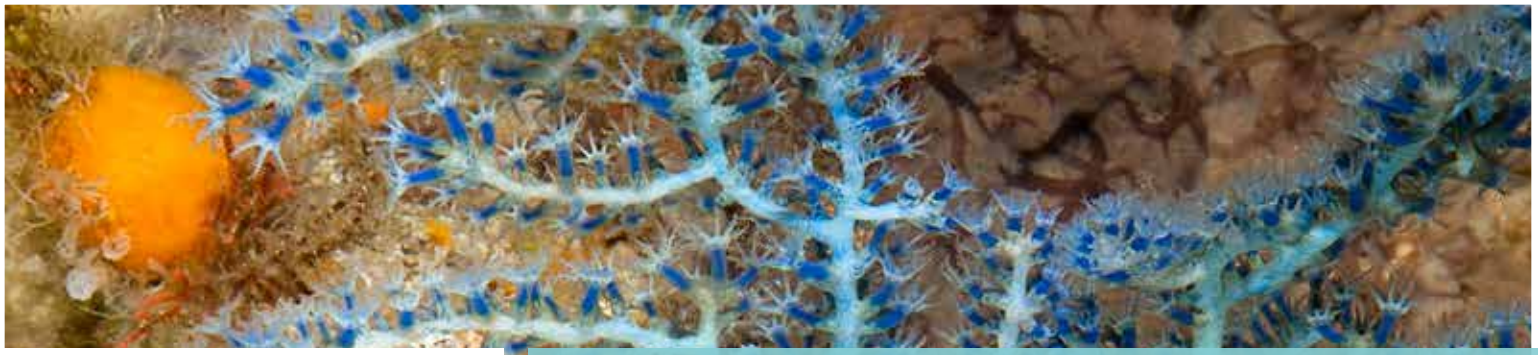


Pharma Mar

Corporate Social Responsibility Report 2016

CORPORATE SOCIAL RESPONSIBILITY REPORT 2016

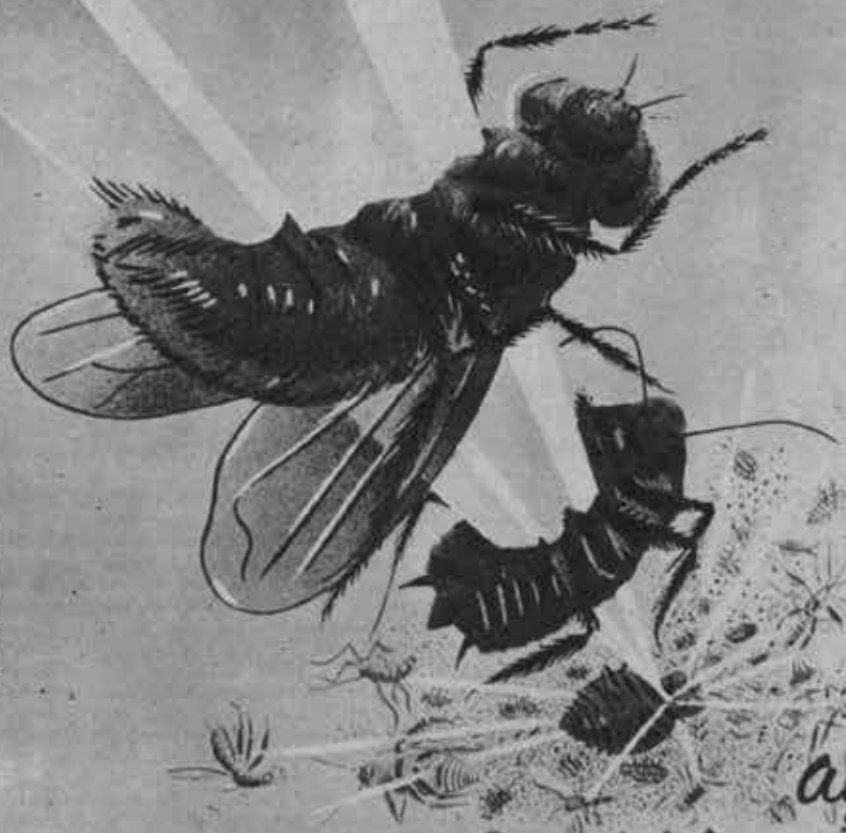
Pharma Mar, S.A.

CONTENTS

GROUP DESCRIPTION

INSECTICIDA 'Zeltia'

DE LA SERIE D. D. T.



MODERNO INSECTICIDA
ENÉRGICO-EFICAZ-PERSISTENTE

Los resultados de su empleo en los ejércitos beligerantes, son demostración plena de su eficacia y han acreditado a este insecticida como un producto de fama mundial.

alce

LABORATORIOS ESPAÑOLES 'Zeltia' S.A.

1. GROUP DESCRIPTION

In October 2015, Zeltia (merged company) was merged into PharmaMar (merging company), which became the parent company of the Group, no changes being made to the consolidation scope. The goal of this transaction, in its first stage, is for the oncology business to be listed directly, as well as to provide PharmaMar with the flexibility required to undertake corporate transactions in the future.

HISTORY OF THE GROUP

- **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. Sulfamide was synthesized 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.

- **1950s.** Zeltia expanded its product range and commenced scientific and commercial alliances with foreign companies such as Imperial Chemical Industries (ICI) and Cooper McDougall & Robertson Limited.

- **1960s.** 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.

- **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.

- **Early 1980s** Antibióticos and ICI Farma were divested.

- **1986.** PharmaMar, a world pioneer in the development of anti-tumor drugs of marine origin, was founded.

- **1990s.** The Group stabilized in most recent configuration, through the definition of the two main business areas in which it currently operates: Biopharmaceuticals and Consumer Chemicals.

- **1991.** Zelnova was spun off from Cooper Zeltia.

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

- **1998.** Zeltia shares were listed in the electronic market of all four Spanish stock exchanges.

- **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 therapeutic 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-tumor drug approved in Europe.

- **2009.** Yondelis® was approved by the European regulator to treat relapsed ovarian cancer.

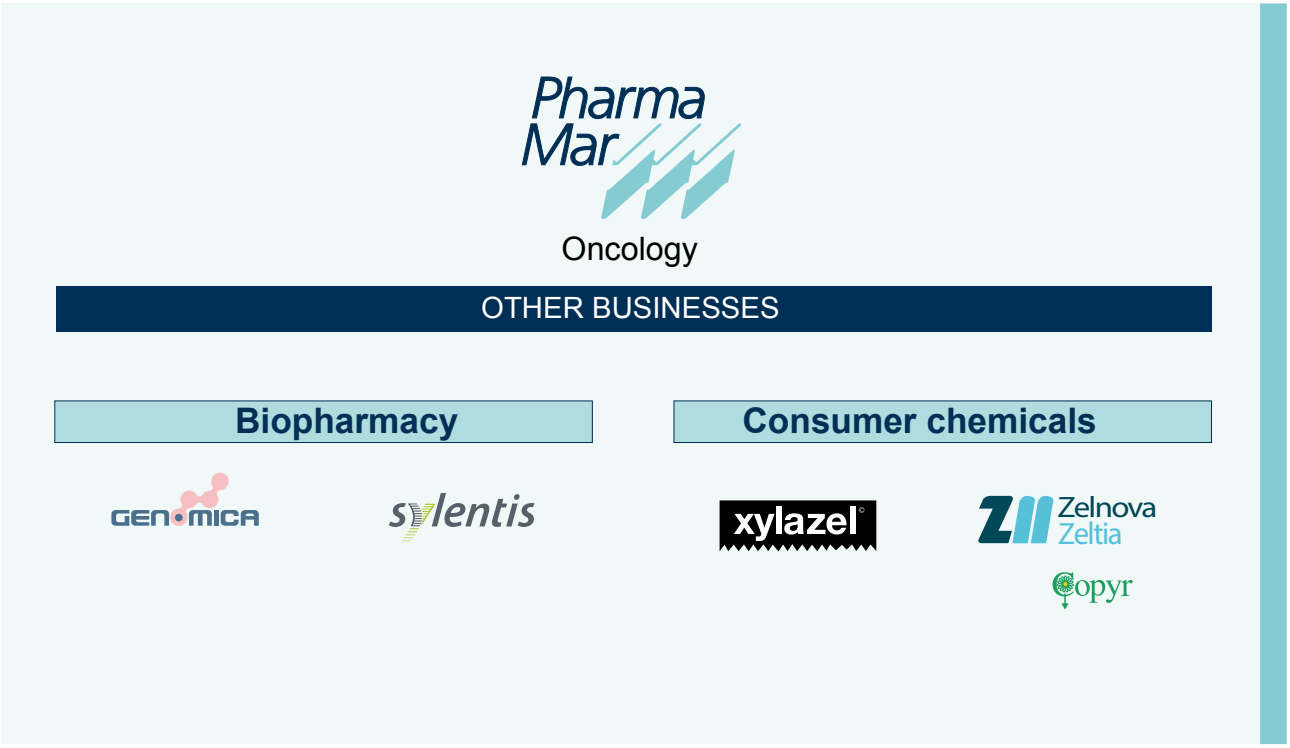
- **2014.** The Group celebrated its 75th anniversary: A long, sound track-record that stands out among Spanish biopharmaceutical companies.

- **2015.** PharmaMar absorbed Zeltia in a reverse merger, and the group was renamed “PharmaMar 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 US and Japanese regulators for the treatment of soft tissue sarcoma. Yondelis® is currently approved for sale in close to 79 countries.

THE GROUP TODAY



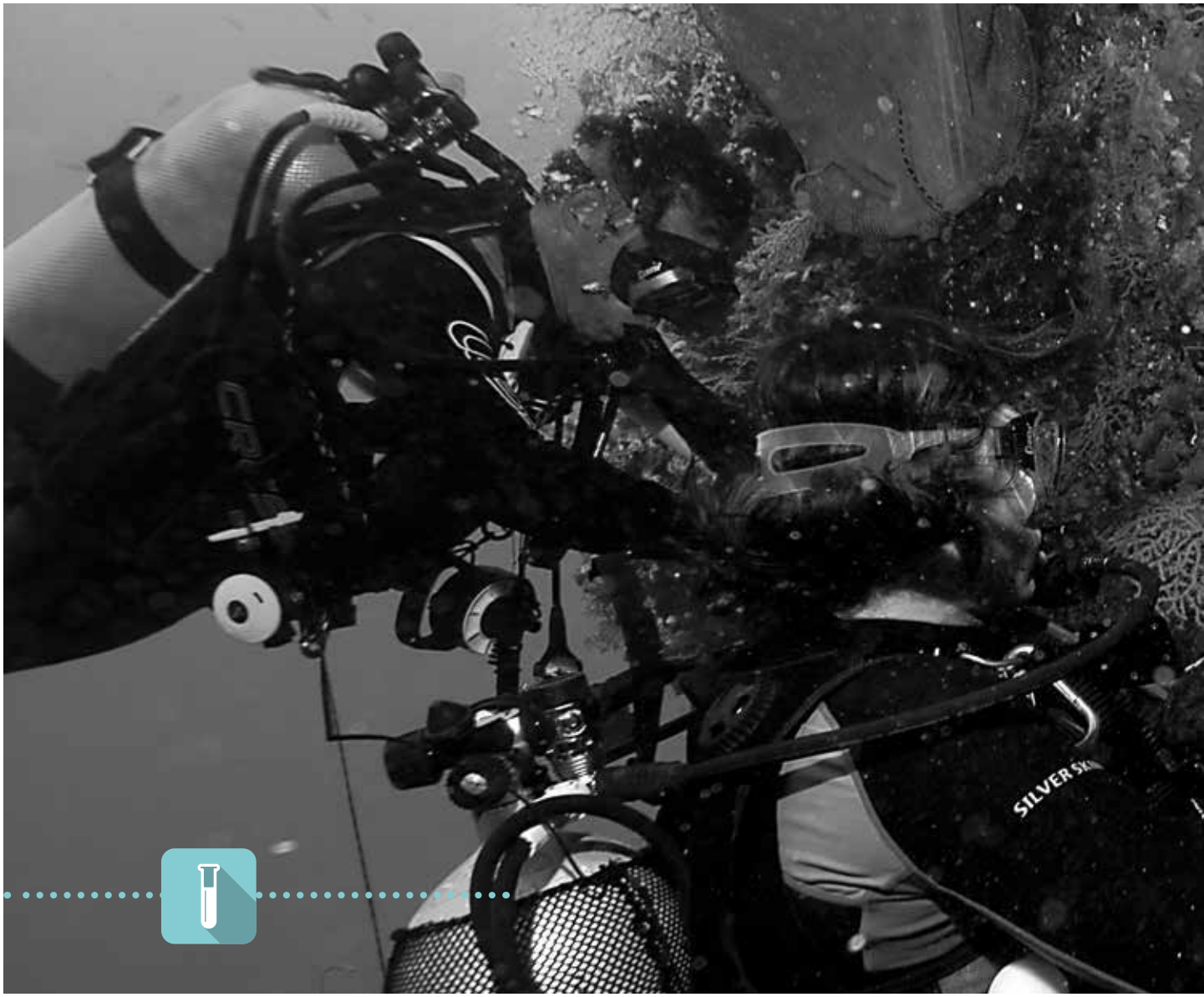
PharmaMar Group comprises the following companies:

PHARMA MAR, S.A. is a company focused on **oncology** and committed to research and development which takes inspiration from the sea to discover molecules with anti-tumor activity. It is an integrated company that seeks innovative products to provide healthcare professionals with new tools to treat cancer. PharmaMar's commitment to patients and to research has made it a **world leader in the discovery of antitumour drugs of marine origin.**

PharmaMar currently has **one approved drug on the market: Yondelis®,** for treating soft tissue sarcoma and relapsed ovarian cancer. It also has a solid pipeline, with various molecules in clinical development (i.e. tests on patients) and others in pre-clinical development (i.e. tests on animal models). One-third of all patents on drugs of marine origin and a similar proportion of academic papers on the subject are the result of PharmaMar's research. PharmaMar currently has the world's largest collection of marine organisms, comprising 200,000 samples of macro- and micro-organisms and growing constantly. From the original marine sample, PharmaMar synthesizes 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.

In order to market Yondelis® in the European Union, PharmaMar has established subsidiaries in Switzerland, Germany, France, Italy, Belgium, the UK and Austria, all of them bearing the Pharma Mar name; the most important ones are Pharma Mar GmbH (Germany) and Pharma Mar S.r.L. (Italy). Their object is to market pharmaceuticals in their respective territories.

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*** technology, which enables simultaneous detection of multiple pathogens and markers in a single test-tube, leading to a rapid, specific diagnosis. 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 also provides technology transfer by installing turnkey genetic fingerprinting and forensic biology laboratories. It is based in the Madrid region and it has a subsidiary, Genómica AB, in Sweden, and a commercial office in China.

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, and other molecules in pre-clinical development in other areas. Sylentis is based in the Madrid region.

XYLAZEL, S.A. manufactures and markets paint and varnish, and is specialized in wood decoration and treatment. Its products protect wood against fungi, mold, wood-boring insects (such as woodworm and termites), rain, sun and other threats. It caters to the DIY, professional and industrial segments. Xylazel is a well-known and prestigious brand; it also produces metal protectors such as rustproof enamels. Its wood protection products include **Xylazel Fondo,**

Xylazel Plus, Xylazel aceites de teca (teak oils) and **Xylazel carcomas** (woodworm treatment), while its metal protection products include **Oxirite,** in a wide range of colors and finishes. The company was founded in 1975 and is headquartered in Galicia.

ZELNOVA ZELTIA, S.A. produces and commercializes 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.** The company is a leader in various segments of the insecticides market (sprays, plug-ins and liquids). ZelnovaZeltia 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). Incorporated in 1991 as a spin-off from Cooper Zeltia, S.A., it has its headquarters in Galicia.

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

2. CORPORATE GOVERNANCE

MANAGEMENT STRUCTURE

José María Fernández Sousa-Faro is the executive chairman of Pharma Mar, S.A. 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**

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:

The Board Secretary, who is not a director, is Sebastián Cuenca Miranda.

For profiles of the Group's directors, their remuneration and the Board committees, their duties and composition, see the shareholders and investors section of website: www.pharmamar.com.

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

CORPORATE GOVERNANCE AND ETHICAL MANAGEMENT POLICY

Code of Conduct

The Board of Directors of PharmaMar approved a Code of Conduct for the entire group, which entered into force on 1 February 2016. This 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 PharmaMar Group, without exception and regardless of their position, responsibility or workplace.

The purpose of the Code of Conduct is to formalize the principles and values that should guide the conduct of all people forming part of companies in the PharmaMar 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 field 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, labor 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 centers, and agreements are reached with contract research organizations (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. Examples of these measures:

- Regular backups are made and stored in a secure specialized off-site facility.
- Data is encrypted while undergoing physical transportation and electronic transmission.
- Access to premises and systems housing data is controlled and logged (physically and electronically).
- Employees are trained in their legal obligations under the Data Protection Law.

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, additional measures are applied to data from genetic analyses, including:

- 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 by PharmaMar and Sylentis are conducted on volunteers and 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' rights, safety and welfare take precedence over the interests of science and the company; consequently, 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 or their US equivalent, The Institutional Animal Care Committee (IACUC), to guarantee the welfare and humanitarian treatment of the animals during the trial.

PharmaMar has also adopted the Farmaindustria Ethics 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.

Membership of platforms

PharmaMar, Genómica and Sylentis participate in the Spanish Technology Platform "Nanomedicinas". 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.

Progress in these disciplines requires closer cooperation with other companies in the industry and the involvement of public authorities, hence the need to integrate into those platforms.

DISTINCTIONS

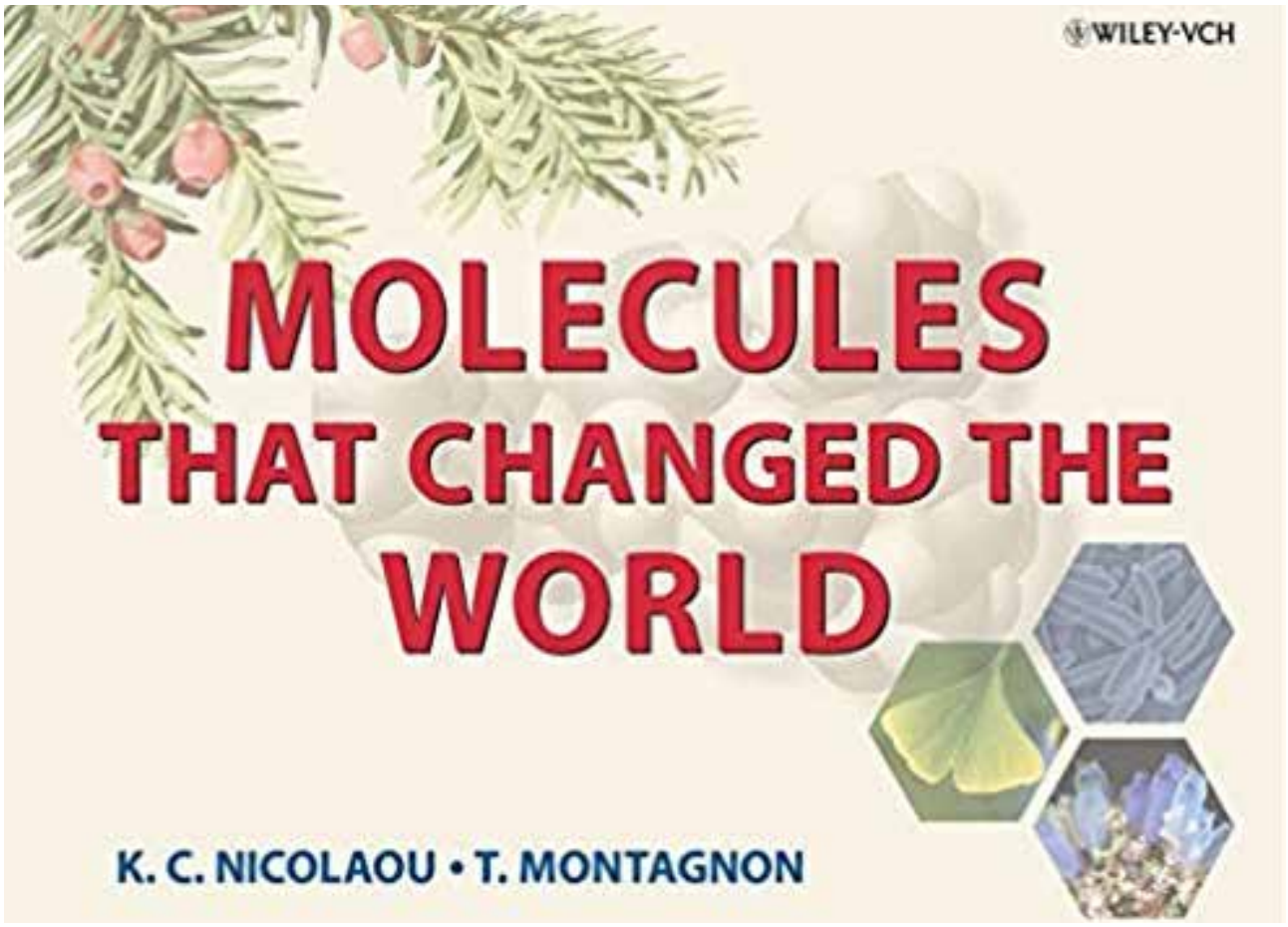
In 2016, El Economista newspaper named PharmaMar's Chairman, Mr José María Fernández Sousa-Faro, as "Pharma industry entrepreneur of the year" based on a reader survey.

That same survey ranked PharmaMar third among the top pharmaceutical companies of the year.

In the last few years, the Group has received, among others, the following awards:

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 PharmaMar 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 PharmaMar “Pharmaceutical company of the year” in the newspaper's special edition featuring the best companies of 2015.
Madrid Healthcare Silver Plaque for PharmaMar in 2014.
Ejecutivos Award for Zeltia as "Company of the Year 2014".
“Universidad Empresa 2014” award for the Zeltia Group from *Red de Fundaciones Universidad Empresa* (REDFUE).
“El Confidencial-KPMG 2014” award for the Zeltia Group for best business practices in Innovation.

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.



Cover of the book "Molecules that changed the world", which mentions Yondelis® as a molecule with considerable impact.

In 2016, PharmaMar ranked first among biotechnology companies in Spain, for the fourth consecutive year, in the MERCO survey of corporate reputation.

PharmaMar 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 32.8% of revenues on R&D — nearly double that of the second-placed Spanish company (16.9%); the average among Spanish companies is 5%. **Furthermore, the Group also ranks first in Spain in terms of R&D expenditure per employee: While other Spanish companies invested €17,965 per employee in 2016, PharmaMar invested €191,412 in the same period.** It ranks 321st in terms of private investment in R&D in the European Union, and 3rd among Spanish pharmaceutical companies in terms of outright R&D investment. PharmaMar ranks number 1,221 on the European Union's Industrial R&D Investment Scoreboard[1].

PharmaMar was granted the category of Excellent within Group A – "Companies with significant research activity and their own production plant or R&D facility" within the Spanish government's 2016 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 stated goals. The goals relate to R&D expenditure, investment in production, and the ratio of R&D expenditure to revenues, among others.

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

[1] Source: The 2016 EU Industrial R&D Investment Scoreboard.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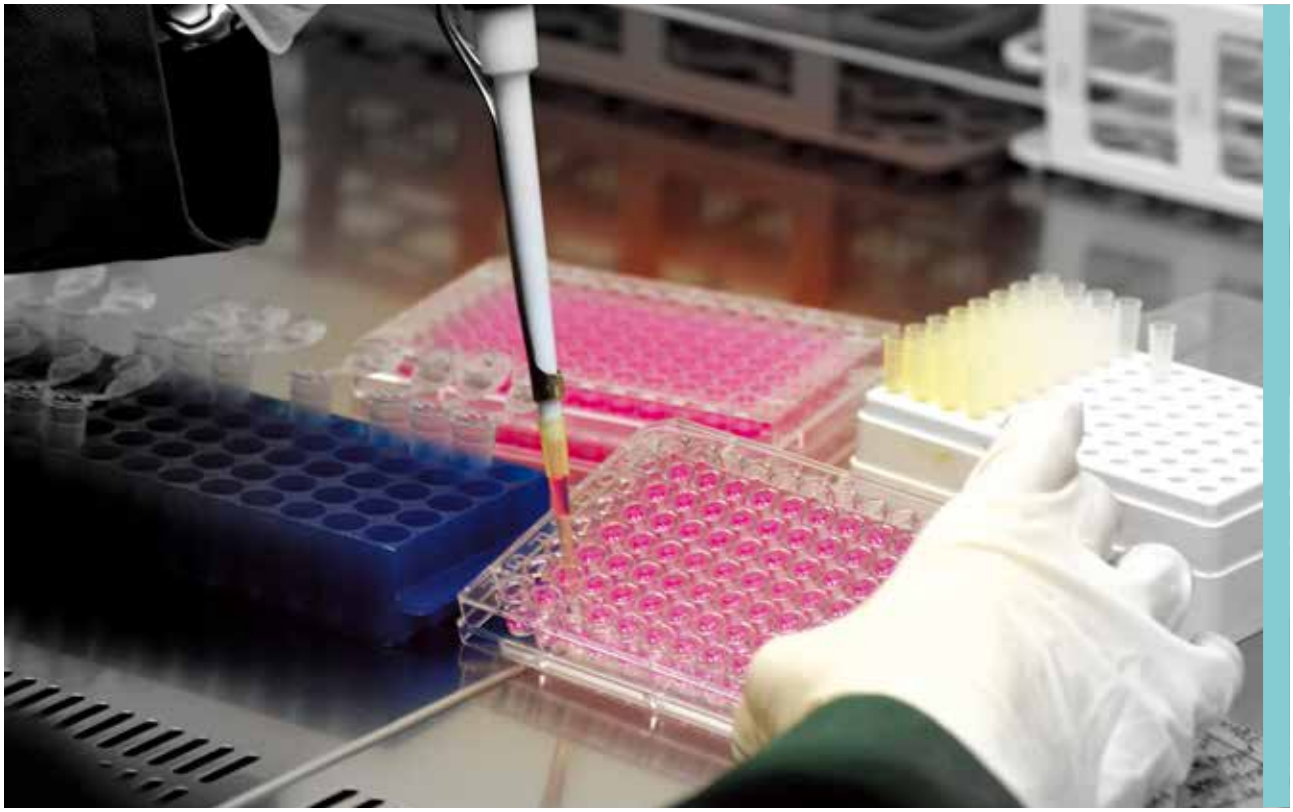
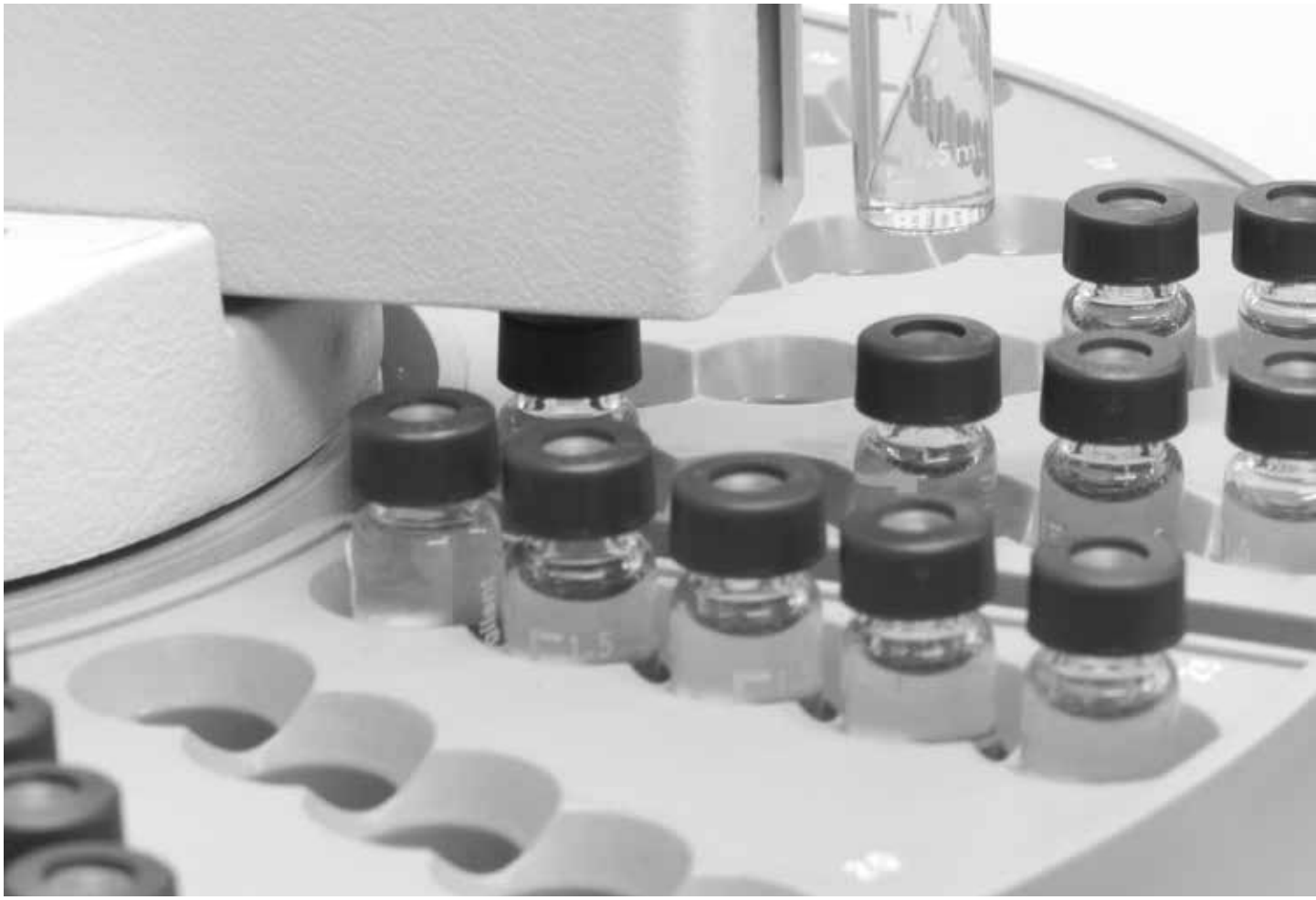


3. COMMITMENT TO R&D

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 PharmaMar Group has made a firm commitment to advance in researching drugs that can palliate and cure certain pathologies in the area of oncology (PharmaMar) and ophthalmology (Sylentis).

The year 2016 brought positive developments for our product R&D and for oncology patients and people with eye diseases: A Marketing Authorization Application (MAA) for Aplidin® was presented to the European regulator and the company is awaiting its approval in order to market the drug in Europe. Additionally, PharmaMar and Sylentis have obtained very promising results with their clinical trials. These results aroused considerable interest in conferences where they have been presented and among companies in other countries, with which important licensing and marketing contracts have been signed. The agreements of this type that PharmaMar signed in 2016 are as follows:

- Licensing agreement with Specialised Therapeutics Australia (STA) for the commercialisation of Aplidin® in Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, Philippines, Vietnam, Singapore, East Timor, Thailand and Papua New Guinea.
- Licensing agreement with Boryung Pharm to market Aplidin® in South Korea.
- Licensing agreement with Chugai Pharma Marketing for PM1183 commercialisation in Japan.



Drug research and development by PharmaMar commences with undersea expeditions to gather samples. Extracts are generated from the samples and a selection is made of those that present interesting activity *in vitro*; pure compounds are isolated from the extracts, their structures are elucidated and they are then synthesized chemically. The compounds then progress to pre-clinical development, where the action mechanism is elucidated and the molecule is tested on animal models. Compounds that successfully pass this stage are tested on patients in clinical trials. Clinical trials comprise three phases (I, II and III) which are conducted on growing numbers of volunteers, and they provide information about a compound's efficacy and safety. Research and development at Sylentis is different: it commences with the choice of target for which to design interference RNA (RNAi), and progresses through pre-clinical and clinical development.

The PharmaMar Group's tireless research efforts were recognized in 2016 by the concession of support by a number of public agencies: Spain's Centro de Desarrollo Tecnológico Industrial (CDTI) gave an additional subsidy to PharmaMar for an individual project. Additionally, Spain's Ministry of Economy and Competitiveness and the European Regional Development Fund (ERDF) financed PharmaMar and Sylentis in four new public-private partnerships, which are in addition to the existing partnerships and are detailed in the section on each company's R&D.

Internationally, PharmaMar and Sylentis are participating in projects under the EU's framework program. In 2016, PharmaMar participated in a project of the Innovative Medicines Initiative (IMI), which was approved by the European Commission in 2017. As in previous years, during 2016 the Group tracked the new Horizon 2020 program closely with a view to optimizing the participation by Group companies in innovative collaboration projects between European countries.

PharmaMar

Cancer

Cancer is a set of diseases characterized by abnormal cell proliferation. Its malignancy arises from its capacity to invade organs and tissues.

Scientists have established a number of factors which can trigger the development of tumors, such as genetic predisposition, exposure to chemicals or viruses, and even stress, although the causes of the illness are not known for certain.

At least 280 different types of cancer have been recognized, which complicates the search for a cure. Although the different types of cancer behave similarly as regards their rapid uncontrolled growth and ability to invade other tissues, each cancer differs in terms of prognosis and treatment depending on the tissue where it arose and the parts of the organism which it invades.

Five- and ten-year survival rates for cancer have increased in the last few decades and, on average, it is estimated that more than 46% of patients diagnosed with cancer will survive for more than ten years after the diagnosis, although it depends on the type of cancer and the country. Constant research and a steady flow of new drugs provide hope of an increase in cancer patient survival rates.

Research and development

PharmaMar explores the sea's ecosystems as a source of new chemical substances with anti-tumor 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 four molecules in various phases of clinical development.

There is also a move towards personalized medicine based not just on the histological characteristics of the tumor 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 tumors 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 and Competitiveness 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 four joint projects under the European Union framework program: "**MACUMBA:** Marine Microorganisms: Cultivation Methods for Improving their Biotechnological Applications", "**BLUEPHARMTRAIN:** Co-Cultivation of Sponge Cells & Microorganisms" e "**INMARE:** Industrial Applications of Marine Enzymes: Innovative screening and expression platforms to discover and use the functional protein diversity from the sea". The latter project, which was approved recently, is part of the second "Innovative Medicines Initiative" (IMI-2). This project, "**ITCC-P4:** ITCC Pediatric Preclinical POC Platform" seeks to create animal models for researching cancer in children and includes major pharmaceutical companies.

In 2016, PharmaMar spent over €78 million on R&D, 30% more than in 2015 and its largest-ever R&D expenditure in a single year.

Researching new pharmaceutical forms

PharmaMar's research work in drug discovery culminates with the isolation and synthesis of new chemical entities with strong anti-tumor potential. However, many of these potential drugs have characteristics that hamper clinical development: specifically, low solubility and high chemical instability in aqueous medium are the most common obstacles in the process of developing these potential drugs into therapeutic agents.

The latest progress with pharmaceutical technology—particularly new release systems and "nanodrugs"—is very promising in this connection. These approaches can improve the compounds' solubility and tissue permeability, protect the molecules from chemical degradation, selectively direct the cytotoxic drugs towards tumor 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-stabilized nanocapsules, solid nanodispersions obtained using supercritical fluid techniques, and alternative routes for administering insoluble drugs, such as subcutaneous.

This research developed and performed pre-clinical evaluations of new nanosystems designed specifically to address the problems posed by PharmaMar's novel molecules. PharmaMar's ongoing interest in these drug release strategies enhances the enormous potential of our molecules.

Clinical trials

PharmaMar is currently conducting clinical trails on the following types of cancer: subtypes of sarcoma, ovarian cancer, leiomyosarcoma, multiple myeloma, angioimmunoblastic T-cell lymphoma, breast cancer, small cell lung cancer, head and neck cancer, neuroendocrine tumors, germ cell cancer, bile duct cancer, endometrial cancer, cancer of unknown primary (CUP) and Ewing sarcoma.

PharmaMar is conducting clinical trials on Yondelis®, which has already been authorized for sale (these trials are supervised by the Medical Department); and also on Aplidin®, PM1183 and PM184, which have not yet been authorized for sale (these tests are conducted by the Clinical Development Department). PharmaMar currently has the following molecules undergoing clinical trials:

- **Yondelis®:** PharmaMar develops and markets Yondelis® in Europe, while Janssen Products, L.P. has the rights to develop and sell Yondelis® in the rest of the world except Japan, where PharmaMar has signed a licensing agreement with Taiho Pharmaceutical. A number of post-authorization trials are under way which seek to optimize the drug's clinical use in the two indications for which it has marketing authorization — soft tissue sarcoma, and platinum-sensitive ovarian cancer (in combination with pegylated liposomal doxorubicin—PLD) — and to identify new indications. The trials which commenced in 2016 are as follows:

  - **GENESIS-1:** Retrospective trial to obtain the genomic characterization of the response to trabectedin in patients with sarcoma.

  - **TrObs:** Retrospective analysis of the use of trabectedin in sarcoma.

  - **LMS-04:** Randomised Phase III trial comparing the efficacy of doxorubicin and trabectedin as first-line treatment in patients with metastatic leiomyosarcoma, both uterine and non-uterine.

  - **ReTraSarc:** Retrospective analysis of the efficacy and safety of using trabectedin in sarcoma patients.

  - **MITO-23:** Randomized Phase III trial comparing trabectedin with the therapy of investigator's choice in treating ovarian, peritoneal or fallopian tube cancer that is recurrent with mutated BRCA or BRCAness.

- **Aplidin®:** Trials are being conducted in multiple myeloma and lymphoma.

  - **Multiple Myeloma**
    The ADMYRE Phase III clinical trial completed patient monitoring in 2016 and the primary endpoint was analyzed. Aplidin® (plitidepsin) in combination with dexamethasone vs. dexamethasone as monotherapy in patients with relapsed or refractory multiple myeloma revealed a statistically significant 35% reduction in the risk of progression or death vs. the comparator, thereby achieving the primary endpoint.

    A Marketing Authorization Application (MAA) for plitidepsin to treat multiple myeloma was filed with the European Medicines Agency (EMA) in September 2016.

    With regard to the combination of Aplidin® with bortezomib in patients with relapsed or refractory multiple myeloma, recruitment continues in the expansion phase with the goal of enrolling 15-20 additional evaluable patients.

    Centers have begun to open in the Phase II trial with Aplidin® in combination with bortezomib and dexamethasone in patients with double refractory multiple myeloma.

A new Phase I trial with Aplidin® in combination with bortezomib, pomalidomide and dexamethasone in patients with multiple myeloma exposed to proteosome inhibitors who are refractory to lenalidomide will commence in the first half of 2017.

These latest trials with Aplidin® in combination with other drugs are aimed at obtaining the necessary information to support its use in the various stages of treating multiple myeloma.

- **Lymphoma**
  The registration trial with Aplidin® as monotherapy in patients with angioimmunoblastic T-cell lymphoma has commenced recruitment.

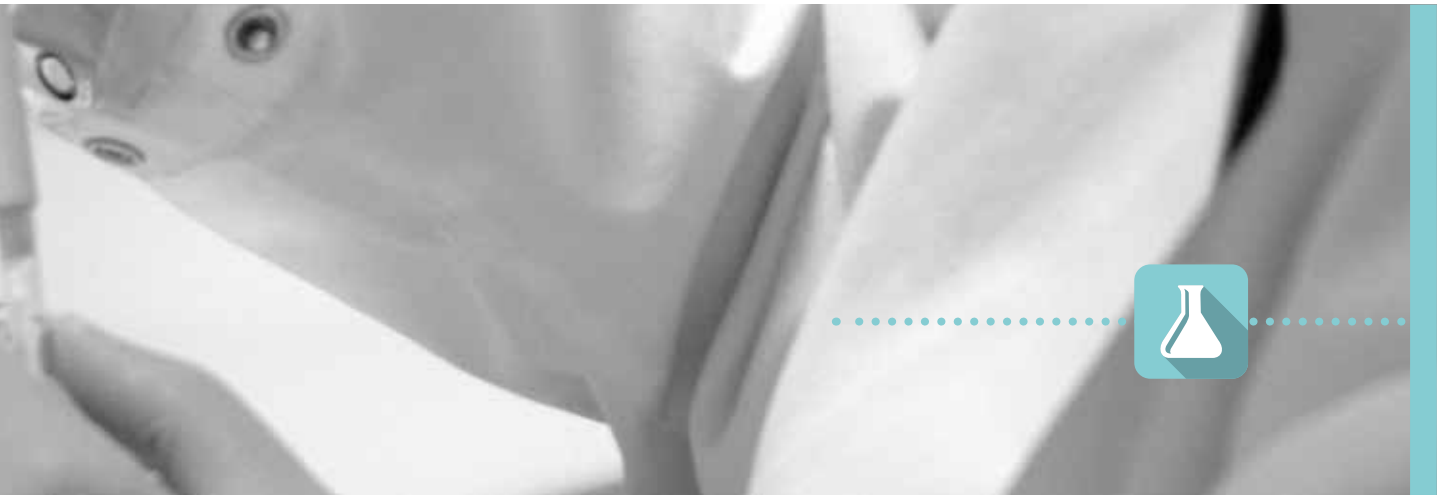
- **PM1183:** Trials are under way in platinum-resistant ovarian cancer, small-cell lung cancer and breast cancer as well as a basket trial in advanced solid tumors that include small cell lung cancer, neuroendocrine tumors, cancer of the head and neck, germ cell cancer, endometrial cancer, bile duct cancer, cancer of unknown primary (CUP), and Ewing sarcoma.

  - **Platinum-resistant ovarian cancer**
    The CORAIL Phase III pivotal trial with PM1183 as monotherarapy vs. topotecan or pegylated liposomal doxorubicin in patients with platinum-resistant ovarian cancer completed recruitment in October 2016. The primary endpoint of the trial is to assess progression-free survival (PFS). It will also analyze overall survival, objective response rate and patient quality of life variables.

  - **Small-cell lung cancer (SCLC)**
    In 2016, PharmaMar commenced the ATLANTIS Phase III registration trial that compares the activity and safety of the combination of PM1183 (lurbinectidin), a drug of marine origin, plus doxorubicin with topotecan or CAV (cyclophosphamide, adriamycin and vincristine) for treating patients with small-cell lung cancer who have relapsed after a first round of platinum treatment. Topotecan is the only drug approved in the US and Europe for this indication. In February 2016, the Food and Drug Administration (FDA) gave regulatory approval to start this trial.

    The primary endpoint of the trial is to demonstrate an increase in progression-free survival. Secondary endpoints include overall survival, response duration, quality of life variables, response rates, and the correlation between pharmacokinetics and pharmacodynamics.

  - **Advanced breast cancer**
    The Phase II clinical trial in advanced breast cancer is recruiting in the A1 arm, consisting of breast cancer patients with BRCA 1 or 2 mutations who have been pre-treated with PARP inhibitors. The registration strategy for PM1183 in breast cancer patients with the BRCA gene mutation was discussed and



agreed upon with the FDA at a meeting in December 2016.

- **Combination trials**
  As regards Phase I combination trials, recruitment was completed 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 breast cancer types, among others; consequently, the next stages of development for this indication are currently being assessed. Recruitment continues on schedule for the Phase I trial in combination with irinotecan.

- **Basket trial in advanced solid tumors**
  Recruitment is continuing for the Phase II trial with PM1183 as monotherapy in indications chosen on the basis of the drug's action mechanism or of its activity as observed previously in combination trials. Those indications are: small cell lung cancer, neuroendocrine tumors, cancer of the head and neck, germ cell cancer, endometrial cancer, bile duct cancer, cancer of unknown primary (CUP), and Ewing sarcoma.

- **PM184:** The Phase I dose escalation trial assessing the combination of PM184 with gemcitabine is recruiting on schedule. There are plans to enroll patients with specific diseases in which clinical benefit has been observed, such as non-small-cell lung cancer, breast cancer and tumors of the head and neck.

  The Phase II trial with PM184 is being conducted in hormone-receptor positive advanced breast cancer patients; recruitment is advancing on schedule.

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

The definition of rare diseases varies from region to region: The European Union (EU) classifies them as illnesses affecting less than 5 out of every 10,000 people, whereas the USA uses the figure of less than 200,000 people affected nationwide. Orphan drugs are those that help to diagnose, prevent or treat rare diseases.

PharmaMar's commitment to developing drugs 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. One of these compounds has also been

designated as an orphan drug in Switzerland for treating soft tissue sarcoma and ovarian cancer, and in Korea and Japan for soft tissue sarcoma.

Quality management

PharmaMar has been authorized 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 authorized to commercialize drugs and as a manufacturer of active ingredients for human use, including the manufacture of radiopharmaceuticals.

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.

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 specialization.

Bioprospection efforts are assisted by universities, centers 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 preventive and/or corrective measures are taken to safeguard patients' welfare where necessary.

There was an incident in 2016 in the process of producing Yondelis®, which PharmaMar had outsourced to Belgian laboratory Cenexi Thissen Laboratories, resulting in the recall of several batches of the commercial product, although no adverse effects in patients have been reported to date. The incident is described in detail below:

In June 2016, a complaint was received from a German hospital in connection with a bulk batch of Yondelis® 0.25 mg in which a piece of glass was visible inside the vial after it was reconstituted. This quality defect took place in a single bulk batch (no. 15I02, theoretically comprising 15,000 vials), which was used to produce 24 commercial batches. The bulk batch had been manufactured in 2015 by Belgian lab Cenexi Thissen Laboratories, with which PharmaMar had signed supply and quality agreements for the purpose of producing Yondelis®.

In line with European regulations on quality defects in centrally authorized products, PharmaMar immediately notified the EMA and AEMPS. Based on a proposal by PharmaMar, the AEMPS ordered a recall of all batches of Yondelis® 0.25mg made up from the aforementioned bulk batch 15I02 in order to minimize the risk to patients. The defect was also notified to PharmaMar subsidiaries.

Information on the recall of the affected vials was reported periodically to the health authorities: EMA, AEMPS and local European authorities. The recall was conducted within the deadlines imposed by the AEMPS. The recalled vials that were returned to PharmaMar were destroyed by an authorized firm, which issued a certificate of destruction. In exceptional cases, for logistics reasons, the Technical Department authorized on-site destruction of some of the affected units.

An investigation at Cenexi Thissen Laboratories revealed that the glass particle matched the composition of the glass of which the vials are made. It also transpired that a number of vials broke during the production of the bulk batch, specifically during the vial washing and filling process. It was concluded that, in all likelihood, the glass particle came from the breakages that had taken place at the washing stage and that it had gone undetected by the controls established throughout the process. The manufacturer defined and implemented corrective measures to avoid a recurrence of the incident.

PharmaMar's Department of Pharmacovigilance, in cooperation with the Technical Department, performed a meticulous investigation to identify all possible adverse effects that might arise from this quality defect. No adverse effects on patients have been reported to date, either to PharmaMar or to the health authorities of the countries where the batches in question were distributed.

Sylentis

Dry eye syndrome

Dry eye syndrome results from an alteration in the tear film, which damages the external part of the eye. This leads to general discomfort, including eye pain, the sensation of having a foreign body in the eye, burning, itching, sensitivity to light, seeing colored halos, the sensation of heavy eyelids, etc.

Dry eye syndrome is generally associated with a lack of teardrops and of moisture in the eye. External factors, such as the use of contact lenses or excessive exposure to cold or hot air, can exacerbate symptoms and discomfort. This is the most common eye disorder, and it is estimated that more than 30 million people worldwide suffer from dry eye syndrome.

Glaucoma

Glaucoma is a group of eye disorders characterized by damage to the optical nerve that leads to progressive loss of eyesight and can ultimately cause blindness. The disease is asymptomatic until the sufferer begins to note a reduction in their field of view. It is estimated that half of glaucoma sufferers do not know they have it. It is usually associated with higher intraocular pressure, which damages the optical nerve and seriously and irreversibly compromises the field of view.

Glaucoma is one of the main causes of blindness. Over 67 million people worldwide have glaucoma, and the figure is expected to reach 80 million by 2020. There are approximately one million glaucoma patients in Spain at present. There is no cure for the disease, and medicine has only managed to slow its progress.

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 revolutionized 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, which prolongs the drug's action over time, 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, ocular allergies and other diseases of the eye.
- Inflammatory: inflammatory bowel diseases (Crohn's disease and ulcerous colitis).
- Central nervous system: cerebral ischemia, 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 2015, the company initiated a new line of research in the ophthalmology area, focusing on drugs for treating problems of the retina. That line of research continued in 2016, addressing new treatments based on RNA interference to treat such diseases as diabetic retinopathy and retinitis pigmentosa.

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

Among the numerous research and development projects being undertaken by Sylentis, the following

public-private partnerships funded by Spain's Ministry of Economy and Competitiveness and the European Regional Development Fund (ERDF) are particularly noteworthy:

- **SEKEYE** consortium: Sylentis heads this consortium, which includes 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 personalized treatments for glaucoma, focusing particularly on children and the elderly.

- **SURFEYE** consortium: Sylentis heads this consortium, which includes Biotechnology Institute IMASD, BioDan Science, Bioftalmik, Fundación de Investigación Oftalmológica, University of Santiago de Compostela and University of the Basque Country. The objective is to establish innovative treatments for eye inflammation and personalized treatment for eye surface regeneration. It will also develop personalized diagnostic systems to be able to apply the most appropriate treatment in each case.

- **TERET** consortium: comprising Sylentis (as consortium leader), with Leadartis, LEITAT Technological Center, and the Biomedical Research Networking Centers (CIBER). The goal of this project is to research new treatments for degenerative illnesses of the retina, focusing on macular degeneration associated with age, diabetic retinopathy and retinitis pigmentosa.

- **INDREYE** consortium: Sylentis heads the consortium, which includes SALVAT Laboratories, the Foundation for Biomedical Research at San Carlos Clinical Hospital, the Microelectronics Institute of Barcelona-National Microelectronics Centre, part of the Spanish National Research Council (CSIC), and the University of Oviedo. This project aims to change the traditional approaches for diagnosis and treatment of dry eye syndrome with a view to specifically addressing each type of illness that causes this syndrome.

Sylentis is also participating in two cooperation projects under the European Union framework program: "**NANOPILOT**: *A* Pilot Plant for the Production of Polymer-based Nanopharmaceuticals in Compliance with GMP" and "**NABBA**: *D*esign and Development of advanced Nanomedicines to overcome Biological Barriers and to treat severe diseases".

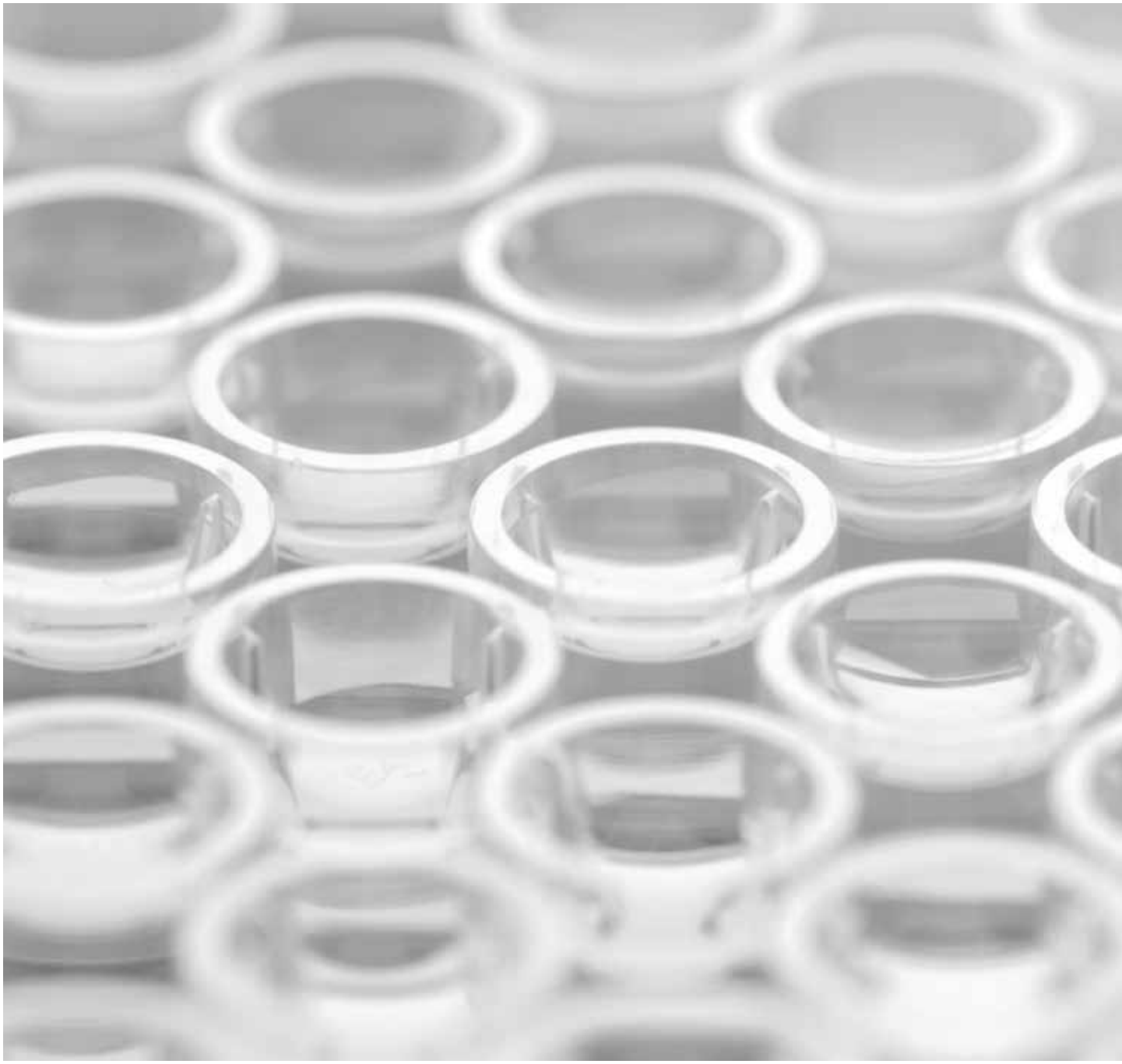
Clinical trials

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, is for the treatment of ocular pain associated with dry eye syndrome. A Phase I clinical trial was completed, with optimal results in terms of local and systemic safety. Development continued with a Phase II dose-seeking and efficacy trial, whose results were quite satisfactory: The primary endpoints in terms of eye pain and reduction of hyperemia were attained with the 1.125% dose. The compound was well tolerated at all evaluated doses and the percentage of adverse events was similar to the placebo group. The results justify advancing this product to the next phase of development; accordingly, a Phase III clinical trial is currently being developed.

Quality research

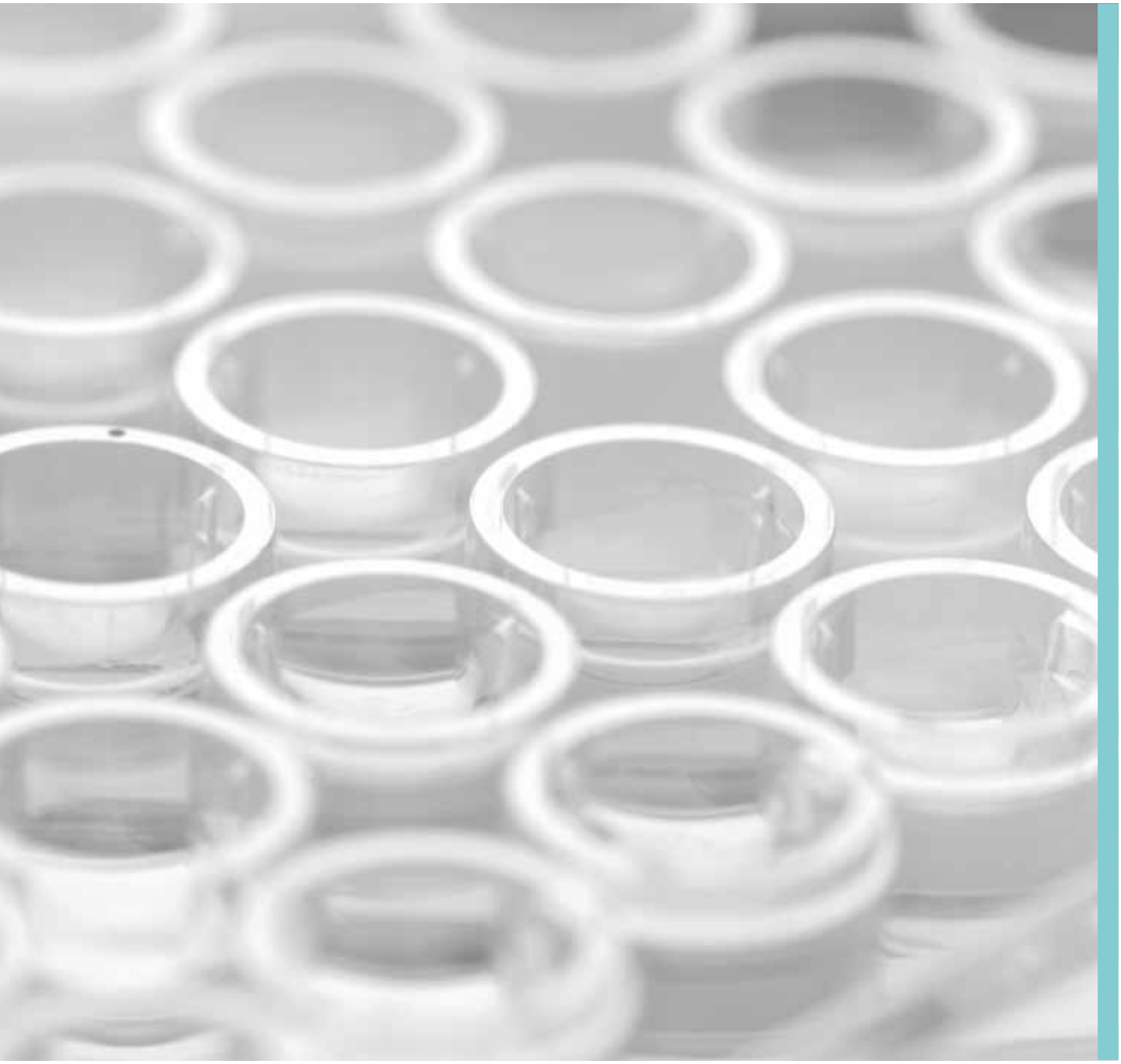
Sylentis obtained the "Madrid Excelente" distinction. Madrid Excelente is a mark granted by the Madrid Regional Government in recognition of companies' quality and excellence with a view to fostering competitiveness. The mark does not refer to a specific product or service but is



based on an analysis of the company's overall management 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) authorized 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 its project is generating. Inspections by the Spanish Agency for Medicines and Healthcare Products (AEMPS) for renewal of the authorization 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 participation in clinical trials also conforms to Good Clinical Practices, as required by law, and it



ensures that contract research organizations 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 centers as well as private contract research organizations to conduct its trials.


Splash
Con la garantía
casa jardín
Trampa
DETECTORA DE
POLILLAS
de los alimentos
Sin insecticidas
ni olores
3 trampas
cada trampa
dura
3 MESES
Food moth detector trap
Con la garantía
casa jardín
Splash

4. CUSTOMERS

The PharmaMar Group's current customers are the users of ZelnovaZeltia, Xylazel, Genómica and PharmaMar products and services. In chemicals, molecular diagnostics and antineoplastics, our companies make a commitment to customers from the outset: to guarantee a quality service, provide consumers with products that meet their needs, maintain satisfactory communications, and solve their problems as efficiently as possible.

Our customers are fundamental to the PharmaMar Group and, consequently, we direct all our efforts, both human and technical, to meeting their needs. By developing innovative products, we steadily improve our offering and enhance the quality we provide.

In line with its international growth strategy, in 2016 PharmaMar established a commercial subsidiary in Austria, in addition to those it already had in France, Germany, Switzerland, Italy, the United Kingdom and Belgium, as well as its base of operations in the US (Pharma Mar), a subsidiary in Sweden and a sales office in China (Genómica). All of these are markets with high growth potential where the Group seeks to increase its sales.

ZelnovaZeltia

ZelnovaZeltia has approximately 966 direct customers.

ZelnovaZeltia's products are air fresheners, domestic insecticides and cleaning products, which are marketed via two divisions: household products (insecticides, air fresheners, odor neutralizers, rat poison, wax, impregnators, cleaners, bathroom products, grease removers, furniture cleaners, etc.) and environmental hygiene products for industrial use (hospitality industry, etc.).

Xylazel

Xylazel has approximately 1,100 direct customers.

It manufactures and distributes paints and varnishes. It provides paints and varnishes for protecting wood and metal, as well as fillers, oils, etc. and a technical service to handle customer queries, advice, complaints, etc.

Genómica

Genómica has approximately 104 direct customers.

The company provides its customers with 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-tumor therapy), genetic identification analysis (paternity tests, genetic fingerprinting and filiation), and technology transfer (turnkey installation of genetic fingerprint labs).

PharmaMar

PharmaMar has approximately 1,009 customers.

Following the launch of Yondelis® in Europe in 2007 for soft tissue sarcoma and in 2009 for ovarian cancer, PharmaMar's customers are hospitals and clinics in Europe which are served by PharmaMar's own sales network or its sales and distribution partners. Sales queries are handled directly by account managers in each country's commercial structure.

Communication with customers

Customers can obtain information through a variety of channels: The main (and the most direct and personal) channel is via area sales representatives.

Internationally, sales are channeled through subsidiaries or distributors, which are selected on the basis of their technical and financial capacity and signed under contract.

End consumers can visit each company's web site to obtain information about the variety of products that the Group manufactures and markets. They may also contact the companies by phone or e-mail to clarify queries. The company's product packages, brochures and advertising material all carry the e-mail address, website and phone number.

In the case of the Oncology unit (PharmaMar), contact with the professional customers (healthcare professionals) is conducted via the commercial structure or by telephone, e-mail etc. Because of the pharmaceutical industry's peculiar features and the high degree of specialization in oncology, clinical queries from patients are channeled through the doctor responsible for their treatment. Technical queries are answered with the support of the Medical Information Service and the Medical Department to ensure that replies are rigorous on the basis of clinical experience.

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

and takes account of consumer feedback obtained via the sales force, the quality and complaints handling system, distributors, market experience and knowledge, and regular surveys. Customers' opinions are very important when making decisions about any product (development, design, production, labeling, manuals and marketing) and, where necessary, product literature and labels are corrected on the basis of customer feedback.

In the Oncology unit (PharmaMar), scientific information and promotional materials provided to healthcare professionals are produced in several languages and undergo a rigorous approval process that conforms to best practices in individual countries and Europe-wide.

Customer satisfaction

It is important to ascertain customers' opinions and identify aspects of our services that can be improved. Our companies conduct regular surveys of customers and end consumers to gauge their satisfaction with the products. Once the results are quantified, the Commercial Department analyses the data and, based on complaints and reject counts, takes the appropriate measures to address the least positive aspects.

Any complaint or claim from a customer is registered in writing. All complaints are channeled through the Commercial Department, which, based on the nature and characteristics of the issue, refers it, with a full dossier, to the departments it considers appropriate, in order for the problem to be analyzed, 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, based on commercial criteria. A written reply is sent to 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 (ZelnovaZeltia), José Manuel Cortiñas Viñas (Xylazel), Antonio Sevilla and Juan Bataller (Genómica), and Juan Nogués Ortuño (PharmaMar).

Advertising and competitors

A variety of methods are used to reach end consumers, depending on the company and sector: ZelnovaZeltia and Xylazel products are advertised on television and in specialist press 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.

In the case of Genómica and PharmaMar, since their pharmaceutical and diagnostic products are highly specialized, their advertising is targeted very directly at customers to emphasize technical and product quality, as well as the benefits with respect to those of the competition, but without mentioning

the latter. For this purpose, the company uses published independent scientific studies that support its message, as well as demos and small comparative surveys. Similarly, the company also advertises at scientific conferences which are attended by product advisers familiar with the industry. Competitors deserve our utmost respect, and sales arguments are purely technical, enabling the customer (who is technically sophisticated and knows the advantages and disadvantages of each product) to assess the best technique or product on the basis of his/her needs and the available analytical and therapeutic options.

Compliance

New legislation is being implemented, including the Biocidal Products Directive (BPD), amendments to the European Agreement concerning the International Carriage of Dangerous Goods by Road (ADR), the regulation on the Registration, Evaluation, Authorisation of Chemicals (REACH), and the new Regulation on Classification, Labelling and Packaging of substances and mixtures (CLP Regulation). This requires the company to comply with a broad range of rules over the long term, all of which are aimed at eliminating any type of impact on the environment or people.

Compliance with this legislation is costly, in terms of both direct costs and of human resources and relationship costs. The products must comply with the legislation in force on the classification and labeling of hazardous products and with the regulations limiting emissions of volatile organic compounds.

There were no incidents in 2016 stemming from non-compliance with legal or internal regulations regarding product information and labeling, advertising, promotion or sponsorship. Furthermore, there were no complaints with respect to customers' privacy or personal information leaks.

Product quality

The 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 returns or recalls for health or safety reasons in 2016, except for one incident at PharmaMar involving a batch of Yondelis®, which is described in detail in the section on Commitment to R&D.

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

ZelnovaZeltia, Xylazel and Genómica are certified to ISO 9001:2008, and their product quality management and quality control processes conform to that standard. That is the most comprehensive standard, since it covers quality in design, production, installation and service. ZelnovaZeltia also has the Higher Level certification under the IFS HPC standard.

IFS HPC CERTIFICATION

ZelnovaZeltia 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 (cosmetics) and household products and sell them to consumers under their own brand names (private label).

It is an internationally-recognized standard which ensures that IFS-certified companies deliver products that adhere to defined specifications with a view to continuously improving product safety and quality. It helps reduce costs and ensure transparency throughout the entire production chain of household and personal care products.

The number of companies that have obtained this certification is very small, both in Europe and in Spain; ZelnovaZeltia's certification evidences its commitment to developing high-quality innovative products and provides a clear competitive advantage over other manufacturers.

Large retail chains with IFS certification include Carrefour, Auchan, Aldi, Casino, Lidl, Leclerc, Metro, Migros, Wal-mart, Coop, etc.

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.

- The A+ Seal from the French Ministry of Ecology, Sustainable Development, Transport and Housing, supporting the new line of Xylazel Air Sano paints as acceptable 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, supporting Xylazel Aire Sano paints due to their low VOC content.

- Certification of compliance with the EN71:3 standard on toy safety, and the migration from certain 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 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 (SEMPSPH) for Xylazel Aire Sano paint for healthcare environments.

- Testing by Laboratorio CONTROL MICROBIÓLOGICO, S.L. according to protocol JIS Z 2801, which confirmed that the dry film of Xylazel Aire Sano paint for healthcare environments does not support the proliferation of micro-organisms.

- Cooperation agreement with the Spanish Pediatric 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, CLART® STIs, in accordance with Directive 98/79/EC 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 to ISO 13485:2003, as well as adaptation and certification to the new version of ISO 13485:2012, which ensures that the quality management system complies with the regulatory requisites of any country in the world.

- ISO 9001 Certification: 2008, granted by TÜV *Rheinland.*

- GMP (Good Manufacturing Practices) certification in Brazil by ANVISA.

New product research and development

ZelnovaZeltia

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 optimized toxicological and environmental profiles are being developed. Work is also ongoing to register new formulae in accordance with the latest legislation on biocides. At the same time, the goal is to expand the offer of innovative formats, perfumes in line with market trends, and new applications and dispensing systems.

ZelnovaZeltia is working on the following lines, among others:

- Full development of a number of registration dossiers in accordance with the European Biocidal Product Regulation (BPR).
- Development of electronic mosquito killers not requiring the GSH08 pictogram.
- Launch of a range of products bearing the EU Ecolabel.
- New application formats for air fresheners, and expansion of the range of available fragrances in line with trends.
- New insecticide application formats (gel bait, tablets, etc.).

Xylazel

The company seeks to develop innovative products that take advantage of real business opportunities in the market, comply with increasingly demanding legislation and improve both personal and environmental safety. As a manufacturer of wood preserving products, we are currently seeing major changes due to implementation of the directive regulating the classification and marketing of biocides. The range of wood protection products is being adapted to comply with the new requirements.

In 2016, Xylazel completed registration of its entire range of wood protection products under the European Biocidal Product Regulation (BPR).

The company worked on the following lines in 2016:

- Modification of formulae to adapt to new legislation on the classification and labeling of hazardous products: major changes have been made in certain substances that may be classified as of very high concern under REACH in the future.

- Development of new formulas in the Oxirite line for satin finish, water-based paint for iron, and matt solvent-based paint for high-performance corrosion resistance.
- Development of new water-based and solvent-based varnishes for universal indoor and outdoor use.
- New water-based paints in the Xylazel Soluciones line: Anti-condensation and Anti-mold paint.
- New water-based wood protectors.
- Development of a water-based floor varnish that adheres to floating wood floors.
- Development of a new water-based sealant to avoid leaching of wood tannins.
- Development of a water-based paint for multiple surfaces that enhances the properties of Xylazel Protective Paint.
- Formulation enhancements for certain paints, such as Xylazel Soluciones Pintura para Suelos (for floors) and Xylazel Soluciones Impermeabilizante Elástico (waterproofing).
- Development of a new oil to treat indoor woodwork that is suitable for contact with food.
- Development of a new product to paint outdoor wood decks.

Genómica

Genómica worked on the following lines in 2016:

- Development of NEDXA, a lab-on-a-chip technology based on multiple miniaturized amplification and electrochemical detection, all in a disposable cartridge. This technology offers new applications in microbiology and oncology by providing a compact system for detecting mutations or micro-organisms in slightly over one hour without the need for a lab technician.

- In oncology, two new products for *in vitro* diagnosis based on CLART® technology were launched: CLART® CMA ALK.ROS1 and CLART® CMA EGFR LB. The latter is the company's first product to be developed with the CLART® technology that can detect mutations in liquid biopsies, specifically circulating tumor DNA.

- These new products are in addition to the four kits that Genómica already marketed in the oncology field: CLART® CMA KRAS.BRAF. PI3K and CLART® CMA NRAS.iKRAS for metastatic colon cancer, CLART® CMA EGFR for non-small-cell lung cancer, and CLART® CMA BRAF.MEK1.AKT1 for melanoma. These products detect spot mutations in solid biopsies, enabling a more targeted choice of anti-tumor treatment.

  The new **CLART®CMA ALK-ROS1** kit detects and provides genetic identification of the main chromosome translocations in the ALK and ROS1 genes in patients with lung cancer, using a solid biopsy.

  The new **CLART® CMA EGFR BL** kit determines mutations in the EGFR oncogene from a liquid biopsy (blood) to enable the right treatment to be chosen for non-small-cell lung cancer. This technology enhancement makes it possible to monitor response to treatment using a sample obtained with a non-invasive method, with the resulting benefit for the patient.

- Genómica has implemented liquid biopsy analysis using next-generation sequencing (NGS). This makes it possible to analyze individual gene panels in the coding region (exome), selected a la carte or already established in the market, and thereby provide evidence of the marker's clinical utility.

GENÓMICA AND PERSONALIZED MEDICINE

Rather than implementing standard treatments, personalized medicine “offers each patient the right treatment at the right time”. This concept is especially significant in oncology, where the genes involved in the disease are being studied in increasing detail and at molecular level.

The involvement of one or other genes in the onset of cancer results in clinical subdivisions that enable doctors to use different strategies to treat the disease. For example, there are subtypes of lung cancer that respond to certain treatments, but not to other general therapies used to combat lung cancer. Consequently, if the particular subtype of cancer can be identified, a more suitable specific treatment can be offered. There are multiple advantages to this: starting with an efficient treatment as soon as possible, avoiding using unnecessary medication that will have side effects on the patient, saving on the cost of applying a treatment that is not effective, etc.

Years ago, Genómica decided to take diagnosis a step further, by exploring personalized 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. Those products are CLART® CMA KRAS.BRAF.PI3K and CLART® CMA NRAS.iKRAS for metastatic colon cancer, CLART® CMA EGFR for non-small-cell lung cancer and CLART® CMA BRAF.MEK1.AKT1 for melanoma, plus the newly-added CLART® CMA ALK.ROS1 and CLART® CMA EGFR LB for 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 optimizing clinical management in oncology. The partnership seeks to strengthen Genómica's activity in order to yield reliable molecular diagnostic tools that are optimized in clinical practice and fully aligned with Fundación ECO's goals to drive progress in Spanish oncology.

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.

5. SUPPLIERS

PharmaMar Group's chemical and biopharmaceutical companies interact with a large number of suppliers who provide a broad range of products and services to 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 organization.

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 suppliers.

In some cases, 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 organization. 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 delivery dates; 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. Likewise, raw materials suppliers must comply with the regulation on the registration, evaluation, authorization and restriction of chemicals.

PharmaMar Group companies reserve the right to conduct audits to verify suppliers' quality systems.

The International Standards for Phytosanitary Measures (ISPMs) contain 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.

We maintain close relations with our suppliers via meetings at trade fairs, visits, telephone calls, mail, fax, e-mail and the web.

Company	PharmaMar	Genómica	Sylentis	Xylazel	ZelnovaZeltia
No. of suppliers	**450**	**163**	**458**	**147**	**129**
Of which:					
Spanish	385	148	353	115	100
Rest of Europe	48	12	65	32	23
Developing countries	--	--	--	--	--
Rest of the world	17	3	40	--	6

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

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

6. EMPLOYEES

At the end of 2016, the PharmaMar Group, including subsidiaries outside Spain, had 713 employees. We are fortunate to have a valuable team which brings us closer to our goal of being the best in our fields of endeavor and makes our achievements possible, such as our high market share, ongoing progress with research and expansion of our product portfolio.

We are proud of the loyalty and trust of the employees at our chemical companies — Xylazel and ZelnovaZeltia — where the average length of service is 16 years, providing us with the invaluable experience accumulated over time. We are also very pleased that our biopharmaceutical companies — PharmaMar, Genómica and Sylentis — 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 this occasion to publicly thank each and every one of our employees for deciding to work with the PharmaMar 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 2016 and 2015

Figures at 31 December

Chemical Companies	Xylazel		ZelnovaZeltia	
	2016	2015	2016	2015
No. of employees	105	97	87	90
Average age (years)	47	47	46	47
Average length of service (years)	16	16	16	17
No. of employees from other countries	1	2	0	0
No. of employees with disabilities	2	1	2	2
Breakdown by gender				
% of men in total work force	66	68	60	63
% of women in total work force	34	32	40	37
% of men in management	100	100	83	80
% of women in management	0	0	17	20
Academic qualifications				
% Graduates & PhDs	24	24	19	17
Breakdown of total work force by area				
Administration	23	22	19	20
Commercial & Marketing	36	35	16	16
R&D/Quality/Control	6	5	12	11
Production & Distribution	38	33	38	41
General services	2	2	2	2

Biopharmaceutical companies	PharmaMar			Genómica		Sylentis	
	2016		2015	2016	2015	2016	2015
	Spain	Subsidiaries		Spain and subsidiaries		Spain	
No. of employees	363	69	349	58	64	21	19
Average age (years)	43	45	43	38	37	37	38
Average length of service (years)	8	2	8	6	6	6	6
No. of employees from other countries	18	69	19	4	4	3	2
No. of employees with disabilities	5	1	5	1	1	0	0
Breakdown by gender							
% of men in total work force	41	35	41	36	32	28	21
% of women in total work force	59	65	59	64	68	72	79
% of men in management	67	50	67	40	40	5	5
% of women in management	33	50	33	60	60	95	95
Academic qualifications							
% Graduates	49	72	49	45	38	47	47
% PhDs	18	0	17	26	23	38	37
Breakdown of total work force by area							
Administration	53	12	59	6	9	2	2
Commercial & Marketing	35	57	35	15	13	0	0
R&D/Quality/Control	232	0	222	19	20	17	17
Production & Distribution	30	0	23	18	22	2	0
General services	13	0	10	0	0	0	0

PharmaMar subsidiaries: Germany, France, Italy, Belgium, United Kingdom, United States and Austria (created in November 2016).

Genómica subsidiaries: Sweden, sales office in China, and a commercial agent in Brazil .

The PharmaMar Group adheres to the principles of the International Labour Organisation (ILO), the global body responsible for drawing up and overseeing international labor standards and which receives worldwide support and recognition in promoting fundamental labor rights as an expression of its founding principles.

Employment contracts, collective agreements and remuneration

Over 93% of the Group's employees have indefinite contracts. Employees are normally hired on a one-year contract, with the probation period established by law in each case, after which they are hired on an indefinite basis if their work is satisfactory. 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 labor 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 organize 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 at the beginning of each year. Each objective is susceptible to specific, measurable objective assessment in line with its importance. 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 labor matters are: Gonzalo Durán (ZelnovaZeltia), Jesús Lorenzo Silva (Xylazel), Luis Rupérez (PharmaMar), Rosario Cospedal (Genómica) and Ana Isabel Jiménez (Sylentis).

CREATING STABLE EMPLOYMENT

The PharmaMar Group was particularly active in creating long-term jobs in 2016. A total of 55 persons were hired on indefinite contracts by Group companies during the year, as follows: 36 by Pharma Mar, 4 by Genómica, 1 by Sylentis, 9 by ZelnovaZeltia and 5 by Xylazel.

PROMOTING YOUTH EMPLOYMENT

We have numerous agreements with universities and educational centers to provide internships. these agreements are signed directly with the universities or in cooperation with employer federations, business schools or business-university foundations.

In 2016, the Group had 40 interns, five of whom were subsequently hired after graduating.

Sylentis is part of the *Mentoring* initiative, a project of the University of Santiago de Compostela that seeks to guide students approaching the end of their studies and must face 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, describe how they got to their current position and what kind of profile they look for when hiring a person, answer their questions and, ultimately, help them find their first job.

Developing talent

We develop training plans that determine staff training needs in this area, ensure that nobody performs a task that requires specific training without having received such training, and that staff receive the appropriate initial training for 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.). In 2016, the PharmaMar Group invested over €763,000 in training, 20% more than in 2015. Employees also participated in many free training activities.

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

	Genómica		Sylentis		PharmaMar		ZelnovaZeltia		Xylazel	
	Hours	€	Hours	€	Hours	€	Hours	€	Hours	€
Scientific training			467	24,022	4,879	507,762				
Executive training	120	34,069			16	3,200	12	1,035		
Administrative training					134	977			503	4,994
Languages	861	9,022			12,139	74,085				
Other types of training					7,695	100,899	60	3,246		

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. In general, the Chemical Industry General Wage Agreement is complied with while meeting employees' wishes as far as possible.

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 ZelnovaZeltia 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 a staff dining area 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 ZelnovaZeltia buildings have eliminated architectural barriers or have installed ramps at the accesses. In April 2015, Genómica relocated within the Madrid region, to Parque Empresarial Alvento, Europe's first green business park. Its new, larger facilities have 1,809 m2 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.

Internal communications

Internal communications are a modern management tool of increasing importance in business. Communications are generally channeled via e-mail, the intranet, regular meetings, and notice boards.

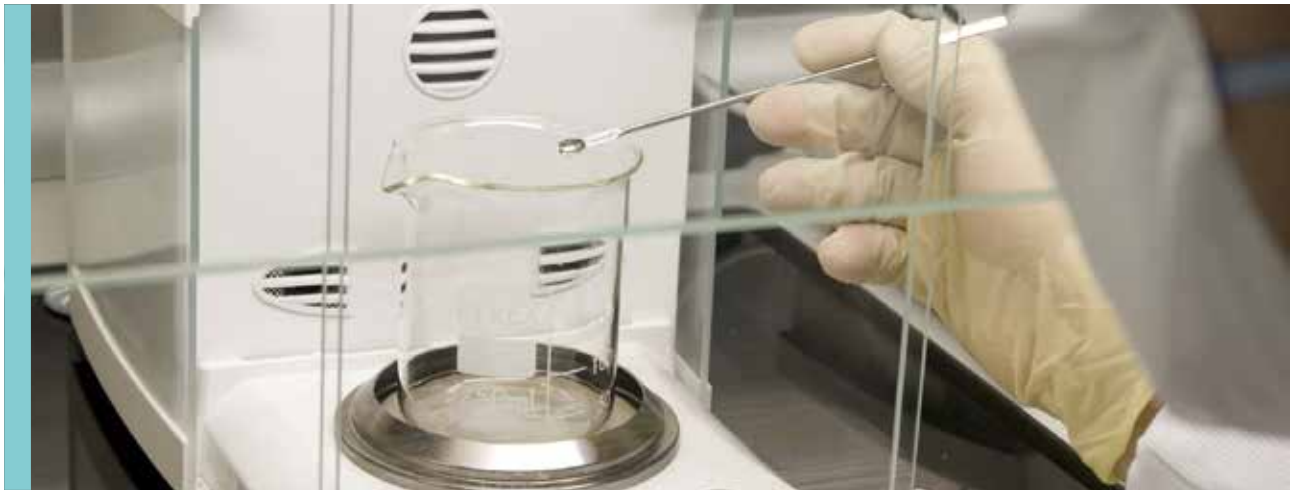
Employees have easy access to management. There is a structured communications plan involving regular meetings between the various echelons (division heads, managers and department heads) to track and manage the objectives of the company and of each individual area and project.

Informal meetings are held frequently with teams from different areas to report on project progress. At Genómica, employees give regular lectures each month about some 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.

PharmaMar conducts employee satisfaction surveys every two years.

Workplace health and safety

Safety at work is a necessity from both an ethical and an economic standpoint. All Group companies have workplace safety programs



that conform to current regulations, and they conduct regular evacuation drills and simulacra. All personnel receive instruction on 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 at Zeltia in charge of Health and Safety issues are Pedro Torrens (ZelnovaZeltia), 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 2016:

	Number	Days lost
Incidence		
Due to illness	168	5,748
Accidents with medical leave	5	128
Accidents without medical leave	11	---
Accidents on the way to/from work	7	105

Xylazel and ZelnovaZeltia 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. This international standard confirms the company's commitment to the health and safety of its workers; in this context, the Zeltia Group 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	Sector	PharmaMar	Sector
Incidence index				
No. of accidents with lost days per 1,000 workers	18.80	28.23	0	10.20
Frequency index				
No. of accidents with lost days per 1,000,000 hours worked	10.73	16.12	0	5.82
Severity index				
No. of lost days per 1,000 hours worked	0.02	0.38	0	0.21

Employee health

All employees are offered an annual medical check-up; all tests, examinations and analyses 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 labor legislation, the Group's medical check-up includes blood and urine analysis, a blood pressure measurement, and nutritional counseling. 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 2016, PharmaMar offered flu vaccination to its employees free of charge.

'Zeltia'

SOCIEDAD ANÓNIMA

Constituida por escritura pública de 3 de Agosto de 1939, modificada por otras del 6 de Mayo y 25 de Junio de 1940, todas ante el Notario de Porriño Don Diego Pombo Somoza, e inscripta en el Registro Mercantil de Pontevedra.

CAPITAL SOCIAL

4.000.000

DE PESETAS

DIVIDIDO EN 4.000 ACCIONES NOMINATIVAS DE 1.000 PESETAS CADA UNA, NUMERADAS DEL 1 AL 4.000

TÍTULO DE UNA ACCIÓN Nº 000001

a favor de Don José Fernández López

MIL 1000 PESETAS

Se reconocen al poseedor de este título todos los derechos que corresponden a los accionistas según las escrituras y Estatutos sociales.

VIGO de de 1940

EL PRESIDENTE DEL CONSEJO DE ADMINISTRACIÓN

EL SECRETARIO DEL CONSEJO DE ADMINISTRACIÓN

ESTE TITULO ESTA COMPLETAMENTE LIBERADO

Artes Gráficas Grijalbo, S.A. Bilbao

7. SHAREHOLDERS

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

At 31 December 2016, PharmaMar's market capitalization was €602 million. Its shares are traded on the four Spanish stock exchanges (Madrid, Bilbao, Barcelona and Valencia).

Number of shares and share performance

At 31 December 2016, the Company's capital stock amounted to €11,110,244.35, represented by 222,204,887 shares with a par value of €0.05 each.

The company's outstanding shares have been listed in the electronic market since 20 October 1998.

In 2016, PharmaMar's share price fluctuated between €1.72 and €3.19 (closing prices), ending the year at €2.71 euro.

In 2016, trading in PharmaMar stock totaled €550 million, with an average of 550,406 shares changing hands each day; trading reached its low in December and peaked in February.

In macroeconomic and market terms, 2016 was a year of uncertainties that had a clear impact on the financial markets. The two principal geopolitical events of 2016 were indisputably the UK vote in June to abandon the European Union (Brexit), and the impact of the US presidential election campaign on the markets throughout the year, culminating with the election of Donald Trump in November. Other notable macroeconomic factors in the year were the monetary policies implemented by the main central banks. In Europe, the European Central Bank (ECB) maintained its expansive monetary policy in view of weak European economic growth; meanwhile, on the other side of the Atlantic, in December the Federal Reserve resumed its policy of increasing interest rates after seven consecutive years of GDP growth and given the improved prospects for the following year as well as the robust recovery by employment in recent years, among other macroeconomic indicators.

In Spain, the political uncertainty in 2016 caused by the need to hold a second general election, while the country spent almost one year under an interim government, was reflected in market performance, as the indices underperformed their European counterparts. This occurred even though Spain achieved 3.2% GDP growth, putting it at the head of the developed countries, with prospects of continued improvement. Nevertheless, Spain still faces major challenges in the coming years, such as the high unemployment rate (although this datum continues to improve), a government deficit that must be controlled in line with Europe's instructions, and the rising government debt, among other issues.

As a result, until mid-December the IBEX-35 index (the main index of the Spanish bourse) had accumulated a moderate 2% decline, after gaining 8% since the end of November, but it finally ended 2016 down -2.2%.

In 2016, PharmaMar's first full year of trading following the inverse merger with Zeltia, the share gained 8%, contrasting with a decline of 2.2% by the IBEX-35 index and of 21% by the Nasdaq Biotech index, one of the world's main biotechnology indexes. PharmaMar's share price recovered from the outset, supported by positive corporate news and despite the difficult market situation.

Notable events in the year included progress with clinical trials with its most strategic product, Lurbinectedin (PM1183), and also with Aplidin®. In March, the Company announced that the ADMYRE Phase II trial with Aplidin® in multiple myeloma had attained its primary endpoint. This resulted in the presentation of a marketing authorization application to the European Medicines Agency (EMA) for Aplidin® in Europe for this indication. The share's good performance

in the second half of the year was driven by Lurbinectedin's clinical progress. Firstly, the Phase III registration trial with Lurbinectedin in combination with doxorubicin for treating patients with small-cell lung cancer commenced at the end of the summer. Shortly afterwards, it was announced that the Independent Data Monitoring Committee (IDMC) had approved continuation of the CORAIL pivotal Phase III trial with Lurbinectedin to treat platinum-resistant ovarian cancer. Enrolment of the 443 patients in this trial concluded in October.

The year 2016 concluded with the signature of an exclusive licensing, development and marketing agreement for Lurbinectedin in Japan with Chugai Pharmaceutical Co, Ltd. This agreement and the related revenues represent strong support for Lurbinectedin's development and had a positive impact in the market.

Distribution of capital

PharmaMar'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 Mª Fernández Sousa-Faro owns 11% (4.6% through Ms Montserrat Andrade Detrell), Rosp Corunna Participaciones Empresariales, S.L. owns 5%, and Mr Pedro Fernández Puentes owns 4.5% (3.9% through Safoles SA).

Shareholders' rights

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

Under law, shareholders have the following rights:

- 1. The right to attend Shareholders' Meetings and to challenge decisions by the Shareholders' Meeting. An Ordinary Shareholders' Meeting is held once per year.
- 2. The pre-emptive right to acquire new shares or convertible bonds.
- 3. The right to share in the corporate profits and in the proceeds from its liquidation.
- 4. The right.

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, the motions submitted to the meeting, and any other reports and documentation that must be made available to shareholders.

Where the law so provides, 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.

From the date of notice of the Shareholders' Meeting and up to and including the seventh 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.

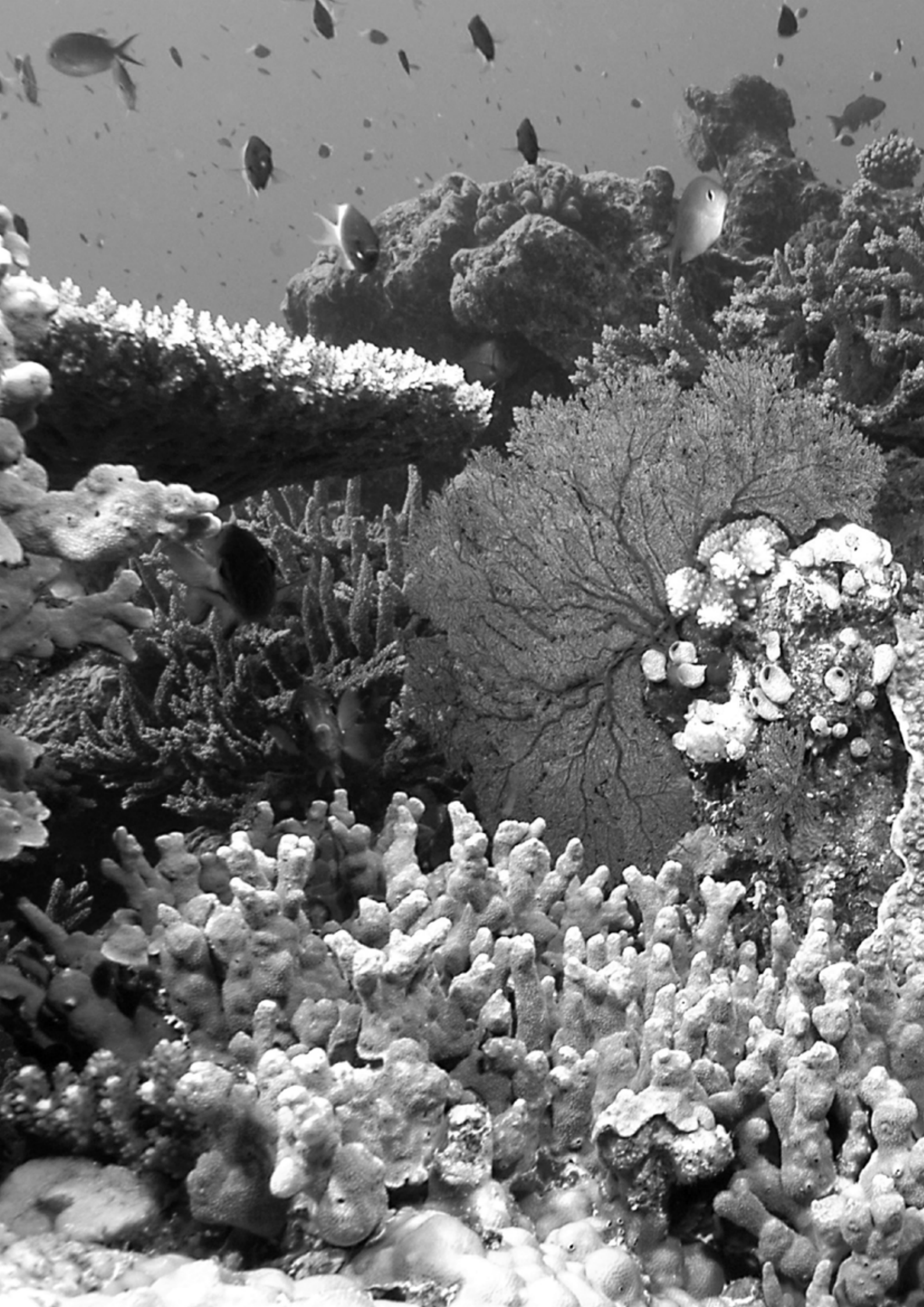
During the Shareholders' Meeting, shareholders may verbally request any information and clarification they wish about the items on the agenda.

Communications with shareholders

All material information about PharmaMar is kept up to date and is available to shareholders and the general public on the company's website, 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



8. ENVIRONMENT

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, which is the source of their compounds; molecules of interest are synthesized. Once a compound is identified, synthesis provides a supply without having to resort to the original marine organisms. 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. By protecting, conserving and making sustainable use of these resources, PharmaMar not only contributes to the development of possible new pharmacological treatments from just a few grams of marine 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 68% of the PharmaMar Group's revenues and 75% of its workforce.

There were no environmental incidents or sanctions at any of our companies in 2016. The Group companies are located in industry parks and have very little environmental impact in terms of noise or smells, electromagnetic emissions, influence on biodiversity, leaks or risk activities affecting ground or surface water in the areas where they are established.

The Group attaches great importance to saving and recycling plans; it uses photovoltaic panels and insulation on factory and warehouse roofs and separates its waste by type, with the participation of the staff. There are specific waste bins for separating waste, which are managed by specialized companies. Additionally, the staff (particularly production personnel) receives training in waste management.

In seeking to support respect for the environment, this Social Responsibility Report will be issued in electronic format only, thus saving the paper of a print edition.

The waste policies of the Group's largest companies, PharmaMar, ZelnovaZeltia and Xylazel, 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. This internationally-recognized accreditation evidences PharmaMar's commitment to the environment and its decision to implement policies and actions that encourage continuous improvement and conservation of the sea. 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. From an environmental protection standpoint, there are two existing international documents whose principles are reflected in the criteria applied in sample collection: The Red List of Threatened Species, which is the work of the International Union for the Conservation of Nature and Natural Resources (IUCN), and the CITES list (Convention on International Trade in Endangered Species of Wild Fauna and Flora).

We collect samples manually and selectively via scuba diving for marine invertebrates; we do not use any mechanical systems such as drag nets or dredging, thereby eliminating the impact on the natural environment. We also use an underwater robot with an umbilical cord which is operated from the surface and provides a real-time view of the seabed, allowing for the selection of sample zones and minimizing 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 which ensure that all employees are highly qualified in safety and environmental management.
- Minimization 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 minimization of the impact using waste separation programs.
- Control of process water using a purifying plant that homogenizes 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 2016, PharmaMar ratified the commitment of the Spanish Green Growth Group, which it joined in 2014.

The Spanish Green Growth Group is an association created to foster public-private cooperation in addressing environmental challenges. This platform encourages the participation of business in the most important debates on the environment, shares information and identifies opportunities for Spanish companies.

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 in the private sector and establish a channel of communication with government with a view to international negotiations on climate change. Explore ideas for public-private partnership in combating climate change.
- Influence the creation of favorable conditions for the development of a low carbon economy that is compatible with the goal of economic growth and job creation.
- Contribute to the creation and distribution of the necessary knowledge to drive changes that contribute to sustainable development.

PACT FOR THE BIOSPHERE

The PharmaMar 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, centers 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 classified by PharmaMar researchers[2].

As an expression of its commitment to the biosphere, the PharmaMar Group has signed the Pact for Biodiversity, which aims, in cooperation with business, to promote economic development that is compatible with biodiversity conservation.

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

The Company also supports Spain's ratification of the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization.

ZelnovaZeltia

- Waste treatment: The use of a solid waste separation center, 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 center).
- Reduction in electricity consumption: Adoption of measures such as improving natural lighting; controlling energy usage times so as to reduce electricity consumption; scheduling manufacturing by synchronizing the start-up and stoppage of boilers, compressors and agitators; and making optimal use of machinery operating periods with a view to saving energy.
- 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.
- Issuance of annual reports on transportation and hazardous wastes produced during the year and disposed of through authorized waste managers.
- Measurements of CO and NO emissions every six months, which are sent to the Galicia Regional Government.
- Modifications in product composition to avoid classification as carcinogens.
- Segregation of chemicals on the basis of danger and installation of containments in each specific risk area. It is a priority for ZelnovaZeltia to avoid chemical spillages and contain any that occur; to

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

this end, it has catchment pans around all fixed solvent tanks.

- Water separation: process cleaning water is subjected to a specific treatment process to separate sludge from clean water (waste water). Wastewater, sewage and storm water are channeled separately to allow for better control over discharge quality.

- Reduction of production tank wash water production: a water spray system has been installed which greatly reduces the volume of water used for cleaning.

- An energy efficiency audit in 2016 confirmed that measures taken in previous years had been appropriate, and improvements will continue to be made.

Xylazel

Xylazel is certified to the ISO 14001:2004 standard. That certification is audited annual by BUREAU VERITAS to ensure that Xylazel's environmental management system conforms to the standard.

As for compliance with the requirements of the standard, Xylazel has defined an environmental policy which is integrated with the pre-existing quality policy and establishes general guidelines for the organization's environmental management. In this framework, it has implemented several environmental management and emergency plans for the event of environmental accidents:

- Application of the 2013-2016 hazardous waste abatement plan, originally presented to and approved by the competent environmental authority.

- Use of the system to periodically evaluate the consumption of raw materials and of ancillary utilities (diesel, electricity, water, paper, etc.) in manufacturing. The system also monitors Xylazel's emissions, discharges and waste production.

- Implementation of a new water recirculation system for firefighting in the factory, notably reducing water consumption.

In recent years, Xylazel has continued to modernize lighting equipment by replacing conventional sodium vapor lamps with LED lamps, which consume less electricity.

Resources Use

	PharmaMar	ZelnovaZeltia	Xylazel
Electricity (MWh)	5,000	1,034	579
Gas oil (l)	---	37,845	6,945
Natural gas (fuel) (l)	309,497,000	---	---
Water (m3)	9,847	15,000	1,643

9. COMMUNITY ACTION

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.

However, we also cooperate actively with numerous initiatives to promote research, disseminate knowledge and support education. The PharmaMar Group's contributions in this area include:

Scholarships	279,704 €
Donations (mainly to hospitals)	75,294 €
Sponsorship of conferences, seminars and exhibitions	786,648 €
Cooperation with organizations	165,688 €

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

- Collaboration with **patient associations,** including **FEDER** (*Federación Española de Enfermedades Raras*), Sarcoma Patients Euronet (**SPAEN**), *Asociación Española de Afectados por Sarcomas* (**AEAS**), *Asociación de Afectados por Cáncer de Ovario* (**ASACO**), *Grupo Español de Pacientes con Cáncer* (**GEPAC**), *Rare Cancers Foundation* (**RCF**) and *Cura e Ricerca in Oncologia Ginecologica* (**IRIS**). Specifically, PharmaMar took part in the FEDER 2016 campaign "*Creando redes de esperanza*" (Creating networks of hope), coinciding with world Rare Disease Day.

  The company works with FEDER in a number of ways:

  - Donations.
  - Organisation of a panel of experts entitled "Reference Centers and Care Quality in Rare Diseases", held in February 2016.
  - Employee participation in the Hope Race in March 2016. PharmaMar paid the entry fee for its employees who participated.

- 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.

- **Signature of an agreement between PharmaMar, RedeLA, the Severo Ochoa Foundation and the research group of Dr. Luis Carrasco** to continue with the "Etiology of neurodegenerative diseases" research project, which will advance understanding of sclerosis.

- **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, PharmaMar is the Spanish company with the third-largest number of publications in high-impact scientific journals.

- Publication of the book **"El mundo submarino de PharmaMar",** (PharmaMar's Undersea

Carlos Galmarini, Head of Cell Biology at PharmaMar (rear, first from right) at the signature of the agreement between PharmaMar, RedELA, the Severo Ochoa Foundation and the Dr. Luis Carrasco research group.

World), which contains photographs of numerous marine organisms taken on expeditions by our marine biologists, from which the company extracts the compounds for R&D and innovation.

- Sponsorship of a number of **research bodies,** including the Spanish Conquer **Cancer Campaign** and the **Mari Paz Jiménez Casado Foundation,** a non-profit organization that helps people with sarcoma and incentivizes training and scientific research.

- Sponsorship of, and participation and presentations at numerous **scientific conferences and meetings.** They included the **Spanish Society of Medical Oncology (SEOM),** held in Madrid in October 2016. Additionally, PharmaMar **sponsored BioSpain,** held in Bilbao in September 2016, at which representatives of the PharmaMar Group participated in significant roundtable discussions.

  The Company also sponsored the **"Detener el glaucoma"** (Stop glaucoma) **campaign,** held during World Glaucoma Week in March 2016, which included a number of events to raise awareness of this disease. Sylentis did not just sponsor this event; its Chief Operations Officer, Ana Isabel Jiménez, took part in a roundtable discussion on upcoming therapies for glaucoma to be marketed in Europe and the United States.

- 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 **AEFI** (Spanish Industrial Pharmaceutical Association) and **EBE** (European Biopharmaceutical Enterprises), which represent the pharmaceutical sector in Spain and Europe.

In the area of **education,** PharmaMar undertook the following actions:

- Agreements with numerous universities, business schools and institutes in Spain and other countries as part of a **training program**

Panel of experts entitled "Reference Centers and Care Quality in Rare Diseases", organized by PharmaMar in cooperation with FEDER.

for interns at PharmaMar, Genómica, Sylentis and Xylazel.

- Participation **in post-graduate seminars and courses** organized by universities and in Master's programs and conferences in the fields of biomedicine and biotechnology. These courses facilitate the exchange of technical knowledge in the pursuit of science and research, thus contributing to the future of our society.

  A good example of this is the *Blue Biotech Master* program at Universidad Católica de Valencia San Vicente Mártir. This master's program 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.

- **Guided visits** of PharmaMar and Xylazel laboratories and facilities for students, with educational talks pitched to the appropriate level. Student groups that visited PharmaMar facilities during the year included Instituto de Enseñanza Secundaria Ángel Corella, Albacete Pharmacy School, and the CESIF Master program. Xylazel received visits from students receiving vocational training in the areas of Sales, Administration, Finance and Management.

- Cooperation with **FEUGA** (Fundación Empresa-Universidad Gallega). This is a not-for-profit entity specialized in transferring knowledge, innovation and technology from Galicia's universities to business and society at large.

- Delivery of material to Madrid Complutense University for **"Science Week".**

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

BioSpain conference, sponsored by PharmaMar.

- Outsourcing of advertising materials and graphic design to sheltered **workshops for people with disabilities,** such as Trébore, a Paideia Galiza Foundation initiative. It also works with the Integral AV travel agency, which employs people with disabilities (from which it acquired services amounting to €69,055 in 2016).

- Blood donation **drives in cooperation with** Spain's Red Cross: PharmaMar organized a blood donation session in cooperation with Madrid's Transfusion Centre, in which 34 employees donated.

- Donation by PharmaMar of the residual value obtained from recycling IT equipment to **Federación de Padres de Niños con Cáncer.**

- Contribution by Xylazel to the **Vigo Food Bank** donation drive. Within the framework of an agreement between the food bank and the companies belonging to the Tui Chamber of Commerce, arrangements were made to collect the food that employees of those companies had donated. The company matched employees' donations, in the form of food or cash.

- Participation by Sylentis employees in **"Operación Kilo",** a food bank program.

- Collection of toys at Genómica for "**Asociación Caminar",** an NGO.

- 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.

- Cooperation with the **Spanish Broadcasters Association and the Spanish Association for Investor Relations.**

- Cooperation with the **Family Business Association of Madrid,** an independent group which defends the interests of family businesses in the Madrid region.

- Cooperation with **ASEYACOVI,** Association of Entrepreneurs, Business-owners and Self-employed persons of Colmenar Viejo.

10. COMMUNITIES

The PharmaMar Group companies are established in the municipalities of Colmenar Viejo, Tres Cantos and Coslada (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 programs — and providing a range of services. Additionally, the companies take the necessary steps to minimize 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 €90,000 in Galicia and €86,000 in Madrid in 2016.

Our companies are also a major source of employment. We employ 163 people in Galicia. Xylazel and ZelnovaZeltia also create jobs in other regions: a total of 32. We employ a total of 438 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 organized 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:

- Visits by students to the laboratories and facilities of PharmaMar and Xylazel, including educational talks pitched to the appropriate level.
- Cooperation with ASEYACOVI (Association of Entrepreneurs, Business-owners and Self-employed persons of Colmenar Viejo) and the Madrid Association of Family Firms.

11. REGULATORY BODIES

Regulatory bodies are authorities with responsibility for drafting and enforcing the law relating to the development and authorization of new drugs. PharmaMar's relations with the regulatory bodies that govern its various activities are fluid, transparent and efficient.

Relations with regulators are based on direct contacts, frequent meetings and conference calls in which open communication and the exchange of knowledge make it possible to ascertain the authorities' opinion and set out the company's viewpoint in defense of its interests. As part of this constructive dialogue, scientific and technical advice is sought, doubts are resolved, information requested by regulators is presented, and regulator's proposals and questions are noted for consideration in future actions. With a view to responding to constant changes in legislation due to directives and regulations issued by the European Union and other legal provisions in countries where the Group operates directly or through subsidiaries or agreements with third parties, the Group companies regularly update their procedures and documentation to ensure rigorous compliance with the legislation in force.

A number of initiatives were taken to increase transparency in relations between the regulatory authorities and the industry. For example, PharmaMar cooperates with regulatory bodies in drafting guidelines 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 involves the revision of draft new guidelines, directives and regulations.

As a listed company and issuer of securities, PharmaMar is subject to the supervision of the National Securities Market Commission (CNMV). The Commission is entrusted with supervising and inspecting Spain's securities markets and the activity of all market participants.

The main regulatory bodies and institutions with which the PharmaMar 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 and Competitiveness, Industry, etc.), Madrid Regional Government Ministry of Health, regional healthcare services (SER+MAS in Madrid, SAS in Andalucía, SALUD in Aragón, CatSalut in Catalonia, etc.), the Spanish Agency for Medicines and Healthcare Products (AEMPS), 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.

The main issues discussed with regulatory authorities are:

- PharmaMar: Authorisation and performance of clinical trials, inspections, drug development (including pediatric and orphan drugs), scientific advice, maintenance of commercialisation authorization for Yondelis® and price and reimbursement negotiations. In 2016, a marketing authorization application for Aplidin® was presented to the European authorities in connection with the treatment of multiple myeloma.

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

- Sylentis: Drug development, including the launch of clinical trials and trial authorization by ethics committees and regulatory agencies. Organization of a pre-IND meeting with the FDA to discuss clinical trials in the US. Inspection by the Spanish Agency for Medicines and Healthcare Products (AEMPS) to renew its authorization as a pharmaceutical laboratory to manufacture research drugs.

- Genómica: Registration and obtainment of the CE mark for diagnostic kits.

- ZelnovaZeltia: Obtainment of approval to market its products.

- Xylazel: Register of Biocides and Pesticides, cooperation with the paint industry association ASEFAPI (Asociación Española de Fabricantes de Pinturas y Tintas de Imprimir) and its actions before the Health Ministry, and new legal provisions such as the Law on Solvent Emissions to the Atmosphere, the Biocide Law and the Hazardous Products Law.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