Marine-inspired Oncology
“Nature distributed medicine everywhere.”

Pliny the Elder.
74 AD
PharmaMar is a biopharmaceutical company, focused on oncology and committed to research and development which takes inspiration from the sea to discover molecules with antitumor activity. It is an integrated company that seeks innovative products to provide healthcare professionals with new tools to treat cancer. Its commitment to patients and to research has made it one of the world leaders in the discovery of antitumor drugs of marine origin.

PharmaMar has a pipeline of drug candidates and a robust R&D oncology program. With subsidiaries in Europe and the United States, PharmaMar develops and commercializes Yondelis® in Europe, along with Aplidin®, approved for the Australian market, also having other clinical-stage programs under development for several types of solid cancers: lurbinectedin (PM1183), PM184 and PM14.

PharmaMar fully owns other companies: GENOMICA, a molecular diagnostics company; Sylentis, dedicated to researching therapeutic applications of gene silencing (RNAi); and a chemical enterprise, Zelnova Zeltia.
The sea as a source of inspiration

The sea covers 70% of the planet and holds 80% of all life. Down through the millennia, marine organisms have evolved a range of substances with biological activity that they use for survival, defense, attack and communication. These substances hold great potential for the development of new drugs. PharmaMar conducts activities from, for example, basic research with marine expeditions, compound isolation, chemical synthesis, and in vitro and in vivo studies to discover and develop new antitumor compounds of marine origin.

Initially, the samples of marine organisms (mostly invertebrates), are gathered studying later their taxonomy and beginning to assess their biological activity in tumor cells. Nowadays, the company has probably the world’s largest collection of marine organisms: nearly 200,000 samples of macro- and microorganisms.

Subsequently, the substance identified as being responsible for the activity is isolated and its chemical structure is established. A chemical synthesis process for its industrialization is designed. Then, the pharmaceutical formula of the new compound is defined and where possible patents are filed. “In vivo” models are designed to test the efficacy in a range of different tumors. If the results are positive, research may begin with cancer patients.

As a result of this research process, the company has a portfolio of products that are at various stages of clinical development.
From **Spain** to the rest of the **world**

From its facilities in Madrid, PharmaMar produces Yondelis® and Aplidin®, for the rest of the world, synthesizing the active molecules for drug manufacturing, and undertaking secondary conditioning to meet the commercial demand and forecasted needs for clinical trials and compassionate use programs. The process is done with the agility and rigor required to guarantee industrial scale manufacture and supply of its products, always in strict compliance with Good Manufacturing Practices (GMP), regulatory requirements and the regulations on protecting our workers and the environment.

PharmaMar has developed the marine derived cancer drug Yondelis®, which has been approved for treating soft tissue sarcoma in around 80 countries, including the US, EU and Japan. PharmaMar has also obtained approval for Yondelis® in treating ovarian cancer in the EU and other countries. Under a licensing agreement with PharmaMar, Janssen Products, L.P. has the rights to develop and sell Yondelis® globally except in Europe, where PharmaMar holds the rights, and in Japan, where PharmaMar has granted a license to Taiho Pharmaceuticals. PharmaMar has also developed Aplidin® for treating multiple myeloma, approved in Australia, and licensed by Specialised Therapeutics.

“**In the relatively near future, the marine environment in all of its manifestations will be producing leads to novel treatments against cancer and other diseases**”.

GENOMICA S.A.U.
A company leader in molecular diagnostics

GENOMICA was born in 1990 and it was the first private company in giving support in molecular diagnostics in Spain. It focuses its activities in the field of genetic analysis, and it is also a pioneer in technology transfer. Its objective is to improve current methods for molecular diagnostics and DNA profiling with reliable, automated tools that conform to the highest quality standards.

GENOMICA reinvests a significant percentage of their revenues to develop new techniques and products.

GENOMICA was the first Spanish company to obtain accreditation by ENAC (Spain’s National Accreditation Agency).

The company has the following lines of business:

1. Design, development and sale of in-vitro diagnostic kits based on low-density microarrays, which can then be automatically read and interpreted with the proprietary SAICLART® software. This reliable, robust platform, called CLART®, permits the detection of multiple targets in a single run, allowing for quick and effective clinical decision-making.

2. Genetic identification and filiation, an area in which the company is a leader in this field.

3. NGS (Next Generation Sequencing Service): services and sequencing led by tailored panels (R&D).

GENOMICA is firmly committed to internationalization. It currently operates in more than 40 countries worldwide and continues to expand actively.
SYLENTIS S.A.U.  
Understanding RNA interference

SYLENTIS, founded in 2006, seeks innovative therapeutic agents based on RNA interference, a technology whose discoverers were awarded the Nobel Prize for Medicine in 2006. Sylentis focuses primarily on treatments for ophthalmology.

The company has finalized a phase III clinical trial for treating the signs and symptoms of Dry Eye Disease, which has demonstrated an improvement in reducing central corneal staining. Sylentis also has other molecules undergoing preclinical development for the treatment of eye allergies and diseases of the retina.

RNA interference (RNAi) has revolutionized biology by making it possible to design and develop drugs from a totally new perspective. It can be used to selectively silence genes through post-transcriptional degradation of the messenger RNA that would lead 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.

1. Some diseases, such as glaucoma, appear when a specific protein is altered or produced in excess.

2. DNA. The information required to produce each protein is stored in the DNA molecule, in the cell nucleus. The DNA, however, is such a large molecule that it cannot leave the nucleus with all the information that it contains.

3. DNA RNAm. The DNA information is transferred to smaller molecules, known as the messenger RNA (RNAm), which contain the information required to generate the protein.

4. RNAm Protein. The mRNA leaves the nucleus and is used as the template to produce the proteins. But, sometimes, altered proteins or high concentrations can cause a disease.

Drugs based on RNA interference (RNA) block expression at this point reducing and regulating protein levels (Gene Silencing Process).

These RNAi products are designed with computer tools using information from DNA databases and synthesized by chemical processes.
“Overall, it is estimated that between 0.4% to 1.8% of natural extracts (from terrestrial plants to marine animals respectively) of natural materia may contain anti-cancer principles.”
