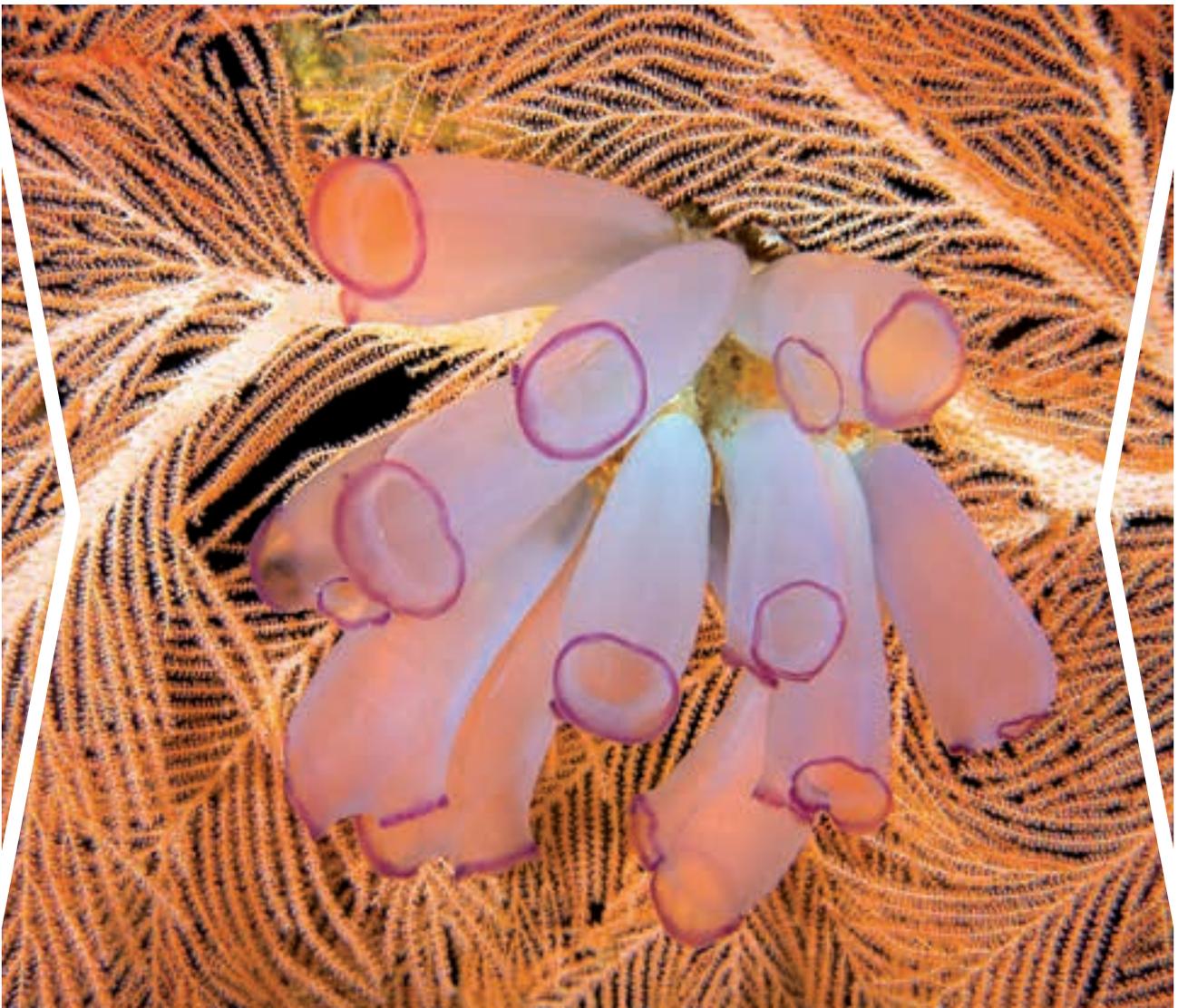
The taxes paid to municipal and regional governments by the Group companies (property tax, business tax, various municipal taxes, etc.) amounted to around €95,000 in Galicia and €75,000 in Madrid in 2017.

Our companies are also a major source of employment. We employ 155 people in Galicia. Xylazel and Zelnova Zeltia also create jobs in other regions: a total of 31. We employ a total of 447 people in the Madrid region.

We also maintain smooth relations and an ongoing dialogue with the governments of the municipalities where we are established, and we participate in numerous events organised to promote and provide services to the community: job banks, seminars on technology and R&D, lectures, meetings, etc.

Services provided to the local communities include:

- ▶ **Guided visits** to PharmaMar and Xylazel facilities for students, with educational talks pitched to the appropriate level. Among the group visits to PharmaMar in 2017 were students from CESIF Business School, the CBM (Autonomous University of Madrid) Master's programme in Biotechnology, and Madrid Complutense University. Xylazel hosted visits from the vocational students in Sales Management and Commercial Space, and International Trade, and students from A Guia high school in Vigo.
- ▶ **Cooperation with the ASEYACОВI**, the Association of Entrepreneurs, Traders and Self-employed workers of Colmenar Viejo, and the **Family Business Association of Madrid**, an independent group which defends Madrid interests and organises activities for its members.
- ▶ Participation by Sylentis and Genómica in the Madrid **Food Bank**.





## Regulators



## 11. Regulators

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Smooth, transparent relations with regulators

Cooperation in drawing up guidelines and regulations

Regulators are authorities with responsibility for drafting and enforcing the law relating to the development and authorisation of new drugs.

Pharma Mar's relations with the regulators that govern its various activities are smooth, transparent and efficient. Open communication and the exchange of knowledge make it possible to ascertain the authorities' opinion and set out the company's viewpoint in defence of its interests. As part of this constructive dialogue, advice is sought, doubts are resolved, information requested by regulators is presented, and regulator's proposals are noted for consideration in future actions. Responding to constant changes in legislation due to new Directives issued by the European Union and other countries where the Group operates, the Group companies update their procedures promptly so as to comply scrupulously with the current legislation.

A number of initiatives were taken to increase transparency in relations between the regulatory authorities and the industry. For example, Pharma Mar works with regulators in drawing up new guides and regulations, which enables us to comment on issues that could be improved and makes it possible for our interests to be taken into account. Through associations such as European Federation of the Pharmaceutical Industries and Associations/European Biopharmaceutical Enterprises (EFPIA/EBE), the company participates in discussions with the European Union, the European Medicines Agency (EMA), local regulators in Europe, and the US Food and Drug Administration (FDA) on proposals for guidelines relating to drug development and commercialisation. This entails reviewing draft versions of new guidelines.

As a listed company and issuer of securities, Pharma Mar is subject to the supervision of the National Securities Market Commission (CNMV).

The main regulatory bodies and institutions with which the Pharma Mar Group has contact—either directly or via subsidiaries, clinical trial

monitors, partners, or associations of which it is a member—are as follows:

- ▶ Spain: Ministries (Health & Social Policy, Environment, Economy, Industry & Competitiveness), Madrid Regional Government Department of Health, the Health Departments of other Spanish autonomous regions, the Spanish Medicines and Health Products Agency, Institutes of Public Health, Pesticide Register, Regional Governments, city governments, and the National Securities Market Commission (CNMV).
- ▶ Europe: EMA, European Commission, the Ministries of Health of the various Member States, National Regulatory Agencies and the Price and Reimbursement Authorities.
- ▶ USA: FDA, directly and through Janssen Research & Development, LLC, a Johnson&Johnson subsidiary.
- ▶ In Japan: Ministry of Health and the Medicine and Health Product Agency, via PharmaMar's representative in that country.



- ▶ Other: ANVISA (Brazilian Health Regulatory Agency) and the Korea Food and Drug Administration (KFDA).

The main issues discussed with regulatory authorities are:

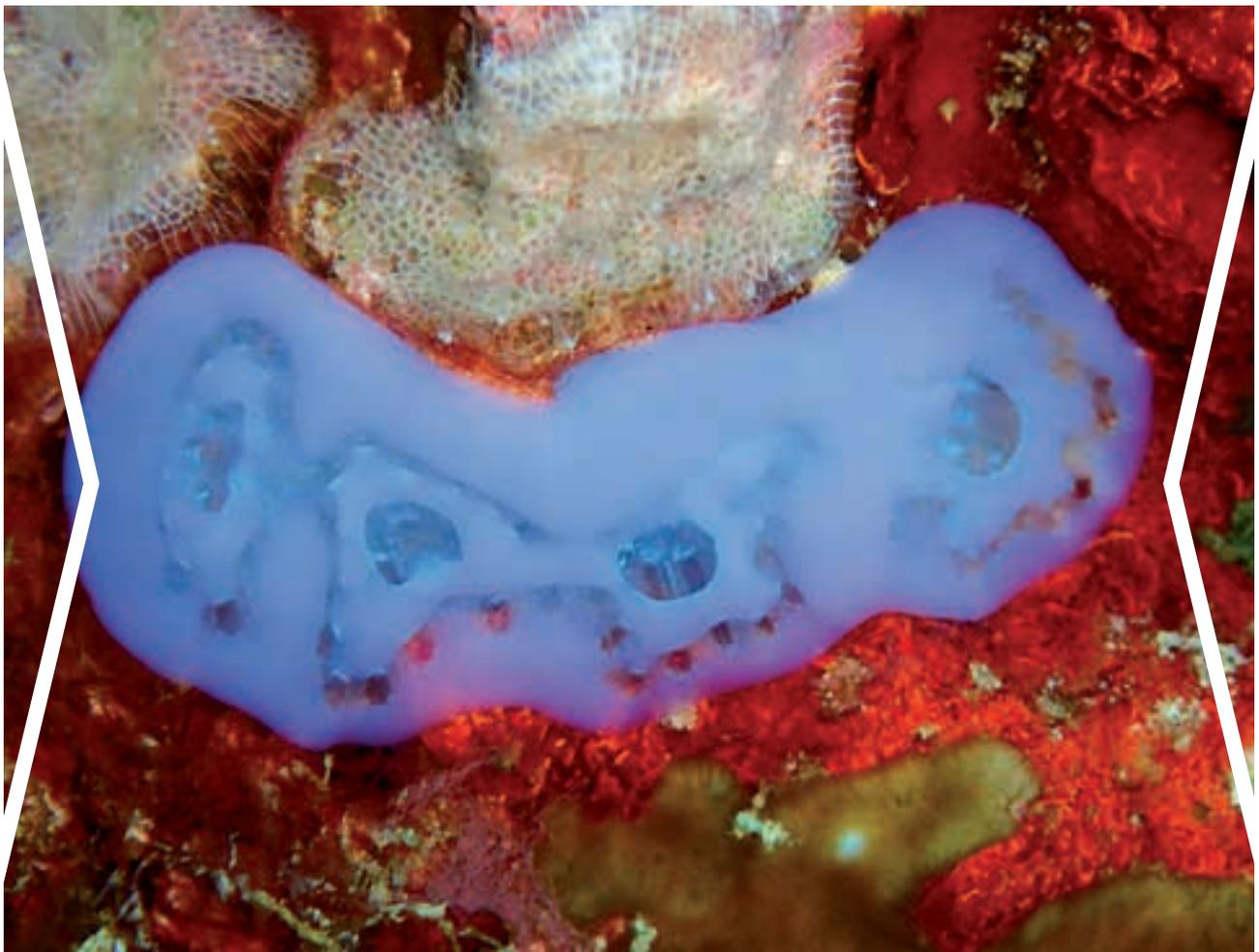
- ▶ PharmaMar: authorisation and performance of clinical trials, inspections, drug development, scientific advice, maintenance of commercialisation authorisation for Yondelis® and price and reimbursement negotiations.

Issuance and listing of securities, and financial and business disclosures in connection with the capital markets.

- ▶ Sylentis: drug development, including clinical trials and trial authorisation by ethics committees and regulatory agencies in Europe and the US. Inspection by the Spanish Agency for Medicines and Healthcare Products (AEMPS) to renew its

authorisation as a pharmaceutical laboratory to manufacture research drugs. In 2017, the company met with the medicines agencies in Spain, Germany and Sweden to discuss the future development of tivanisiran.

- ▶ Genómica: registration and obtainment of the CE mark for diagnostic kits, most recently for CLART® STD. In 2017, the company worked intensely with the Brazilian and Korean regulators to obtain the GMP (Good Manufacturing Practices) certificate required to commercialise health products in those territories.
- ▶ Zelnova Zeltia-Copyr: obtainment of approval to market the company's products.
- ▶ Xylazel: register of biocides and pesticides, cooperating with the Spanish paint industry association ASEFAPI (*Asociación Española de Fabricantes de Pinturas y Tintas de Imprimir*) and its actions before the Health Ministry.



Pharma  
Mar

The logo graphic consists of three parallel, slanted rectangular bars in a teal color, positioned to the right of the text 'Pharma Mar'.