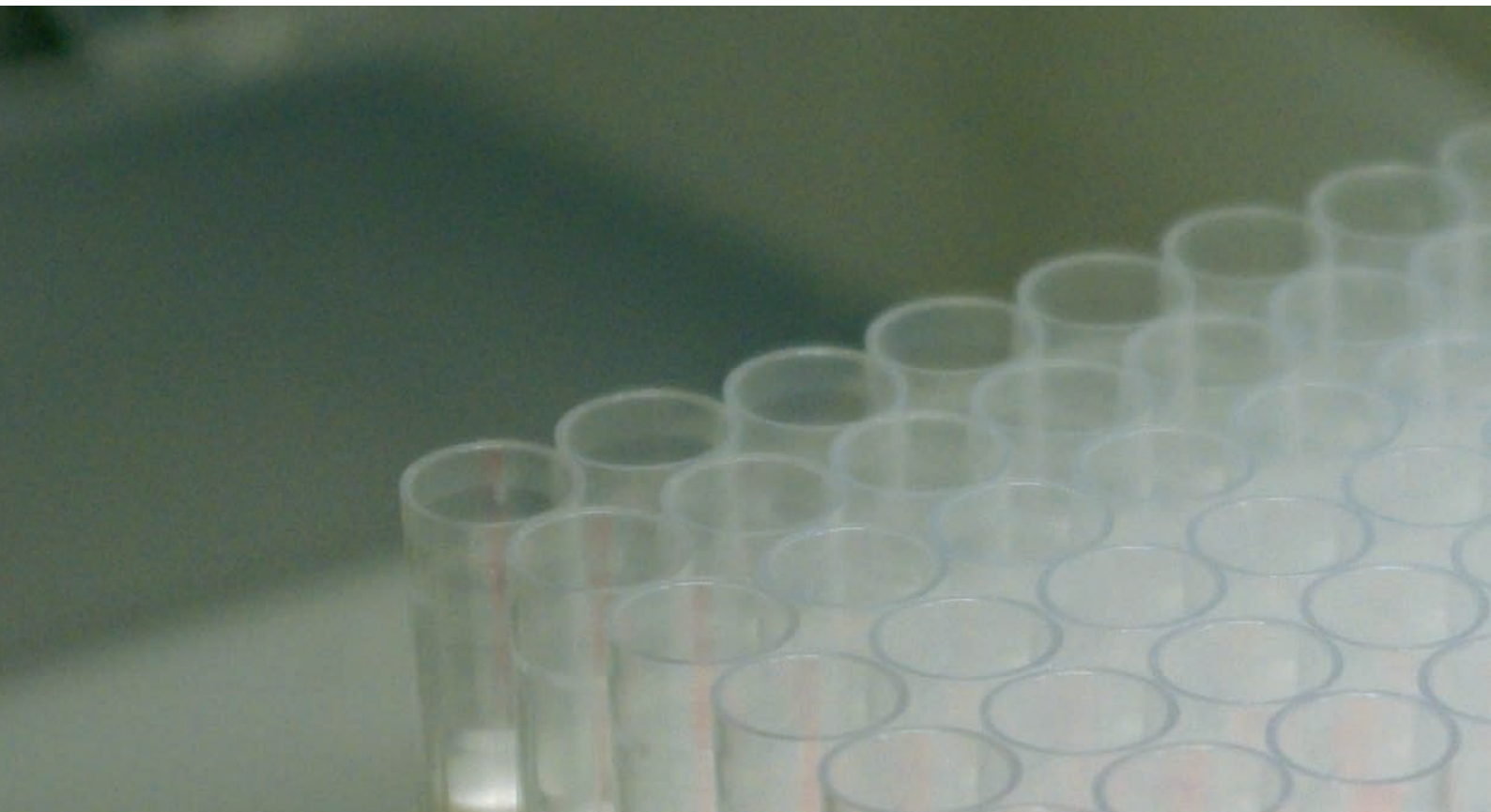




2015

CORPORATE SOCIAL RESPONSIBILITY

REPORT





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GROUP DESCRIPTION





GROUP DESCRIPTION

The Zeltia Group, which existed until October 2015, comprised the following companies: PharmaMar, Genómica, Sylentis, Xylazel and Zelnova. On that date, Zeltia Group was absorbed by its subsidiary PharmaMar, and became PharmaMar Group, comprising the same companies.

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. Sulphamide was synthesised in the Porriño laboratories.

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

- 1942.- Zeltia explored new avenues, manufacturing agricultural products and insecticides. The ZZ brand became leader in terms of market share.



- 1945.- Antibióticos, S.A. was founded, and soon became a major domestic company and exporter. Zeltia owned a stake in Antibióticos until 1985.



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

- 1990s.- The Group stabilised in most recent configuration, through the definition of the two main business areas in which it currently operates: Biopharmaceuticals and Consumer Chemicals.
- 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 therapeutical agents based on interference RNA (RNAi).

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

- 2007.- Yondelis®, a PharmaMar drug, was approved by the European regulator for treating soft tissue sarcoma, and was the first Spanish anti-tumour drug approved in Europe.
- 2009.- Yondelis® was approved by the European regulator to treat relapsed ovarian cancer.
- 2014.- The Group celebrated its 75th anniversary: A long, sound track-record that stands out among Spanish biopharmaceutical companies.
- 2015.- PharmaMar absorbed Zeltia in a reverse merger, and the group was renamed “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 almost 80 countries.



THE GROUP TODAY

On 31 October 2015, Zeltia was merged into its main subsidiary, PharmaMar. 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.

PharmaMar also has a majority stake in other group companies: Genómica, Sylentis, Xylazel and Zelnova Zeltia, which previously belonged to Zeltia Group.

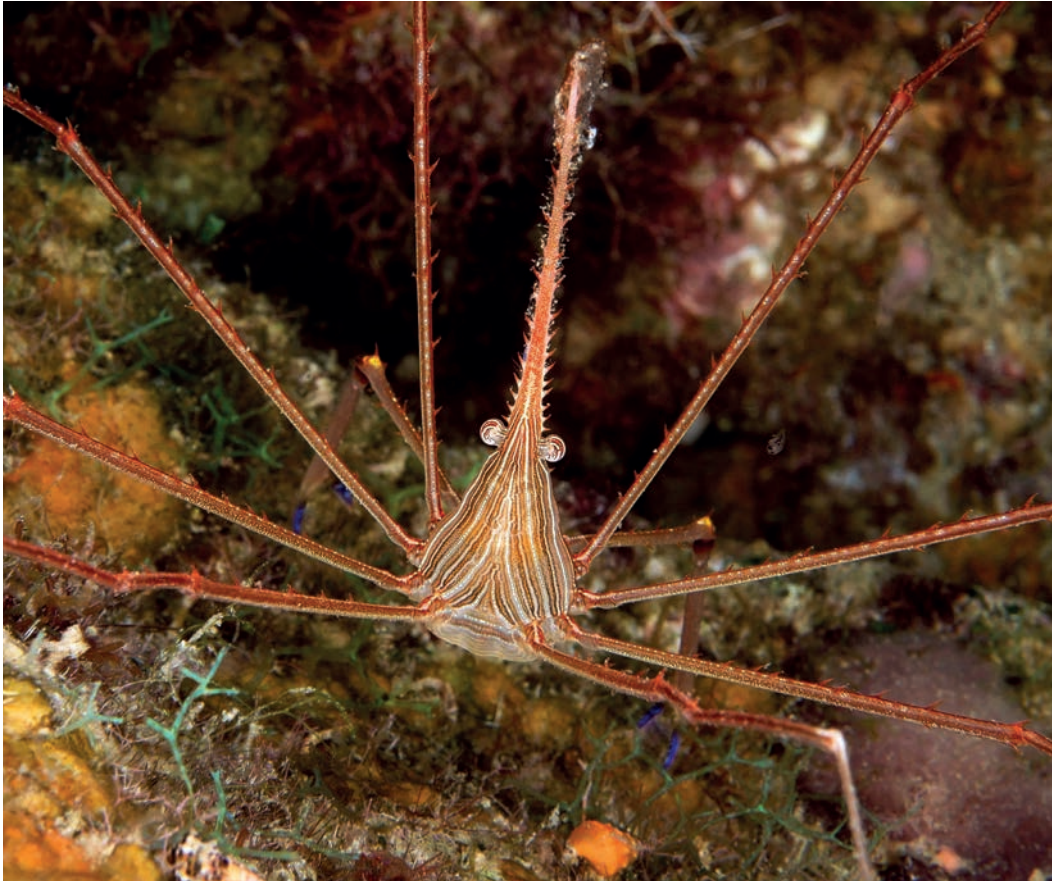


OTHER BUSINESSES

Biopharmacy



Consumer chemicals





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-tumour 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: more than 170,000 samples of macro- and micro-organisms. From the original marine sample, PharmaMar synthesises the active compound so as to have a source of the molecule without affecting the seas or relying on natural sources. Founded in 1986, the company is based in the Madrid region and has subsidiaries in the US, UK, Belgium, France, Germany, Switzerland and Italy.



GENÓMICA, S.A.U.

Was founded in 1990 and was the first private company in Spain to provide molecular **diagnostic services**. In 2015, it celebrated its 25th anniversary. 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.

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 specialised in wood decoration and treatment. Its products protect wood against fungi, mould, 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 colours and finishes. The company was founded in 1975 and is headquartered in Galicia. It celebrated its 40th anniversary in 2015.

ZELNOVA ZELTIA, S.A.

Produces and commercialises chemical products for household and industrial use, such as insecticides, air fresheners, cleaners and disinfectants. It has leading brands such as **Casa Jardín**, **Kill-Paff**, **ZZ Paff**, **Bio-Kill**, **Coopermatic**, **Baldosinin** and **Hechicera**. The company is a leader in various segments of the insecticides market (sprays, plug-ins and liquids). Zelnova Zeltia has been using ozone-friendly propellants for over 20 years. It has also pioneered, in Spain, the use of electric mosquito killers that do not use refill tablets, and the first electric air freshener (based on the Kill Paff system). 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. Despite its acquisition by Zelnova Zeltia 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.

NOTABLE EVENTS IN 2015

Corporate

- Zeltia was absorbed by PharmaMar in a reverse merger. PharmaMar shares began trading on the stock exchange.

Oncology

- Janssen Biotech Inc, (PharmaMar's US partner) received approval from the US Food and Drug Administration (FDA) to commercialise Yondelis® (trabectedin) for treating patients with liposarcoma (LPS) or leiomyosarcoma (LMS). These are the two most common forms of soft tissue sarcoma. This is the first treatment approved specifically for liposarcoma in the US.
- Taiho Pharmaceutical (PharmaMar's partner in Japan) received authorisation from Japan's Ministry of Health, Labour and Welfare to commercialise Yondelis® (trabectedin) in Japan for the treatment of soft tissue sarcoma.

- PharmaMar signed a licensing agreement with TTY Biopharm for the commercialisation of Aplidin® (plitidepsin) in Taiwan.
- PharmaMar signed a licensing agreement with Specialised Therapeutics Australia Pty, Ltd for the commercialisation of Aplidin® (plitidepsin) in Australia and New Zealand.
- Patient recruitment concluded for the pivotal Phase III trial with Aplidin® in multiple myeloma.
- Recruitment commenced for the CORAIL pivotal Phase III trial with PM1183 (lurbinectedin) in patients with platinum-resistant ovarian cancer.
- A phase II basket trial commenced to assess the efficacy and safety of PM1183 (lurbinectedin) in patients with various tumour types at an advanced stage.
- The first patient was enrolled for a Phase II trial with trabectedin in meningioma, a type of brain cancer, which is being conducted in conjunction with the European Organisation for Research and Treatment of Cancer (EORTC).

Diagnostics

- Launch of a kit for detecting melanoma biomarkers.
- Participation in a programme in Turkey for early detection of cervical cancer using Human Papilloma Virus (HPV) genotyping: this will be the largest HPV screening programme in the world.
- Brazil authorised the sale and commercialisation of the CLART® kit for STIs (sexually transmitted infections).
- Genómica and Fundación ECO (*Fundación para la Excelencia y Calidad en la Oncología*) announced a cooperation agreement in oncology.

RNAi

- Sylentis presented the results of its SYLTAG Phase II dose-seeking trial with bamosiran (SYL040012) for treating glaucoma.
- Sylentis completed recruitment for the Phase II clinical trial of SYL1001 for treating eye discomfort associated with dry eye syndrome.

Consumer chemicals

- Sales in this segment increased by 2.7%
- Xylazel Aire Sano, a paint suitable for hospital environments, was chosen as one of the paints for Vigo Hospital.





CORPORATE GOVERNANCE



MANAGEMENT STRUCTURE

Mr. José María Fernández Sousa-Faro is the executive chairman of Pharma Mar, S.A. The other senior executives are:

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 website: www.pharmamar.com.

The Board of Directors is the company's organ of management, administration and representation and it is vested with all powers except those reserved for the Shareholders' Meeting.

Board of Directors

The Board of Directors comprises the following members:

NAME OF DIRECTOR	REPRESENTATIVE	OFFICE
JOSÉ M ^a FERNÁNDEZ SOUSA-FARO	N/A	Executive Chairman
PEDRO FERNÁNDEZ PUENTES	N/A	Executive Vice-Chairman
ANA PALACIO VALLELERSUNDI	N/A	Independent director
ROSP CORUNNA PARTICIPACIONES EMPRESARIALES, S.L.	José Francisco Leyte Verdejo	Proprietary director
JEFPO, S.L.	José Félix Pérez-Orive Carceller	Director (Other external)
JAIME ZURITA SÁENZ DE NAVARRETE	N/A	Independent director
CARLOS SOLCHAGA CATALÁN	N/A	Independent director
EDUARDO SERRA Y ASOCIADOS, S.L.	Eduardo Serra Rexach	Independent director
MONTSERRAT ANDRADE DETRELL	N/A	Proprietary director

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

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

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.

This kind of code is aimed at presenting the principles and ethical values of the organisation. In this case, it formalises the principles and values of PharmaMar Group; principles and values that guide and should continue to guide the conduct of all people belonging to the group companies, 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 current legislation with regard to the confidentiality of the data gathered in our activities and research. The companies most involved in this area are PharmaMar, Genómica and Sylentis, because of the nature of their activities, specifically their involvement in clinical trials and genetic analyses. Patient and client personal data is afforded special protection, as is the personal data collected in the course of the company's ordinary activities: information about employees, suppliers, external scientists, labour representatives, etc.

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

- Regular backups are made and stored in a secure specialised 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.

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 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.

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.

AWARDS GRANTED TO THE GROUP

In 2015, PharmaMar received the following distinctions:

- 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).



María Luisa de Francia, CFO of the PharmaMar Group (front, first from left), collecting the award for business transparency presented to Zeltia by Sociedad Española de Contabilidad y Dirección de Empresas (AECA).



Second Vice-President of ASEBIO and Director of Project Coordination at PharmaMar, Carmen Eibe (second from left) collects the recognition granted by ASEBIO to Zeltia as a founding member. Also shown: Begoña Cristeto (first from left), General Secretary of Industry and SMEs, Carmen Vela (second from right), Secretary of State for Research, Development and Innovation, and Regina Revilla (first from right), President of ASEBIO at the time.

- El Economista readers voted PharmaMar “Pharmaceutical company of the year” in the newspaper’s special edition featuring the best companies of 2015.

elEconomista

PHARMAMAR COMMITTED TO REDUCING WORKPLACE ACCIDENTS

Fraternidad-Muprespa recognises companies committed to reducing workplace accidents and preventing risks in the workplace, as regulated by Royal Decree 404/2010. Within this framework, PharmaMar was awarded the Bonus 2012 diploma.

The main requirements for obtaining this recognition are: having invested in facilities, processes or equipment aimed at reducing risks during the observation period; not exceeding general and extreme accident rates during the observation period; be up to date in obligations relating to Social Security contributions; not having been fined for serious or very serious infractions in relation to workplace safety or social security; and meet all basic requirements in relation to the prevention of workplace risks and accidents.

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

Madrid Healthcare Silver Plaque for PharmaMar in 2014.

Ejecutivos Award for the Zeltia Group as company of the year in 2014.

"Universidad Empresa 2014" award for the Zeltia Group from *Red de Fundaciones Universidad Empresa* (REDFUE).

"El Confidencial-KPMG 2014" award for best business practices in Innovation for the Zeltia Group.

2013 Fundamed Award for R&D and Innovation, awarded to Genómica.

Gold Aspid 2013 Award for the "Best End-to-End Pharmaceutical Product Campaign for Professionals", to PharmaMar for its international campaign to relaunch Yondelis® as treatment for ovarian cancer (in combination with PLD).

"Best Ideas" award, granted by Diario Médico to Genómica for its colorectal cancer diagnostic kit.

2012 National Award for Research, Development and Innovation, granted by the Medical Science and Health Products Foundation (FundaMed) to Sylentis for its innovative RNAi technology applied to drug development.

2012 "100 Best Ideas" Award, granted by Actualidad Económica to Sylentis.

Ejecutivos Award in 2012, granted to Zeltia in the Internationalisation category.

"Concello de Mos 2012" medal, for the Zeltia Group.

2012 Lifetime achievement plaque from ASEBIO, presented to Mr. José María Fernández Sousa-Faro in recognition of his track record in Biotechnology.

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.

Both PharmaMar Group (previously the Zeltia Group) and its Chairman rank consistently in the lists of 100 most prestigious companies and leaders in Spain, drawn up by MERCO. In 2015, PharmaMar ranked first among biotechnology companies in Spain for the third consecutive year, and now occupies 60th position in the overall ranking. The Group Chairman, Mr. José María Fernández Sousa-Faro, also appears on the list, at number 90. MERCO ranks Spanish companies according to reputation after they are evaluated by more than 1,500 senior business executives, financial analysts, NGOs, unions, consumer associations and opinion leaders. MERCO also produces a league table of the 100 companies in Spain that best attract and retain talented employees; the Group is also on that list, in 84th place. Finally, it is also ranked 84th in the "Responsibility and Corporate Governance" category.

POSITION
IN 2015

MERCO Companies	100 companies with the best reputation	Zeltia/PharmaMar Group	60
MERCO Leaders	100 most prestigious companies	José María Fernández Sousa-Faro	90
MERCO Talent	This is a list of the 100 companies that best attract and retain talent	Zeltia/PharmaMar Group	84
MERCO Responsibility	100 most responsible companies	Zeltia/PharmaMar Group	84

The Zeltia/PharmaMar Group 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 37.6% of revenues on R&D — more than double that of the second-placed Spanish company R&D spending as a percentage of revenues (16.6%); the average among Spanish companies is 5.2%. Furthermore, the Group also ranks first in Spain in terms of R&D expenditure per employee: While other Spanish companies invested 13,047 euro per employee in 2015, the Zeltia/PharmaMar Group invested 84,700 euro in the same period. It ranks 330th 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. The Zeltia/PharmaMar Group ranks 1,196th in terms of R&D investment globally .

1. Source: The 2015 EU Industrial R&D Investment Scoreboard.

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 2015 Profarma Plan, the same result as in the previous thirteen 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, we highlight the appointment of Carmen Eibe Guijarro, Director of PharmaMar's Department of Project Coordination, as Second Vice-Chairman of the Spanish Association of Biotechnology Companies (ASEBIO).



COMMITMENT TO R&D





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 glaucoma. Responding to this reality, the PharmaMar Group has made a firm commitment to advance in researching drugs that can palliate and cure certain pathologies and improve the quality of life for patients and their families, in the area of oncology and ophthalmology.

The year 2015 brought positive developments for the R&D of our products and for oncology patients and people with eye diseases: Yondelis® was approved for commercialisation in the United States and Japan to treat soft tissue sarcoma. Additionally, PharmaMar and Sylentis have obtained very promising results with their clinical trials. This progress aroused considerable interest at the conferences where the results of our research were presented, and among foreign companies, with which major agreements are being reached, such as the contracts signed by PharmaMar with Specialised Therapeutics Australia (STA) and TTY Biopharm to market Aplidin® in Australia and New Zealand, and Taiwan, respectively.

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 synthesised 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 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 recognised in 2015 by the concession of support by a number of public agencies: Spain's Centro de Desarrollo Tecnológico Industrial (CDTI) gave three subsidies to PharmaMar and one to Genómica for an individual project. Additionally, Spain's Ministry of Economy and Competitiveness and the European Regional Development Fund (ERDF) financed PharmaMar in a new public-private partnership; the Group's research partnerships are detailed in the section on each company's R&D.

Internationally, PharmaMar and Sylentis are participating in projects under the EU's framework programme. As in previous years, during 2015 the Group tracked the new Horizon 2020 programme closely with a view to optimising the participation by Group companies in innovative collaboration projects between European countries. PharmaMar, Genómica, Sylentis and Zelnova Zeltia aim to contribute to, and lead, many projects, some of which were implemented in 2015 and will come to fruition in the coming years.

PHARMAMAR

CANCER

Cancer is a set of diseases characterised 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 tumours, 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 recognised, 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-tumour activity. Identifying new marine products with biological properties that differ from existing drugs is an essential route to finding molecules with novel action mechanisms that may improve cancer treatment. PharmaMar currently has four molecules in various phases of clinical development.

There is also a move towards personalised medicine based not just on the histological characteristics of the tumour but also on molecular criteria, which will allow a more rational treatment of patients in the future. Consequently, the current goal is for the treatment to be administered only to patients with tumours with a defined

molecular characteristic (e.g. the presence of a target which the antitumour compound attacks), as they would theoretically benefit most from the treatment. PharmaMar is working to identify such patients by applying pharmacogenomic techniques in its trials.

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



- **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.
- **MARINMAB** Consortium: PharmaMar heads this consortium, which includes the Institute for Research in Biomedicine (IRB Barcelona) and the Autonomous University of Madrid. The objective is to research and develop a new type of medicine—antibody-drug conjugates (ADC)—with a view to generating new anti-cancer molecules which are selective, effective and have fewer adverse effects. This project is investigating the ADC compound MI130004, which has shown activity against HER2-positive tumours.

PharmaMar is also involved in three joint projects under the European Union framework programme: “**MaCuMBA**: Marine Microorganisms: Cultivation Methods for Improving their Biotechnological Applications”, “**BLUEPHARMTRAIN**: Co-Cultivation of Sponge Cells & Microorganisms” and “**INMARE**: Industrial Applications of Marine Enzymes: Innovative screening and expression platforms to discover and use the functional protein diversity from the sea”.



In 2015, PharmaMar spent over 63.5 million euro on R&D, 21% more than in 2014.

Researching new pharmaceutical forms

PharmaMar's research work in drug discovery culminates with the isolation and synthesis of new chemical entities with strong anti-tumour potential. However, many of these molecules 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 tumour cells, or modify their toxicological profile.

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

This research has 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 trials on the following types of cancer: subtypes of soft tissue sarcoma, ovarian cancer, multiple myeloma, breast cancer, small cell lung cancer, head and neck cancer, neuroendocrine tumours, germ cell cancer, bile duct cancer, endometrial cancer, angioimmunoblastic T-cell lymphoma, cancer of unknown origin and the Ewing family of tumours.

PharmaMar is conducting clinical trials on Yondelis®, which has already been authorised for sale (these trials are supervised by the Medical Department); and also on Aplidin®, PM1183 and PM184, which have not yet been authorised for sale (these tests are conducted in 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-authorisation trials are under way which seek to optimise the drug's clinical use in the two indications for which it has marketing authorisation—soft tissue sarcoma, and platinum-sensitive ovarian cancer (in combination with pegylated liposomal doxorubicin—PLD)—and to identify new indications. The trials which commenced in 2015 are as follows:
 - GEICO-1402R: a retrospective trial with Yondelis® + PLD based on the data of patients with relapsed platinum-sensitive ovarian cancer patients.
 - GEIS-38: a retrospective trial with Yondelis® based on the data of patients with soft tissue sarcoma.
 - NIMES-ROC: an observational trial with Yondelis® + PLD based on the data with relapsed platinum-sensitive ovarian cancer patients.
 - TRANSITION-1: a Phase II trial with Yondelis® in patients with relapsed ovarian cancer who are partly sensitive to platinum.
 - TARMIC: Phase I/II trial that explores the combination of Yondelis® with metronomic doses of cyclophosphamide in patients with advanced soft tissue sarcoma.
 - PR Trab-PT: evaluates the reintroduction of platinum-based treatment after treatment with Yondelis® + PLD in platinum-resistant ovarian cancer patients.
 - EORTC-1320-BTG (meningioma trial): assesses the efficacy of Yondelis® in patients with high-grade meningioma.
- **Aplidin®:** recruitment for the pivotal trial with Aplidin® in combination with dexamethasone in patients with multiple myeloma concluded in 2015. Once patient tracking for the time established in the protocol had concluded, in view of the positive outcome, a registration dossier will be presented in the fourth quarter of 2016.

The dose for the combination of Aplidin®+bortezomib has been defined. The trial was conducted on patients with multiple myeloma with a view to allowing the use of Aplidin® at earlier stages of the disease.

Additionally, the mass balance trial, which is essential for obtaining information on the metabolism and elimination of Aplidin® for the registration dossier, concluded recruitment in 2015, as expected.

These three trials are part of the clinical development process, aimed at obtaining the necessary information to support the use of Aplidin® in various phases of treatment of multiple myeloma.

As for other indications, the protocol for the Phase II trial with Aplidin® in patients with peripheral angioimmunoblastic T-cell lymphoma has been completed and recruitment is expected to commence in the first half of 2016.

- **PM1183:** because of the excellent results of the Phase II clinical trial with PM1183 as monotherapy in platinum-resistant/refractory ovarian cancer patients, PharmaMar commenced a pivotal Phase III trial in patients with platinum-resistant ovarian cancer in 2015. This trial evaluates PM1183 as monotherapy vs. a control arm with topotecan or liposomal doxorubicin.

Recruitment continues on schedule for the Phase II clinical trial in advanced breast cancer patients with known BRCA 1 or 2 gene mutations, since significant anti-tumour activity was observed in this subgroup.

Also, following the excellent results obtained in the Phase I trial in combination with doxorubicin (70% response rate among patients with small-cell lung cancer undergoing second-line treatment), PharmaMar has designed an international registration trial for this indication.

As regards Phase I combination trials, recruitment was completed for the combinations with doxorubicin, capecitabine and paclitaxel with or without bevacizumab, and recruitment continues for the combination trial with cisplatin in a number of tumour types.

In 2015, recruitment commenced for a Phase II trial with PM1183 as monotherapy against 9 indications: small cell lung cancer, head and neck cancer, neuroendocrine tumours, germ cell cancer, bile duct cancer, breast cancer (BRCA gene mutations), endometrial cancer, cancer of unknown origin, and the Ewing family of tumours.

- **PM184:** the Phase I development trial with PM184 as monotherapy has concluded. The programme of combination trials continues with the current trial in combination with gemcitabine and another planned for 2016 with cisplatin.

The first Phase II protocol with this product for breast cancer was designed and presented to the regulators and ethics committees; authorisation was obtained to commence the trial early in 2016.

In 2015, PharmaMar decided to halt clinical development of compounds Zalypsis® and Irvalec® in order to optimise the company's financial resources and invest in more advanced products.

Communication with patients

The Clinical Oncology Department regularly receives queries and requests from interested patients, which are answered as quickly as possible. We reply to all patient queries, 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 or compassionate use programme, if the patient's specific case is appropriate and complies with the defined protocols.

Compassionate use programmes

All medicines must receive authorisation prior to being marketed. However, one option for patients with an illness for which there is no satisfactory therapeutic alternative available or who cannot participate in a clinical trial is a compassionate use programme, where they can be treated with a non-authorised medical product. Compassionate use programmes seek to provide patients with new treatments that are under development.

Until 2010, PharmaMar offered access to Yondelis® through a compassionate use programme in those European countries where the drug was not yet commercialised, at the request of the hospital or doctor and under a protocol established with the health authorities. PharmaMar does not currently have any compassionate use programmes for Yondelis®. Janssen—which holds the rights to market Yondelis® outside Europe and Japan—has three compassionate use programmes for ovarian cancer and soft tissue sarcoma covering territories where the drug is not yet approved:

- SAR-3002: Phase IIIb from second-line therapy for soft tissue sarcoma. A total of 3,253 patients had been treated under this programme by the end of 2015.
- INV-IND: this programme affords access to the drug for patients not admitted to the SAR-3002 programme. A total of 619 patients had been treated under this programme by the end of 2015.
- Named Patient Program (NPP): a total of 243 patients had been treated under this programme by the end of 2015.

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

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.

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.

As for new quality certifications requested in 2015, PharmaMar applied to the AEMPS for an amendment of its application as a laboratory in order to expand its refrigerated product storage capacity and include a new finished product packaging area at its facilities in Colmenar Viejo, Madrid. The AEMPS approved the request and modified PharmaMar's laboratory authorisation number 4012E.

Also in 2015, the FDA inspected the process of producing trabectedin, the active ingredient of Yondelis®, at PharmaMar's facilities. The inspection pursued two goals: a routine GMP inspection, and a pre-approval inspection as a result of the presentation, by our partner Janssen Pharmaceuticals, of a dossier requesting approval in the US to commercialise Yondelis® for treating soft tissue sarcoma. The inspection involved a full audit of the six systems. Quality, Production, Equipment/Facilities, Materials, Labelling/Packaging and Quality Control. Only one comment arose, and it was addressed properly and within the deadline. Accordingly, PharmaMar retains its FDA certification as an authorised manufacturer of active ingredients.

Also, as a result of the presentation by our partner, Taiho Pharmaceutical, of an application to commercialise Yondelis® for treating soft tissue sarcoma, in 2015 the Japanese regulator conducted a documentary inspection of the quality system,

facilities and equipment, and manufacturing process for trabectedin, with entirely satisfactory results.

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

Cooperation with other bodies

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

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

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

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

Pharmacovigilance

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

During 2015, there was an incident with one of PharmaMar's products:

On 31 March 2015, via its distributor, IDIS Limited, PharmaMar received a complaint from Clinique Saint-Joseph in Liège, Belgium, due to the presence of black particles in a vial of Yondelis® 0.25mg that were visible at the time it was reconstituted. The complaint referred to bulk batch 14F05 of Yondelis® 0.25mg, manufactured in 2014 by Belgian company Cenexi Thissen Laboratories, to which PharmaMar had outsourced the production of Yondelis®.

In compliance with European regulations on responding to possible quality defects in medicines, PharmaMar immediately notified the EMA and the AEMPS and the latter, based on a proposal by PharmaMar, ordered a recall of all batches of Yondelis® 0.25mg made up from the aforementioned bulk batch 14F05 in order to minimise the risk to patients.

All the vials in question were recalled successfully (except for those whose destruction on-site was authorised by the authorities), and the health authorities in the countries in question were notified. The recalled vials that were returned to PharmaMar were destroyed by an authorised firm, which issued a certificate of destruction.

An investigation at Cenexi Thissen Laboratories revealed that the black particles visible in the vials to which the complaint referred were small fragments of plastic wrapping which were burned during the process of depyrogenation of the vials and were not removed during the subsequent washing phase. Cenexi Thissen Laboratories has already implemented the corrective actions designed to prevent a recurrence of this quality defect.

PharmaMar's Department of Pharmacovigilance and the authorities performed a meticulous investigation to identify all possible adverse effects or quality complaints arising from this quality defect. No adverse effects or additional complaints have been reported to date, either to PharmaMar or to the health authorities of the countries where the batches in question were distributed.

SYLENTIS

GLAUCOMA

Glaucoma is a group of eye disorders characterised 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.

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 coloured 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.

Research and development

Sylentis focuses its research on drugs obtained using interference RNA (RNAi) technology. The importance of this novel technique is evidenced by the fact that its discoverers, Andrew Fire and Craig Mello, were awarded the Nobel Prize for Medicine



in 2006. RNAi has revolutionised biology by making it possible to design and develop drugs from a totally new perspective.

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

The RNAi mechanism of action, 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 ischaemia, neurodegenerative diseases and dementia.
- Basic research: formulation and chemical modification of molecular structures to increase stability and efficacy in models *in vivo*.
- Formulation of RNAi products for oral administration.



In 2015, the ophthalmology area commenced a new line of research into drugs for treating diseases of the retina.

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

Among the numerous research and development projects being 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:

- **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 personalised treatment for eye surface regeneration. It will also develop personalised diagnostic systems to be able to apply the most appropriate treatment in each case.
- **TERET Consortium:** Sylentis heads this consortium, which includes 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 programme: “**NANOPILOT:** A Pilot Plant for the Production of Polymer-based Nanopharmaceuticals in Compliance with GMP” and “**NABBA:** Design and Development of Advanced Nanomedicines to Overcome Biological Barriers and to Treat Severe Diseases”

Clinical trials

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

The company's most advanced compound is SYL040012 (bamosiran) in the form of ophthalmic drops to treat elevated intraocular pressure and glaucoma. Phase I and Ib clinical trials have been completed with this compound. The results obtained, in terms of both safety and efficacy, were very promising, with the result that clinical development continued with a Phase II multicentre international trial to demonstrate its efficacy in humans. This trial demonstrated excellent tolerance to the drug, both locally and systemically, as well as statistically significant efficacy of one of the evaluated doses. In 2015, Sylentis conducted a Phase IIb trial with bamosiran to treat glaucoma and ocular hypertension. This clinical trial, which aimed to identify the most effective dose, was performed in 21 hospitals in Spain, Estonia, Germany and the US, recruiting 180 patients. The results justify advancing this product to the next phase of development; accordingly, a Phase III clinical trial is currently being designed.

The company's second 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 hyperaemia 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.

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

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

Cooperation with other bodies

Sylentis has cooperation agreements with numerous public and private institutions in Spain and other countries so as to effectively transfer knowledge and resources and make progress with product research and development. It works with numerous universities and research centres as well as private contract research organisations to conduct its trials.





A close-up, slightly blurred underwater photograph of a coral reef. In the foreground, a large, textured, yellowish-brown coral structure dominates the view. To the left, a smaller, more colorful coral branch with white and pinkish polyps is visible. In the background, a diver in a blue wetsuit is partially visible, swimming towards the right. The water is clear and blue. A teal-colored horizontal bar is overlaid on the right side of the image, containing the word 'CUSTOMERS' in white capital letters.

CUSTOMERS



CUSTOMERS

The PharmaMar Group's current customers are the users of Zelnova Zeltia, 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 PharmaMar Group, and 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 growth strategy, in 2015 PharmaMar opened commercial subsidiaries in the UK and Belgium, in addition to those it already had in France, Germany, Switzerland, Italy and a hub in the United States (PharmaMar); Genómica has a subsidiary in Sweden and a sales office in China. All of these are markets with high growth potential where the Group seeks to increase its sales.

ZELNOVA ZELTIA

Zelnova Zeltia has approximately 989 direct customers.

Zelnova Zeltia's products are air fresheners, domestic insecticides and cleaning products, which are marketed via two divisions: household products (insecticides, air fresheners, odour neutralisers, 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, detection of mutations in the genes associated with the response to anti-tumour therapy, and polymorphisms associated with bone metabolism disorders), genetic identification analysis (paternity tests, genetic fingerprinting and filiation), and technology transfer (turnkey installation of genetic fingerprint labs).

PHARMAMAR

PharmaMar has approximately 1,050 customers.

Following the launch of Yondelis® in Europe in 2007 for soft tissue sarcoma and in 2009 for ovarian cancer, the company's customers are hospitals and clinics in Europe which are served by PharmaMar's own sales network or its sales and distribution partners. 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 channelled 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 website 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 PharmaMar, contact with the customer (healthcare professional) is provided 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, calls with clinical queries from patients are channelled 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, labelling, manuals and marketing) and, where necessary, product literature and labels are corrected on the basis of customer feedback.

The PharmaMar scientific information and promotional material provided to healthcare professionals is produced in several languages and undergoes a rigorous approval process that conforms to best practices in various 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 channelled through the Commercial Department which, based on the nature and magnitude of the issue, refers it, with a full dossier, to the departments it considers appropriate, in order for the problem to be analysed, a report issued and a solution proposed. Once the report has been drafted, it is remitted to the Commercial Department, which decides on the appropriate commercial solution to the problem raised by the customer, 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 (Zelnova Zeltia), 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: Zelnova Zeltia 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 specialised, their advertising is targeted very directly at customers to subtly emphasise the 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 labelling of hazardous products and with the regulations limiting emissions of volatile organic compounds.

There were no incidents in 2015 stemming from non-compliance with legal or internal regulations regarding product information and labelling, 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 2015, except one incident at PharmaMar involving a batch of Yondelis®, which is comprehensively explained in the section on Commitment to R&D.

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

Zelnova Zeltia, 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. Zelnova Zeltia also has the Higher Level certification under the IFS HPC standard.



IFS HPC CERTIFICATION



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


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

It is an internationally-recognised standard which ensures that IFS-certified companies deliver products that adhere to defined specifications with a view to continuously improving product safety and quality. 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; Zelnova Zeltia'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, Walmart, 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 Microbiológico, 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 Paediatric Association (AEP) for Xylazel Aire Sano paint for children's environments. 

Genómica has the following quality certificates:

- EC Conformity certificate for the following products CLART® HPV, CLART® Pneumo Vir, CLART® ENTHERPEX, CLART® MetaBone, CLART® SeptiBac, CLART® EnteroBac, CLART® CMA and 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.
- CMDCAS Certification, issued by TÜV Rheinland North America, for sales in Canada with the following scope: design, development and manufacture of *in vitro* diagnostic kits to detect metabolic disorders, tumour genotyping and infectious diseases.
- ISO 9001:2008 certification by TÜV Rheinland.



New product research and development

ZELNOVA ZELTIA

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

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

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.

The company worked on the following lines in 2015:

- Modification of formulae to adapt to new legislation on the classification and labelling of hazardous products: major changes in some formulae with biocides used to conserve dry film or changes in other very hazardous substances, such as cobalt siccatives.
- Launch of two innovative products in the Oxirite line: Oxirite Quality and Oxirite Xtrem Brillante.
- 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 chalky finish paint.
- 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.

THE XYLAZEL AIRE SANO PRODUCT LINE

The Xylazel Aire Sano product line includes paint for allergy and asthma sufferers, healthcare environments, children's environments and healthy households. This is a unique line of paints in Spain.

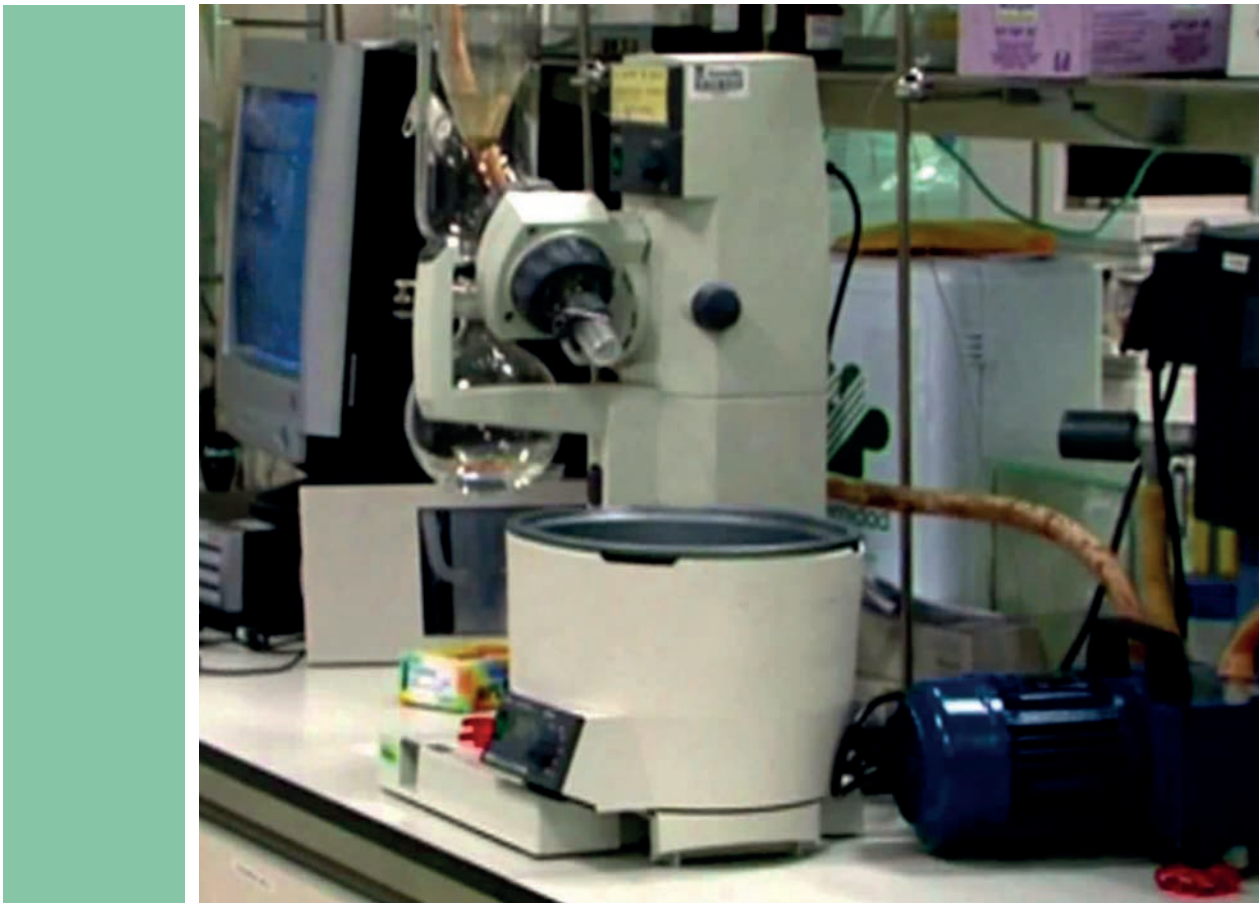
- Xylazel Aire Sano paint suitable for persons with allergies or asthma is an ecological paint with no substances that are detrimental to people's health or the environment. Once dry, the painted surface does not emit volatile compounds which can have a significant sensitising or irritating effect. As a result, people who come into contact with this paint are assured that they will not be exposed to substances that may aggravate the symptoms of respiratory illness, such as allergies or asthma.
- Xylazel Aire Sano paint for healthcare environments helps avoid the growth of bacteria and fungi on painted walls in hospitals. This helps improve the health and hygiene conditions required at hospitals, and prevents a large number of infections that might otherwise develop in such an environment. It is a high-quality paint that can withstand washing and common disinfectants, and contains encapsulated silver ions to avoid the proliferation of bacteria on the painted surface.
- Xylazel Aire Sano paint for children's environments is a special paint which is very low in VOC compounds and hazardous emissions. Having cleaner environments for children helps reduce respiratory illnesses.
- Xylazel Aire Sano-Hogares Saludables (healthy households) is an ecological water-based paint for indoor surfaces. It is very low in volatile organic compounds and hazardous emissions.



GENÓMICA

Genómica worked on the following lines in 2015:

- The microbiology area successfully optimised a lyophilisation process for CLART® HPV-2 for its subsequent implementation by the Technical Department.
- In oncology, a product for *in vitro* diagnosis based on CLART® technology was launched: CLART® CMA BRAF.MEK1.AKT1. This product detects the presence of the most common mutations of the BRAF gene and mutations of the MEK1 and AKT1 genes, which are involved in cell proliferation and the inhibition of apoptosis and are linked to melanoma. The molecular diagnosis of these mutations would enable patients carrying mutated genes to be treated with BRAF inhibitors.
- Also in oncology, Genómica has implemented a project to improve CLART® technology, adapting its use to liquid biopsies (detection of circulating tumour DNA mutations). The protocol enables this type of liquid sample to be analysed using Genómica's various oncological applications.
- Lastly, Genómica has implemented a strict protocol to develop massive sequencing technology to analyse individual gene panels in the coding region, selected a la carte or already established in the market, and thereby provide evidence of the marker's clinical utility. This sequencing is performed using AmpliSeq technology, which requires a small amount of DNA, offering optimal performance and excellent quality (99.5% accuracy, 5% detection sensitivity).



GENÓMICA AND PERSONALISED MEDICINE

Rather than implementing standard treatments, personalised 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 personalised medicine. Evidence of this are the four products it has launched that detect specific mutations, the presence or absence of which allows a suitable treatment to be chosen. These products are CLART® CMA KRAS.BRAF.PI3K and CLART® CMA NRAS.iKRAS for metastatic colorectal cancer, and CLART® CMA EGFR for non-small cell lung cancer, plus the new CLART® CMA BRAF.MEK1.AKT1 for melanoma.

As part of its commitment to researching this area, the company has reached a cooperation agreement with *Fundación para la Excelencia y Calidad en la Oncología* (ECO), a platform comprising the heads of the medical oncology departments of the leading Spanish hospitals. This agreement is aimed at improving cancer treatment by fostering research projects and optimising clinical management in oncology. The partnership seeks to strengthen Genómica's activity in order to yield reliable molecular diagnostic tools that are optimised 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.





The background of the page is a close-up photograph of a sea anemone. The tentacles are long, thin, and translucent, with a yellowish-orange hue. A small, brown, segmented creature, possibly a hermit crab, is visible on one of the tentacles. A semi-transparent teal rectangle is positioned in the upper right corner of the image.

SUPPLIERS

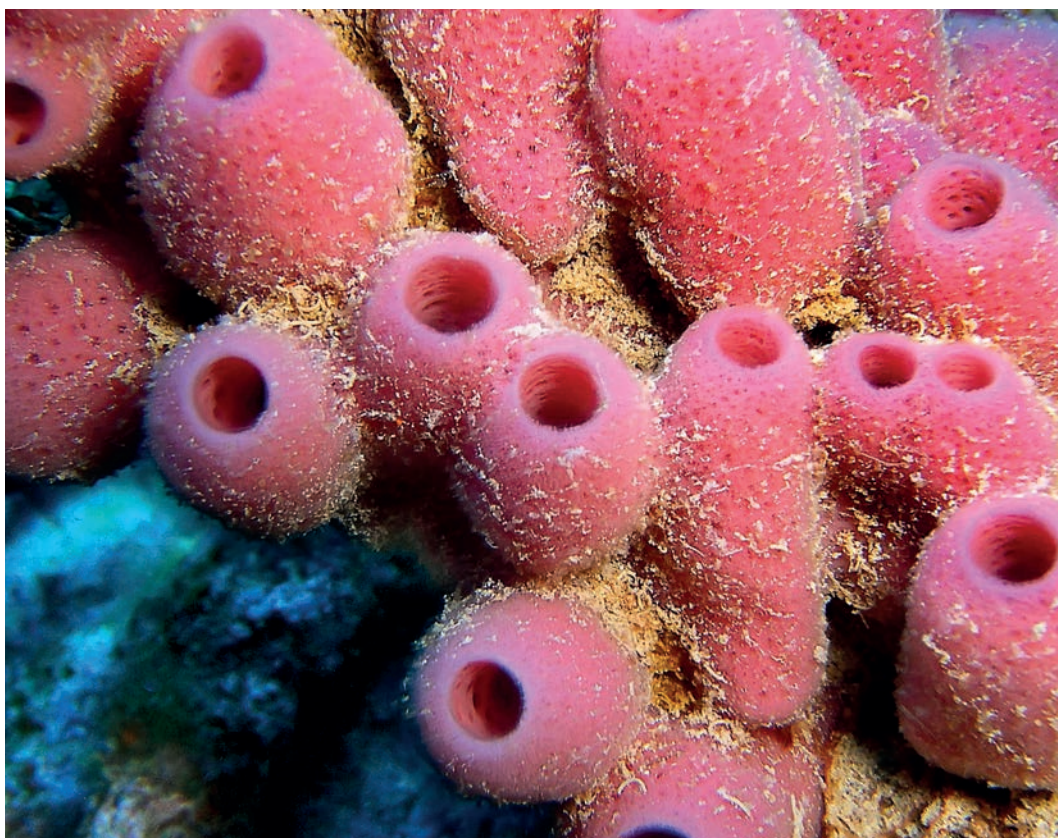


SUPPLIERS

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 organisation.

Suppliers are selected on the basis of compliance with quality standards, reputation in the market, suitability to our needs, and an excellent price-quality ratio. That is to say, we seek suppliers that offer the best combination of quality, service and price using an objective, transparent selection process that takes account of sustainable procurement criteria. Our companies apply purchasing processes certified to ISO standards. There is no discrimination against suppliers for reasons of race, creed, nationality or gender. We use questionnaires to ensure that our services suppliers have the same anti-discrimination values with regard to their 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 organisation. All this information is evaluated by a Supplier Management Committee, which issues a recommendation as to whether or not the supplier is appropriate. Approved suppliers are subject to a system of continuous improvement and scoring based on the number of quality incidents and other factors such as 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, authorisation 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.

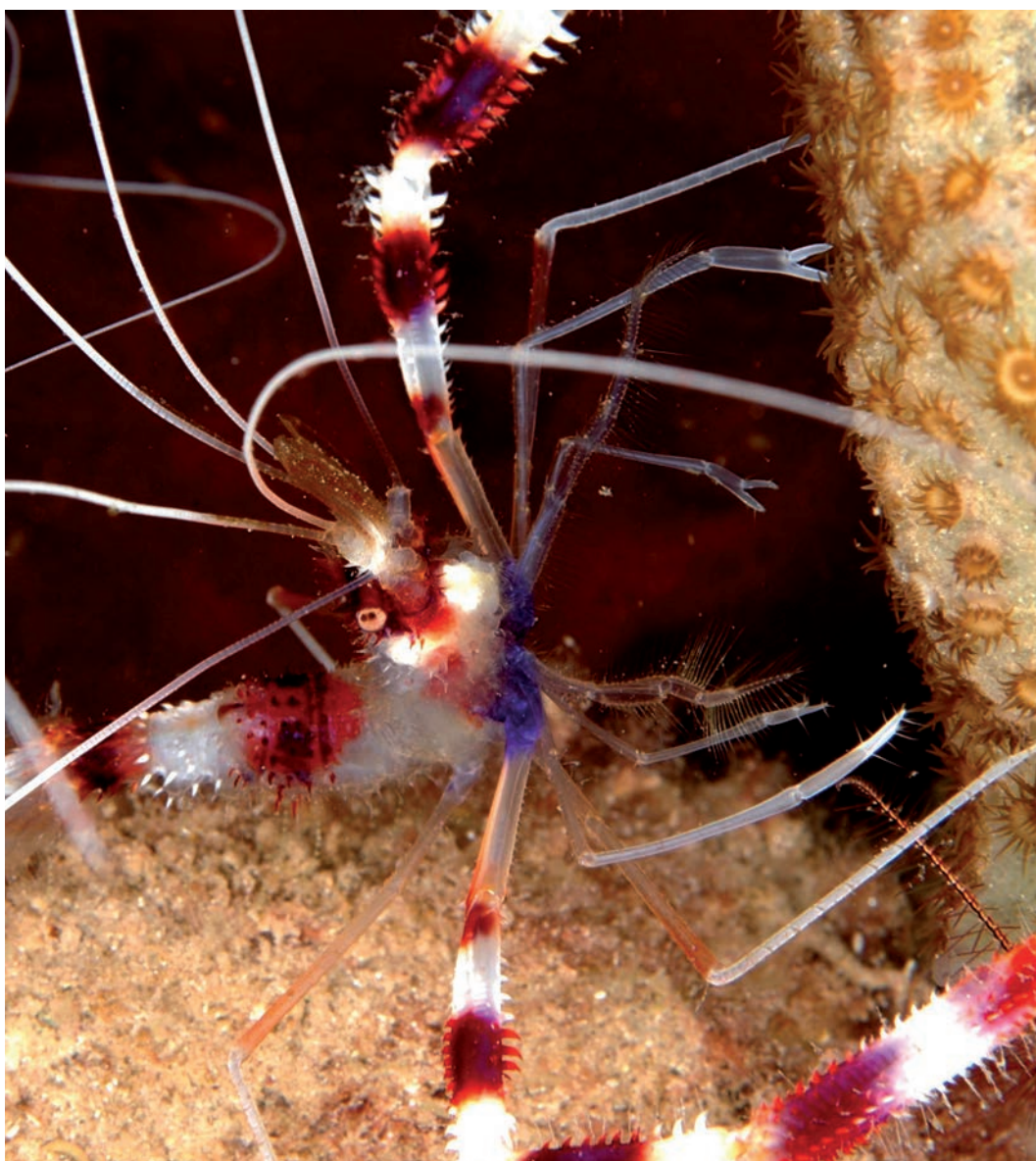
We maintain close relations with our suppliers via meetings at trade fairs, visits, telephone calls, mail, fax, e-mail and the web.



Company	PharmaMar	Genómica	Sylentis	Xylazel	Zelnova Zeltia
No. of suppliers	444	167	454	120	126
Of which:					
Spanish	375	137	352	97	96
Rest of Europe	53	27	63	23	26
Developing countries	--	--	--	--	--
Rest of the world	16	3	39	--	4

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

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





EMPLOYEES





EMPLOYEES

At the end of 2015, the PharmaMar Group, including subsidiaries outside Spain, had 700 employees. We are fortunate to have a valuable team which brings us closer to our goal of being the best in our fields of endeavour and makes our achievements possible, such as our high market share, ongoing progress with research and the commercialisation of our first drug: Yondelis®.

We are proud of the loyalty and trust of the employees at our chemical companies—Xylazel and Zelnova Zeltia—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 2015 and 2014

Data as of 31 December for Spanish subsidiaries.

Chemical Companies

Employees in Spain	Xylazel		Zelnova Zeltia	
	2015	2014	2015	2014
No. of employees	97	94	90	90
Average age (years)	47	47	47	46
Average length of service (years)	16	16	17	15
No. of employees from other countries	2	1	0	1
No. of employees with disabilities	1	2	2	3
Breakdown by gender				
% of men in total work force	68	70	63	63
% of women in total work force	32	30	37	37
% of men in management	100	100	80	80
% of women in management	0	0	20	20
Academic qualifications				
% Graduates & PhDs	24	18	17	17
Breakdown of total work force by area				
Administration	22	23	20	20
Commercial & Marketing	35	34	16	16
R&D/Quality/Control	5	5	11	11
Production & Distribution	33	30	41	41
General services	2	2	2	2

Biopharmaceutical companies

Employees in Spain	PharmaMar		Genómica		Sylentis	
	2015	2014	2015	2014	2015	2014
No. of employees	349*	302	64	53	19	17
Average age (years)	43	42	37	37	38	36
Average length of service (years)	8	8	6	7	6	7
No. of employees from other countries	19	17	4	2	2	2
No. of employees with disabilities	5	5	1	1	0	0
Breakdown by gender						
% of men in total work force	41	39	32	26	21	12
% of women in total work force	59	61	68	74	79	88
% of men in management	67	55	40	40	5	0
% of women in management	33	45	60	60	95	100
Academic qualifications						
% Graduates	49	47	38	43	47	53
% PhDs	17	21	23	19	37	35
Breakdown of total work force by area						
Administration	59	41	9	7	2	1
Commercial & Marketing	35	31	13	11	0	0
R&D/Quality/Control	222	194	20	16	17	15
Production & Distribution	23	23	22	19	0	1
General services	10	13	0	0	0	0

*Includes employees of Zeltia, the group's former holding company.

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

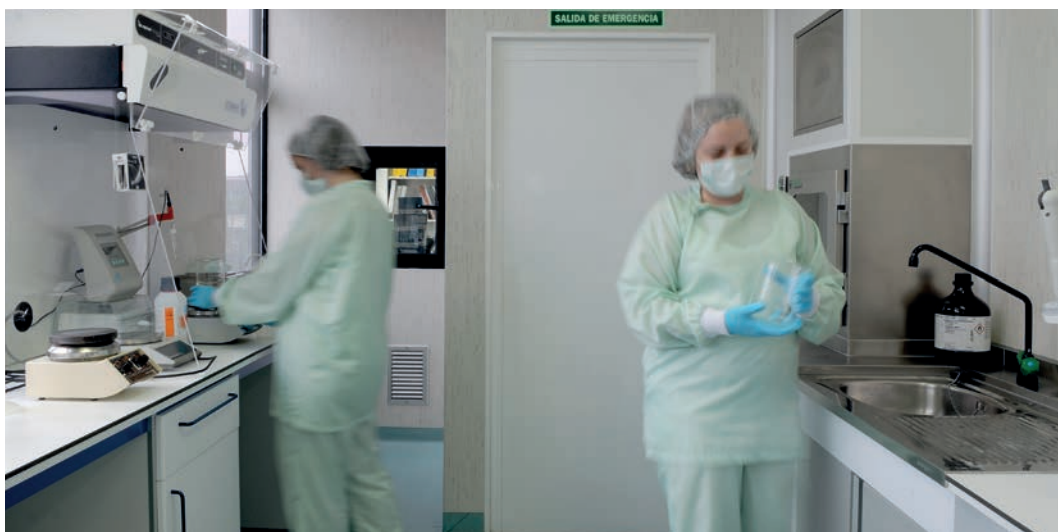
Employment contracts, collective agreements and remuneration

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

Pharma Mar, S.A. has implemented an Equality Plan which seeks to ensure equality between men and women. There is a Standing Committee on Equality comprising



equal numbers of representatives of the company and workers. The committee's purpose is to organise information and awareness campaigns for the workforce and to implement and monitor the Equality Plan. No complaints of discrimination were received and the Group is not aware of any incident in this connection arising in the Group companies.

In order to enhance employee commitment and motivation, many employees receive variable remuneration or a bonus based on targets agreed upon with their supervisor 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 labour matters are: Gonzalo Durán (Zelnova Zeltia), 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 2015. A total of 85 persons were hired on indefinite contracts by Group companies during the year, as follows: 73 at PharmaMar (43 in Spain and 30 in other countries), 5 at Genómica, 2 at Sylentis, 2 at Zelnova Zeltia and 3 at Xylazel.

Incentive plan

In accordance with decision adopted by the Shareholders' Meeting on 27 May 2014, the Board of Directors decided to apply a Stock Ownership Plan under which certain Group executives and employees (excluding members of the Board of Directors) received shares of the company in 2014, free of charge, as a function of the degree of attainment of their 2014 targets.

This Stock Ownership Plan has a double objective: to reward employees and executives whose performance in 2014 was satisfactory, and to incentivate beneficiaries to stay in the Group.

PROMOTING YOUTH EMPLOYMENT

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

In 2015, the Group had 42 interns, four of whom were hired following graduation.

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 draw up training plans that determine staff training needs, ensure that nobody performs a task that requires specific training without having received it, and ensure that staff receive the appropriate initial training for the specific tasks entrusted to them. Training plans include both internal and external training (Master's degrees, courses, conferences, seminars, etc.). In 2015, the PharmaMar Group invested over 627,000 euro in this issue. Employees also participated in many free training activities.

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

		GENOMICA		SYLENTIS		PHARMAMAR		ZELNOVA ZELTIA		XYLAZEL	
		Hours	€	Hours	€	Hours	€	Hours	€	Hours	€
Science training	Conference	42	4,836	394	20,899	2,636					
	Courses			292	6,826	713	400,615				
	Others					1,732					
Management training						354	15,411				
Administrative training						566	9,288			108	266
Languages (English, French, German)		861	12,781			12,069	53,872				
Other types of training						6,100	93,765	564	3,635	204	5,208

Benefits and perks

The Group companies try, as far as possible, to help employees combine work and family life. Mothers have the option of reducing their shifts and 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 Zelnova Zeltia and Xylazel provide study grants for employees' children, an in-house doctor and nurse, a social worker and fitted protective clothing.

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

Improvements are made to facilities each year in an attempt to enhance the working environment. Buildings in the Oncology unit (PharmaMar) and Zelnova Zeltia 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 channelled via e-mail, the intranet, regular meetings, and notice boards.

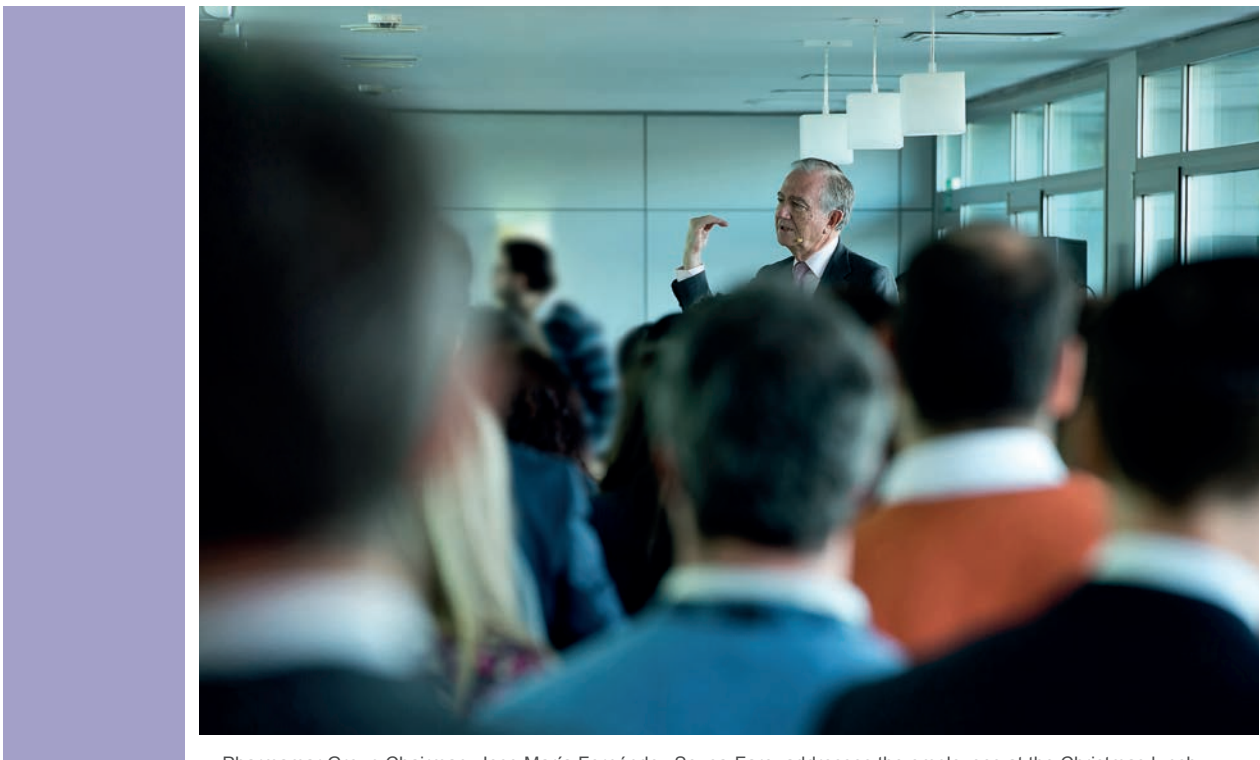
Employees have easy access to management. There is a structured communications plan involving regular meetings between the various echelons (division heads, managers and department heads) to track and manage the objectives of the company and of each individual area and project.

Informal meetings are held frequently with teams from different areas to report on project progress. At Genómica, an employee gives a lecture 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 and Sylentis conduct 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 programmes that conform to current



Pharmamar Group Chairman, Jose María Fernández Sousa-Faro, addresses the employees at the Christmas lunch.

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 Pharmamar Group in charge of Health and Safety issues are Pedro Torrens (Zelnova Zeltia), 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 2015:

	Number	Days lost
Due to illness	86	3,336
Accidents with medical leave	7	179
Accidents without medical leave	5	---
Accidents on the way to/from work	2	30

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

PharmaMar is certified to the OHSAS 18001 Occupational Health and Safety Management System standard by Lloyd's Register Quality Assurance. This international standard confirms the company's commitment to the health and safety of its workers; in this context, the Pharmamar 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	10.31	35.55	6.38	13.13
Frequency index				
No. of accidents with lost days per 1,000,000 hours worked	5.88	20.29	3.64	7.50
Severity index				
No. of lost days per 1,000 hours worked	0.31	0.32	0.03	0.09

In 2015, both PharmaMar and Xylazel received awards for their commitment to workplace safety: PharmaMar received the BONUS diploma for its commitment to reducing industrial accidents from Fraternidad Muprespa, and Xylazel was named the "Safest Company in Galicia" (in the category of undertakings with under 250 employees) by the *Asociación Gallega de Organismos de Control Autorizados* (ASGOCA).

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 labour legislation, the Group's medical check-up includes blood and urine analysis, a blood pressure measurement, and nutritional counselling. The larger subsidiaries also offer an eye test and other specific tests such as PSA, electrocardiograms, etc.; they also have a company nurse to monitor employee health. In 2015, PharmaMar offered free flu vaccination to its employees.

MORE THAN 25 YEARS WITH US

The PharmaMar Group has 72 employees who have been working at its subsidiaries for more than 25 years. The group is very proud of their loyalty. We would like to thank them for their devotion and trust in us with this small tribute. Without them, the PharmaMar Group would not be what it is today, and we would like to recognise the excellent work they do every single day. Thank you!

I started my career at Xylazel in 1975, when the company was founded. I worked in Sales for ten years, and then management entrusted me with the Human Resources Department. Eight years ago, in a restructuring of the departments, I became Director of the Human Resources and Administration Department.

In these 40 years, I have enjoyed a fruitful career. I am proud to belong to the Company and the Group, which have given me the opportunity to grow and develop personally and professionally, working with a brilliant team of professionals at all levels.

Mercedes Rodríguez,
Director of Human Resources at Xylazel

Some of our longest-serving employees are:

Pedro Fernández Puentes	Juan Ramón Lemos Herrero
Isabel Fernández Hoyas	Alfredo Novoa Gallego
Juan Carlos Villalón Gómez	M ^a Mercedes Rodríguez González
María Luisa de Francia Caballero	Jorge Ferreira Ramilo
Serafín Rodríguez Ramos	Francisca Vaquerizo Soriano
Jesús García Sánchez	Antonio Loureiro Pintos
Fernando de la Calle Verdú	M ^a Luisa Lourido Álvarez
Rosa Sánchez González	M ^a Isabel Da Cruz Álvarez
Amor Guerra González	Marian Pujol Gómez
Antonio Sevilla Becerra	José Muñoz Collado
Fernando López Sánchez-Pastor	Lucio Salgado Romero
María Jesus Blanco Giráldez	Rene Petit Martínez
Ramón Fernández Giráldez	Carlos Manuel Rego Fernandes
Aurora Dasilva Ferreira	Carles Oliver Legalina
José Ramón Barbosa Pérez	Alberto Pereiro Lueiro
Ángeles Ramilo Domínguez	Antonio Vega Villar
María Luz Gabeiras Castro	Emiliano Lorenzo Leirós
Jesusa Lorenzo Maceira	M ^a José Pujol Gómez
Carmen Martínez Lorenzo	Francisco Javier González Fernández
Juan Enrique Carrera Barbosa	José Ramón Álvarez Sacristán
Gonzalo Durán Pastor	Silvana Dieguez Romariz
Jaime Boubeta Núñez	José María Moreno Campon
Ana Maria Herranz Herranz	Andrés Peral Jaldo
José Galofre Virgili	Darius Prunera Trave
Francisco Gómez Arenas	Juan Gutierrez Balongo
Jesús Lorenzo Silva	M ^a Carmen Villar Rivera
Anuncia Pereiro Lorenzo	Agustín Casas García

Although people only call Maintenance when something stops working, my colleagues and I work to make sure that all the facility's services work smoothly. There are four of us, and one is on call each week. For example, I had two call-outs last Sunday. One was at 8 am and the other at 4 pm. But when you walk out the door with everything running smoothly, that's a great feeling!.

José María Moreno Campon,
Maintenance Technician at PharmaMar



SHAREHOLDERS





SHAREHOLDERS

Around 80,000 investors have placed their trust in PharmaMar, and we owe them a debt of value-creation and responsibility.

At 31 December 2015, PharmaMar's market capitalisation was 557 million euro. Its shares are traded on the four Spanish stock exchanges (Madrid, Bilbao, Barcelona and Valencia).

Number of shares and share performance

As of 31 December 2015, the Company's capital stock amounted to 11,110,244.35 euro, represented by 222,204,887 shares with a par value of 0.05 euro each.

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

In 2015, PharmaMar's share price fluctuated between 2.51 and 4.32 euro (closing prices), ending the year at 2.51 euro.

In 2015, trading in PharmaMar stock totalled 711 million euro, with an average of 754,957 shares changing hands each day; trading peaked in February and reached a low in December.

The markets on both sides of the Atlantic were dominated by volatility in 2015. After exceeding 11,600 points in the first half of the year, the IBEX-35 index ended the year at 9,544.2 points, a 7.15% decline with respect to 2014, and a departure from the positive trend of the previous two years.

There were several predominant macroeconomic issues during 2015. The year began under the shadow of the Greek economic crisis and the uncertainty as to whether Greece would be able to meet Europe's demands with regard to debt repayment.

However, global growth continued to be the main source of uncertainty in the markets. Market corrections after the summer were driven by doubts about the Chinese economy. There was also a severe correction in commodity markets, particularly a decline in crude oil prices, driven mainly by a demand crisis.

The markets also focused on central banks in 2015. Accordingly, while the US Federal Reserve forewarned of a change in its monetary policy, the ECB expanded its asset purchase programme in view of the European economy's weakness.

Crude oil was the main source of concern at year-end, having reached an 11-year low, with the result that the IBEX-35 closed in negative territory.

During the year, Zeltia was merged into PharmaMar, reflecting the company's decision to focus strategically on its main business: oncology. The merger was successfully completed on 2 November, and PharmaMar's shares commenced trading on that date. PharmaMar's share performance was dominated by the prevailing market volatility. After reaching a 5-year high in October, the stock experienced a sharp correction unrelated to its robust position or good prospects for the coming years.

Notable events in the year included progress with clinical trials with PM1183, its most important strategic product, and Yondelis®. Early in 2015, Taiho Pharmaceutical presented the registration dossier to seek authorisation to commercialise Yondelis® in Japan for treating soft tissue sarcoma. As for clinical development, a Phase III trial with PM1183 in platinum-resistant ovarian cancer commenced mid-year, and the good clinical results presented at ASCO were well received by the stock market. The share reached a 5-year high: 4.3 euro.

On 23 October, the FDA (Food and Drug Administration) finally approved commercialisation of Yondelis® for treating soft tissue sarcoma in the US. This is the first oncology drug from a Spanish company to achieve FDA approval. The share responded very well to the news, rising to over 4 euro.

Breakdown 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: José M^a Fernández Sousa-Faro owns 11% (4.6% through Montserrat Andrade Detrell), Rosp Corunna Participaciones Empresariales, S.L. owns 5%, and 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:

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

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

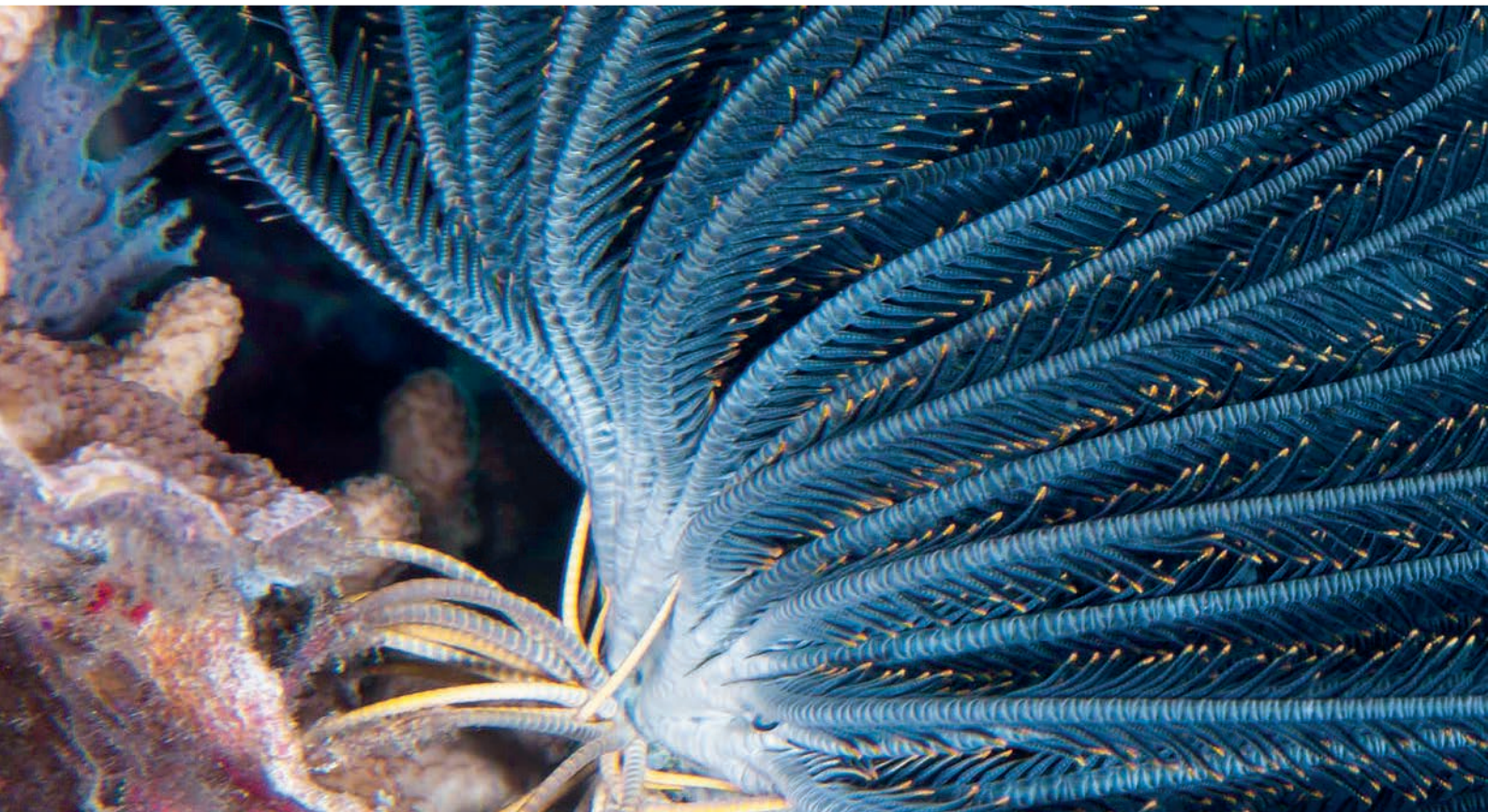
All relevant general information about PharmaMar is kept up to date and is available to shareholders and the general public on the company's website, www.pharmamar.com:

- Regulatory disclosures to the CNMV, press releases, and news items about the PharmaMar Group.
- Annual and quarterly financial statements.
- Corporate Bylaws, Annual Report on Corporate Governance and Annual Director Remuneration Report.
- Information about the Board of Directors: Regulation, committees and composition.
- Information about the Shareholders' Meeting: notice and agenda, motions and documentation circulated prior to the meeting, quorum and decisions adopted, etc.
- Securities Market Commission (CNMV) Internal Code of Conduct.
- General information about the main Group companies, with links to their respective web sites.

The website 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







ENVIRONMENT





ENVIRONMENT

Our companies strive to protect the environment, not just in conducting their activities but also in developing 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 synthesised. 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. These two certified companies account for 70% of PharmaMar Group's revenues and 64% of its employees.

In 2015, none of our companies had material environmental accidents, fines or lawsuits. 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, or 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 materials, all of which are managed by specialised companies. Additionally, the production staff receive special training.

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 environmental policies of the Group's largest subsidiaries, PharmaMar, Zelnova Zeltia 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's oncology business is certified to the ISO 14001 environmental management standard. This internationally-recognised accreditation evidences PharmaMar's commitment to the environment and its decision to implement policies and actions that encourage continuous improvement and the 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 Rio 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 Resource (UICN), 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 minimising human interaction with the ecosystem.

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

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

In July 2015, PharmaMar took part in the fifth edition of the Green Meetings ("Encuentros Verdes"), organised by EFEverde and Fundación Biodiversidad. Participants at this forum debated the relationship between biodiversity and health, the contributions of biological diversity to the world of medicine and research into new drugs to combat diseases. José María Fernández Sousa-Faro, director of the Group and, at the time, Vice-Chairman of ASEBIO, and the head of R&D at PharmaMar, Carmen Cuevas, attended the meeting.

Furthermore, as part of its commitment to protect and conserve the environment, in 2015 PharmaMar sponsored the "Environment Conference" at Colmenar Viejo, within the framework of the European Hercules Project and the Colmenar-Antarctic project.

The Hercules Project is a research project aimed at identifying local landscape management needs and providing a forum for debate and the pooling of project findings. During the working seminars, landscapes in the Colmenar Viejo area were

studied, various stakeholders presented their point of view and actions were proposed to better conserve the natural environment.

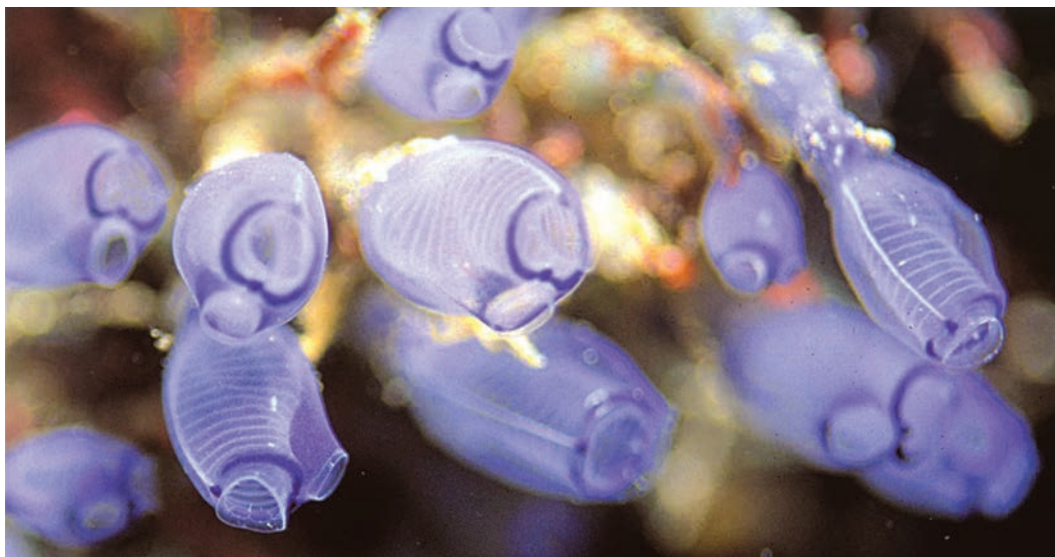
The Colmenar-Antarctic project consisted of conducting an expedition to the Antarctic to complete a mission with a dual purpose: ecological and human. The mission was to symbolically and environmentally twin the town of Colmenar Viejo with the Spanish Antarctic station “Gabriel de Castilla”. The mission was achieved by exchanging environmental projects in the two locations. Persons in charge of the mission won the photo essay prize in the 2015 edition of the Colmenar Viejo Environmental Photography Competition, and the Colmenar Viejo 2015 Environmental Citizen Award.

SPANISH GREEN GROWTH GROUP

In 2014, Zeltia (now PharmaMar) Group joined the Spanish Green Growth Group.

Prior to the Paris Climate Summit in December 2015, the Spanish Green Growth Group issued a statement, which PharmaMar Group signed, setting out the following principles:

- The burden of reducing emissions must be shared among all countries, but in a balanced way, based on their track record in generating the problem. All economic sectors must also contribute their fair share of efforts.
- It is essential to secure commitments to limit global warming to 2° C.
- It is necessary to progress towards models for carbon pricing, so as to develop a low-carbon economy.
- RDI must be supported in order to find technological solutions that facilitate compliance with emissions reduction goals.



BIODIVERSITY PACT

Respect for, and the promotion of, biodiversity are the guiding principles of PharmaMar Group's activities.

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

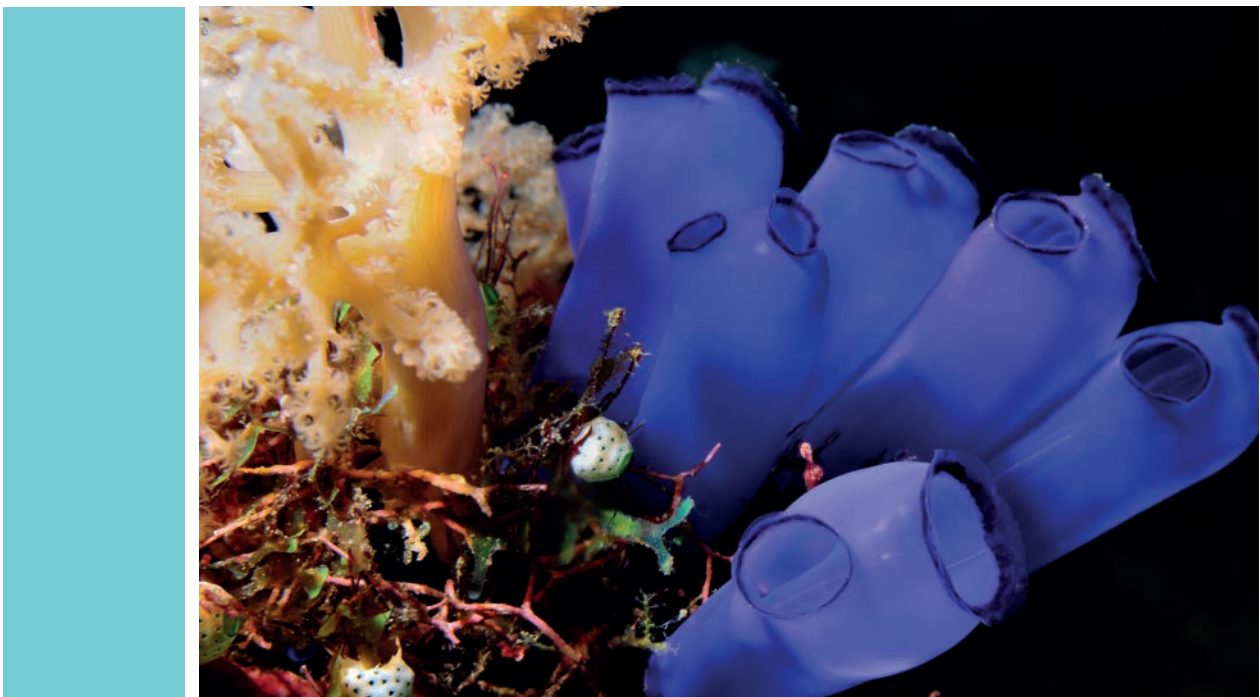
PharmaMar has discovered hitherto unknown marine organisms on its expeditions. For example, the company discovered a new species of deep-sea sponge, *Streptomyces pharmamarensis*, which was isolated from marine sediment and classified by PharmaMar researchers².

Embodying this commitment to biodiversity, PharmaMar has signed the Biodiversity Pact, which, in cooperation with business, aims to promote economic development that is compatible with biodiversity conservation.

As a result, PharmaMar ratifies its practice to date: preservation of biodiversity, sustainable use of their components, and fair and equitable sharing of benefits arising from the appropriate use of genetic resources.

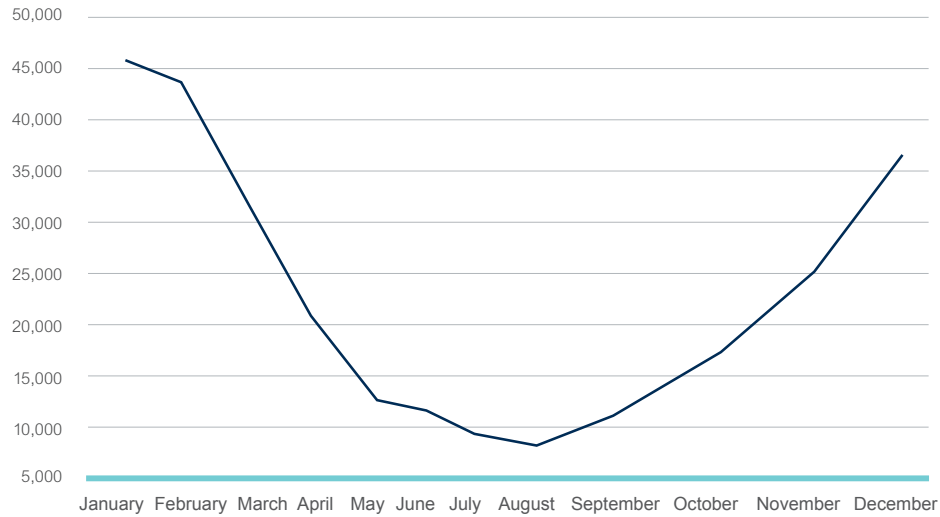
The Company also supports Spain's ratification of the Nagoya Protocol on access to genetic resources and the fair and equitable sharing of benefits arising from their utilisation.

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

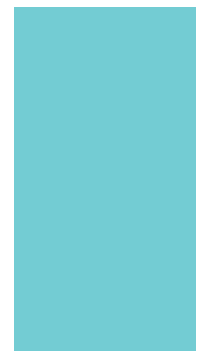
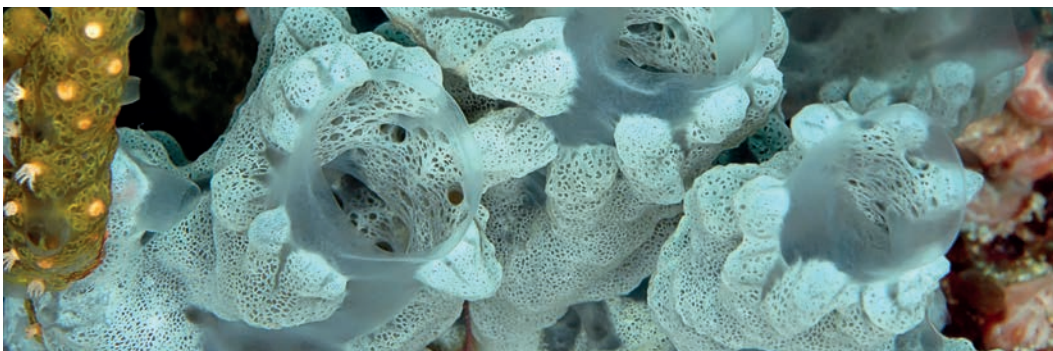
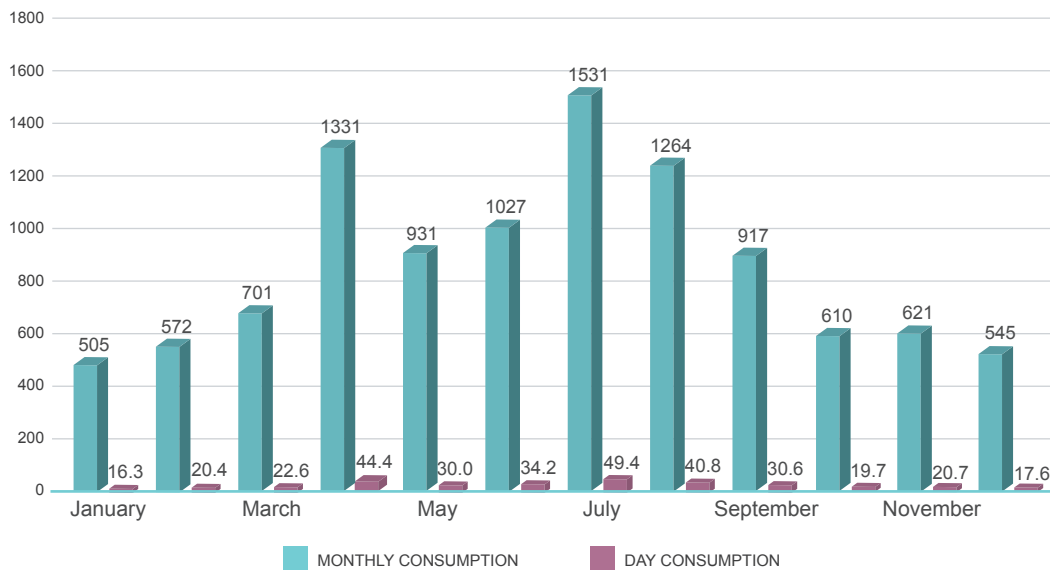


The figures below provide a detailed breakdown of the consumption of resources by PharmaMar in 2015.

Natural gas. Monthly consumption



Water consumption



ZELNOVA ZELTIA

Zelnova Zeltia complies substantially with environmental protection laws. Its environmental policy includes goals relating to the conservation and improvement of the natural environment, mainly in connection with reducing noise pollution and collecting liquid waste at its facilities.

The most significant environmental actions include:

- Waste treatment: Use of a recycling centre to separate solid waste, a water and liquid waste treatment facility, with at-source separation of waste, and membership of the waste management systems ECOEMBES (packaging), ECOLEC (electrical appliances), ECOPILAS (batteries and accumulators) and the SOGARISA industrial waste facility (*Centro de Tratamiento y Eliminación de Residuos Industriales de Galicia*).
- Reduction in electricity consumption: The adoption of measures such as improving natural lighting; monitoring and reducing electricity consumption; scheduling manufacturing by synchronising 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 river authority, respectively.
- Issuance of annual reports on transportation and hazardous wastes produced during the year and disposed of through authorised waste managers.
- Measurements of CO and NO emissions every six months, which are sent to the Galicia Regional Government.
- Changes in raw materials used, to avoid their being classified as carcinogenic.

XYLAZEL

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

As for compliance with the requirements of this standard, Xylazel has defined an environmental policy which is integrated with the pre-existing quality policy and establishes general guidelines for the organisation's environmental management. Under this policy, there are several plans in place for 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 2015, Xylazel has continued to steadily modernise its lighting equipment, by installing new low-energy LED bulbs to replace conventional sodium vapour lamps along one of the roads on site, at a cost of 10,300 euro.

Xylazel took part in the FSC Friday environmental education workshops in October 2015. FSC Friday, an annual celebration of responsible forestry, was held in Madrid in 2015. Xylazel took part in the workshop to build nest boxes made from timber harvested from sustainable sources. Later, in the nest box geolocation workshop, ideal locations for placing these boxes were found using both GPS and paper maps, within Parque Forestal Adolfo Suarez. This teaches children how, using forestry products, it is possible to build boxes for birds to shelter, nest and breed.

ENVIRONMENTAL PARAMETERS

Use of direct energy provided by primary sources:

Company	PharmaMar	Zelnova Zeltia	Xylazel
Consumption 2015			
Electricity (MWh)	4,955	972	525
Gas oil (l)	---	37,849	7,604
Natural gas (fuel) (l)	272,966,000	---	---
Water (m ³)	10,555	20,000	1,750

Discharge parameters:

Legal discharge limits and average values attained. All the parameters were well within the legal limits.

Company	PharmaMar	Zelnova Zeltia	Xylazel
Legal limits 2015			
Susp. solids < 1,000 mg/l	41	5	23
COD < 1,750 mgO ₂ /l	188	318	52
BOD5 < 1,000 mgO ₂ /l	75	52	27
6 < pH < 10	8.3	9	7.5





COMMUNITY ACTION





COMMUNITY ACTION

MAIN CONTRIBUTIONS

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 commitment to R&D.

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

Scholarships	425,563 €
Donations	187,403 €
Sponsorship of conferences, seminars and exhibitions	595,490 €
Cooperation with organisations	112,478 €

We would like to highlight the following actions:

- Agreements with numerous universities, business schools and institutes in Spain and other countries as part of a **training programme for interns** at PharmaMar, Genómica, Sylentis and Xylazel.
- Active participation in associations to **promote biotechnology**, such as **ASEBIO** (Spanish Association of Bioenterprises), of which PharmaMar Group Director of Project Coordination, Carmen Eibe Guijarro, is Second Vice-Chair.
- 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.
- Participation in **ALINNSA** (Alliance for Research and Innovation in Health), an association comprising public and private entities focused on biomedical research and innovation in Spain. The goal is to strengthen science, technology and innovation in life and health sciences in Spain, encouraging cooperation between current players through coordination, joint programmes, internationalisation and strengthening of public-private partnerships. José María Fernández Sousa-Faro, Chairman of the PharmaMar Group, is a member of ALINNSA's initial governing board.
- Cooperation with **FEUGA** (*Fundación Empresa-Universidad Gallega*).
- Creation of the **"Innovation, Health and Communication Chair"** at King Juan Carlos University in Madrid. This chair focuses on education, research and information on healthcare services as well as on labour insertion through the improvement of knowledge and the identification of needs and possibilities for improvement.
- Creation of the **First Master's programme in Drug Research and Development** by PharmaMar and King Juan Carlos University. This course aims to provide participants

with the necessary expertise and experience to work in the pharmaceutical industry and in research centres.

- **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 second-largest number of publications in high-impact scientific journals.
- Publication of the book *"El mundo submarino de PharmaMar"* (PharmaMar's Undersea World), which contains photographs of numerous marine organisms taken on expeditions by our marine biologists, from which the company extracts the compounds for R&D and innovation.
- Sponsorship of the **ASEBIO report**, which describes the situation and trends in Spain's biotechnology sector.
- Participation in **post-graduate seminars and courses** organised by universities and in Master's programmes and conferences in the fields of biomedicine and biotechnology. These courses facilitate the exchange of technical knowledge in the pursuit of science and research, thus contributing to the future of our society.
- 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.
- Collaboration with **patient associations**, including **FEDER** (*Federación Española de Enfermedades Raras*), Sarcoma Patients Euronet (**SPAEN**), *Asociación Española de Afectados por Sarcomas* (**AEAS**), *Asociación Cáncer de Ovario* (**ASACO**), *Infosarcomes* and *Insieme per Realizzare Iniziative di Solidarietà nel Campo della Prevenzione, Cura e Ricerca in Oncologia Ginecologica* (**IRIS**).



Two recipients of science journalism internships financed by PharmaMar (centre of front row) with the team of the SINC science news agency

Specifically, PharmaMar took part in the FEDER 2015 campaign “*Hazlas visibles*” (Make Them Visible), coinciding with world Rare Disease Day.

- Sponsorship and support for several **research entities**: *Asociación Española Contra el Cáncer*, *Fundación de Investigación del Hospital la Fe* and *Fundación Universidad de Navarra*, among others.
- Delivery of material to Madrid's Complutense University for “**Science Week**”.
- PharmaMar signed an agreement with *Fundación Española para la Ciencia y la Tecnología* (FECYT) to finance two of the four **scientific journalism scholarships** which the foundation currently offers at the scientific news agency SINC, the first public agency specialising in science news in Spanish. The scholarship programmes, in which students worked and trained alongside Spain's top scientific journalists, began in September 2015 and lasted for six months.
- Participation by Ana Isabel Jiménez, R&D Director of Sylentis, as guest of honour at the 16th edition of the **TEI Bio conference** in Madrid. This is an informal forum in which the guest is invited to share his or her experiences and opinions with participants, interacting with their questions and opinions, creating an atmosphere conducive to dialogue and generating synergies. This type of event provides a reference framework for investors, scientists and entrepreneurs interested in generating value from innovation in the biomedicine and biotechnology sectors.
- Signature of a **collaboration agreement between Genómica and Fundación ECO (for excellence and quality in oncology)**, which, in addition to fostering research actions, undertakes to promote training courses and conferences, technical information events and the publication of scientific papers.
- **Guided visits** of PharmaMar and Xylazel laboratories and facilities for students, with educational talks pitched to the appropriate level. For example, students enrolled on the Master's in Industrial Pollution at Vigo University visited the Xylazel facility.



Genómica and Fundación ECO announce a framework agreement in oncology.




Attendees at the workshop “*Marine Micr’omics for Biotech Applications*”, which was held at PharmaMar’s facilities.

- Collaboration with **BIOGA**, Galicia’s leading life sciences association, whose goal is to pursue a global strategic vision and foster fluid information exchange and cooperation between players in the field of biotechnology.
- Organization of the **workshop “Marine Micr’Omics For Biotech Applications”** at PharmaMar facilities in March 2015. This workshop served to share knowledge generated in the European projects MicroB3, Macumba and PharmaSea, in which PharmaMar participates in collaboration with other European institutions and companies.
- Sponsorship of, and participation and presentations at numerous **scientific conferences and meetings**. It is worth highlighting the 4th Forum on Ovarian Cancer: Relapse Treatment, held in Cordoba in May 2015, under the auspices of ovarian cancer research group GEICO (*Grupo Español de Investigación en Cáncer de Ovario*), and the 11th Annual Meeting of the Oligonucleotide Therapeutics Society, held in Leiden (The Netherlands) in October 2015.

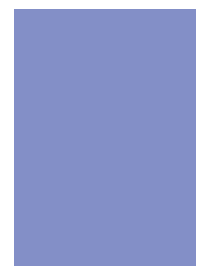
In addition, the Group also engages in the following activities in support of society, outside the field of new drug research and development:

- 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 Integraia travel agency, which employs people with disabilities (from which it acquired services amounting to 77,430 euro in 2015).
- Blood donation **drives in cooperation with Spain’s Red Cross**: PharmaMar organised two blood donation campaigns in cooperation with Madrid’s Transfusion Centre, and Zelnova Zeltia held one campaign in cooperation with the Galicia Transfusion Centre.

- Donation by employees of the company's previous holding company, Zeltia, of the amount earmarked for their "Secret Santa gift" to the NGO "**Aprendices Visuales**", which produces learning materials for children with autistic spectrum disorders.
 - Donation by PharmaMar of the residual value obtained from recycling IT equipment to *Federación de Padres de Niños con Cáncer*. Thanks to this donation, it received accreditation as a "**company with magic powers**", since this aid helps improve the quality of life of many children and adolescents with cancer.
- 
- Participation by Sylentis employees in "**Operation Kilo**", a food bank programme.
 - Collection of toys at Genómica for the "**Ningún niño sin sonrisa**" association.
 - 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.
 - Cooperation with the **Family Business Association of Madrid**, an independent group which defends the interests of family businesses in the Madrid region.
 - Cooperation with the **Association for Management Progress**, which helps companies through executive development.
 - Cooperation with the **Spanish Broadcasters Association** and the **Spanish Association for Investor Relations**.
 - Cooperation with **ASEYACOV**, Association of Entrepreneurs, Business-owners and Self-employed persons of Colmenar Viejo.

PAIDEIA GALIZA FOUNDATION

Trébore is a business initiative created by the Paideia Galiza Foundation as a source of employment and a mechanism for teaching skills to disadvantaged people. Since inception, the Paideia Foundation has been concerned with vulnerable groups in general, and people with disabilities in particular, based on the firm conviction that many people with disabilities could benefit from a work situation which contributes to enhancing their skills.



OTHER GROUP ACTIVITIES WITH AN IMPACT ON SOCIETY

PROMAXSA PROTECCIÓN DE MADERAS, S.L.

Promaxsa Protección de Maderas, S.L. is a PharmaMar Group subsidiary founded in 1981 to treat, protect and restore wood, both structural and ornamental, in monuments and buildings of our national heritage.

Down through the years, these works of art have been attacked by a wide range of xylophages—wood borers, moths, termites and fungi. But for Promaxsa's action to protect and restore these monuments, many would have been lost irretrievably, causing irreparable loss to our cultural heritage. In addition to eradicating the pests, the wood needs to be strengthened to regain the mechanical properties lost over time. Promaxsa also provides civil engineering services.

Promaxsa is the only specialised company with the Quality Seal from AITIM (Association of Investigation of the Industries of Wood and Cork) for restorative and preventive treatments for woodwork.

The company's main services are:

- Preventive and restorative wood treatments against xylophages, including: wood borers, brown rot fungus, and termites, in both furniture and structural timber.
- Termite control using chemical barriers and bait with chitin synthesis inhibitors, which is non-toxic to animals and people, without requiring structural work.
- Strengthening wooden structures with the BETA system, involving epoxy resins and fibreglass rods, which restores lost mechanical strength.
- Bulk fireproofing and paint stripping of timber components.
- Treatment of works of art and furnishings through fumigation in a controlled atmosphere with inert gases. Standard insecticides cannot be used because of the nature of the items to be treated (varnishes, polychromy, parchments).
- Wood structural strength calculations.

Below is an example of one of the unique projects carried out by Promaxsa in 2015 at the Royal Palace of Riofrío (Segovia), in continuation of work performed in previous years.

ROYAL PALACE OF RIOFRÍO (SEGOVIA)

The Royal Palace of Riofrío, located in San Ildefonso, in the province of Segovia, is one of the residences of the Spanish Royal Family, and managed by Spain's National Heritage.

It was commissioned by Isabel Farnese, the second wife of Philip V; fearing that she would be deprived of the palace and gardens of La Granja, she ordered this palace to be built on the Ríofrío estate, surrounded by fields and woodland.

Built in 1752, it is one of the palaces of the period that was most influenced by the Italian style. Unlike most Spanish palaces, Riofrío is austere, sober, and a far cry from the Baroque style. Particularly interesting are the main staircase, the indoor patio, the chapel and the collection of paintings (Velázquez and Rubens), 18th-century tapestries and furniture, as well as sculptures, furnishings and antique weapons of incalculable historical value.

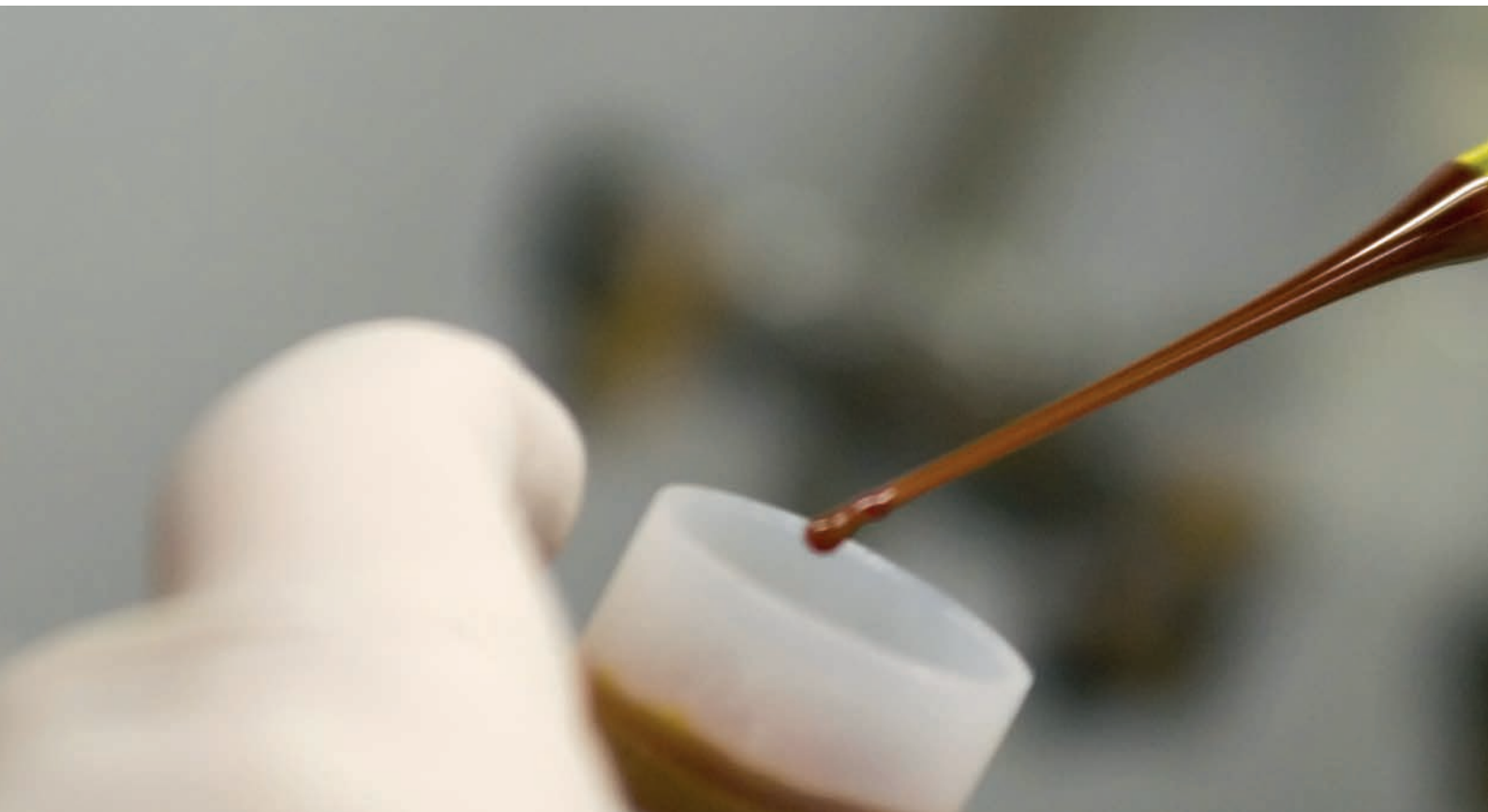
Despite its large size, Riofrío palace was used only as a hunting lodge, with the exception of brief periods of residence by Alfonso XII (who chose the palace as a retreat in which to mourn his wife, María Mercedes) and Francisco de Asís de Borbón, king consort and husband of Isabel II (who retired there). The building currently hosts a hunting museum.

Due largely to its location, surrounded by woodland, for some time Riofrío has suffered the consequences of underground termites, that have eaten into the wood. The termites have had a particularly big impact on the large amount of timber used in the building's roof structure.

In light of this significant deterioration, National Heritage asked Promaxsa to mitigate the damage. In the 1990s, the company treated the entire wooden roof structure of the palace against wood borers. Since the products used are guaranteed for ten years, follow-up treatment is applied every decade. The most recent update, in September to November 2015, included a comprehensive report on the existing pathology and the state of the wooden load-bearing structure, in order to determine potential future actions.

The preliminary inspection revealed timber elements had been attacked by subterranean termites and wood-decay fungus, to the point where some items have actually disappeared. Based on the observations, all structural timber in the roof was reinjected with the anti-wood borer product Xylazel Total IF-T. In addition to this curative treatment, the surface of all woodwork was sprayed, including both the reinjected parts and the wood shingle structure nailed to them, underneath the roof slates. This will protect the treated timber against wood borers for another ten years, after which treatment may be repeated if necessary.





A close-up photograph of a hand holding a yellow highlighter pen. The pen is positioned diagonally across the frame, with its tip pointing towards the bottom left. The hand is holding the pen from the middle, with the thumb and index finger visible. The background is a solid teal color. The word "COMMUNITIES" is written in white, bold, uppercase letters on the right side of the teal background.

COMMUNITIES



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 programmes—and providing a range of services. Additionally, the companies take the necessary steps to minimise the environmental impact of their activities, as detailed in the chapter on the Environment.

The taxes paid to the Galicia region by the Group companies (property tax, business tax, various municipal taxes, etc.) amounted to around 99,000 euro in 2015. Taxes paid to the Madrid region under the same headings amounted to approximately 111,000 euro.

Our companies are also a major source of employment. We employ 153 people in Galicia. Xylazel and Zelnova Zeltia also create jobs in other regions: a total of 31. We employ a total of 432 people in the Madrid region.

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

MADRID REGIONAL GOVERNMENT MINISTER OF THE ECONOMY VISITS PHARMAMAR

The Madrid Regional Government Minister of the Economy and Finance, Enrique Ossorio, visited PharmaMar's facilities in March 2015. During his visit, he was informed about the company's firm commitment to internationalisation, as well as the clinical development of PharmaMar's products, most notably PM1183, which is in Phase III of development for the treatment of relapsed ovarian cancer and small-cell lung cancer, and in Phase II for non-small-cell lung cancer.

Services provided to the local communities include:

- PharmaMar sponsored an environment conference in Colmenar Viejo, as well as other projects in the town, such as the European Hercules Project and the Colmenar-Antarctic Project.
- Visits by students to the laboratories and facilities of Pharma Mar and Xylazel, including educational talks pitched to the appropriate level.
- Cooperation with ASEYACOVl, Association of Entrepreneurs, Business-owners and Self-employed persons of Colmenar Viejo.

In 2015, the Group received the Award for Chemical Business Excellence in recognition of “the initiatives and work carried out over 70 years in pursuit of the development and welfare of Galician society”, to quote the dean of the Galicia Official Association of Chemists.



A photograph of laboratory glassware, including several brown glass vials and two green glass pipettes, arranged diagonally. A teal-colored rectangular overlay is positioned in the upper right quadrant, containing the text 'REGULATORY BODIES'.

REGULATORY BODIES



REGULATORY BODIES

Regulatory bodies are authorities with responsibility for drafting and enforcing the legislation relating to the development and authorisation 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 defence 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.

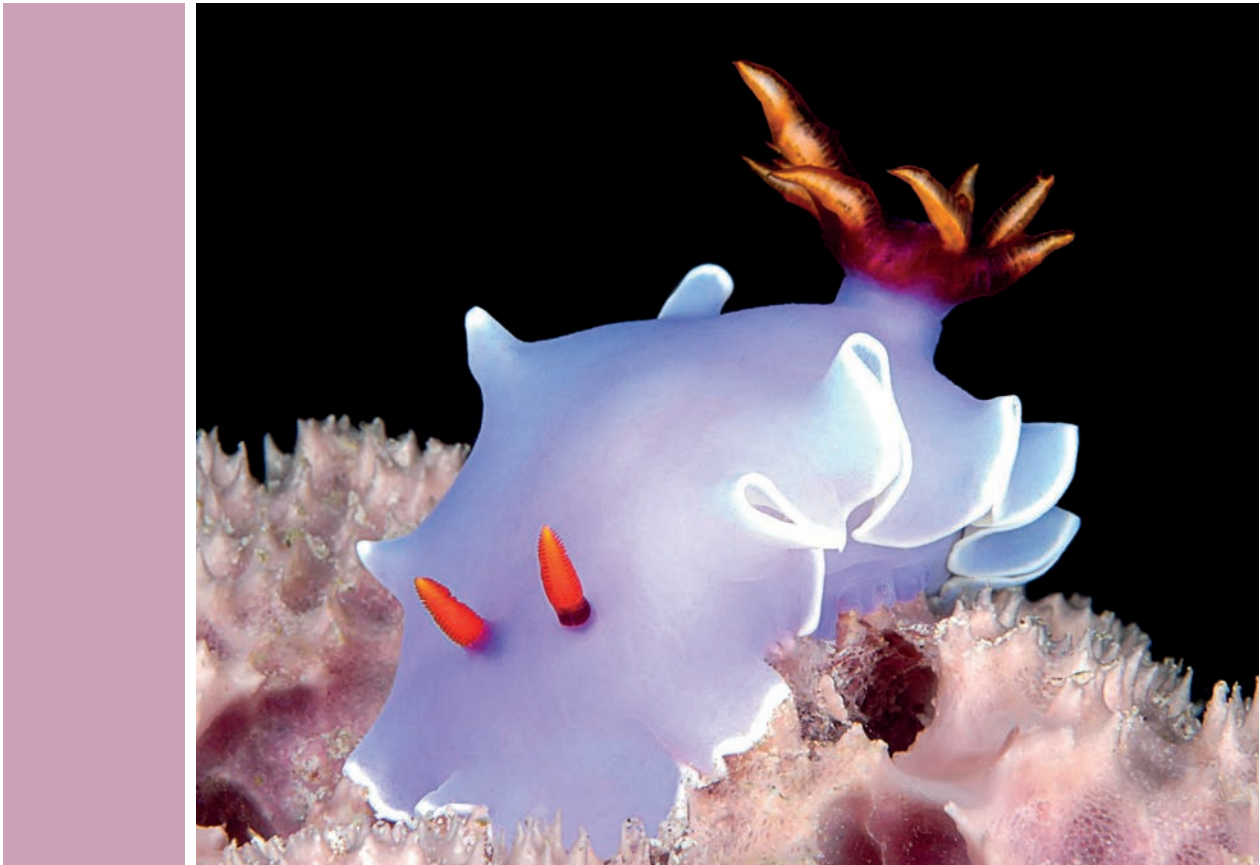
A number of initiatives were taken to increase transparency in relations between the regulatory authorities and the industry. For example, PharmaMar cooperates with regulatory bodies to draft guidelines and regulations, which enables us to comment on issues that could be improved and makes it possible 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 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, Culture, 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 Medicines Agency, Institutes of Public Health, Pesticide Register, regional governments, city governments, and the National Securities Market Commission (CNMV).
- Europe: EMA, European Commission, the Ministries of Health of the various Member States, National Regulatory Agencies and the Price and Reimbursement Authorities.
- USA: FDA, directly and through Janssen Research & Development, LLC, a Johnson&Johnson subsidiary.
- 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 (Oncology business unit): Authorisation and performance of clinical trials, inspections, drug development (including paediatric and orphan drugs), scientific advice, maintenance of commercialisation authorisation for Yondelis® and price and reimbursement negotiations.

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 authorisation by ethics committees and regulatory agencies in Spain, Germany and Estonia. Organization of a pre-IND meeting with the FDA to discuss plans to commence the forthcoming clinical trial in the US. Inspection by the Spanish Agency for Medicines and Healthcare Products (AEMPS) to renew its authorisation as a pharmaceutical laboratory to manufacture research drugs.
- Genómica: Registration and obtainment of the CE mark for diagnostic kits.
- Zelnova Zeltia: 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.

