

## REPORT AS OF 31 DECEMBER 2016

Madrid, 23 February 2017

### 2016 MILESTONES

#### Corporate (stet)

- In December 2016, Pharma Mar, signed a licensing and development agreement relating to its compound Lurbinectedin (PM1183) with Chugai Pharmaceutical Co. Ltd. for Japan which saw a non-refundable upfront payment to PharmaMar amounting to €30 million. Under the IFRS 15, only a part of that upfront payment (€6 million) were recognised as revenues in 2016, based on the degree of progress with the clinical trials referred to in the agreement. The rest of the pending amount will be accrued in line with the development of those clinical trials. As for the cash, PharmaMar collected the entire upfront payment (€30 million) in the first weeks of 2017; consequently, the accrual portion of this payment will be reported in the cash flow statement for the first quarter of 2017.
- Net commercial sales of Yondelis (thus, excluding the effect of raw material sales to Yondelis partners Janssen Pharmaceutical and Taiho Pharmaceutical) increased by 7% compared to 2015.
- Royalties from our partners for Yondelis sales continue to grow.
- Revenues in the Consumer Chemicals segment increased by 4% to €69.88 million in 2016 vs. €67.4 million in 2015.
- Net R&D expenditure increased by 30% year-on-year to €78.3 million vs. €60.3 million in 2015, of which €72 million corresponded to oncology.

#### Oncology

- Lurbinectedin (PM1183):
  - Licensing, development and marketing agreement for Lurbinectedin PM1183 signed with Chugai Pharmaceutical Co. Ltd. for Japan.
  - CORAIL pivotal (registration) trial: in August, following an interim analysis for safety and efficacy, PharmaMar received the green light from the Independent Data Monitoring Committee (IDMC) to continue with this pivotal trial in patients with platinum-resistant ovarian cancer. Enrolment for the trial concluded in October.
  - In August, a Phase III trial commenced to compare the efficacy and safety of the combination of PM1183 and doxorubicin for treating small-cell lung cancer patients who had been treated previously with a platinum based therapy.
  - The Phase II trial with Lurbinectedin (PM1183) in patients with metastatic BRCA 1/2 breast cancer who had previously received at most three rounds of chemotherapy saw an overall response rate of 41%. The subgroup of patients with the BRCA 2 mutation had a 61% overall response rate, compared with 26% in the BRCA 1 group.
- Aplidin (plitidepsin):
  - Signed a licensing agreement with Specialised Therapeutics Asia Pte, Ltd. (STA) to market Aplidin® for the treatment of haematological tumours in 12 Asian countries.
  - Signed a licensing agreement with Boryung Pharm to market Aplidin® for treating haematological tumours in South Korea
  - The ADMYRE Phase III trial in patients with relapsed multiple myeloma concluded in the first quarter of the year, and attained its primary endpoint. Consequently, in September, PharmaMar filed an application with the European Medicines Agency (EMA) for authorisation to market Aplidin® (plitidepsin) in combination with dexamethasone for treating relapsed or refractory multiple myeloma.

- A registration trial commenced in June with Aplidin® in angioimmunoblastic T-cell lymphoma, a rare haematological cancer.
- PM 184:
  - A Phase II trial in patients with advanced breast cancer commenced in the first quarter

#### **Diagnostics alignment**

- The new CLART® PneumoVir2 kit for detecting viral respiratory infections was launched.
- Launched the CLART® EGFR kit for detecting oncological mutations associated with lung cancer in liquid biopsies.
- Launched a second CLART® ALK / ROS-1 kit for detecting oncological mutations associated with lung cancer in solid biopsies.

#### **Consumer Chemicals**

- The Consumer Chemicals division increased revenues by 3.5% over 2015

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## DECEMBER 2016 FIGURES

	December 2016	December 2015
<b>REVENUES</b>		
<b>Sales</b>	<b>164.034</b>	<b>161.992</b>
Biopharmaceutical Area	94.374	94.644
<i>Oncology Segment</i>	<i>88.194</i>	<i>88.442</i>
<i>Diagnostic Segment</i>	<i>6.180</i>	<i>6.202</i>
Consumer Chemicals Segment	69.660	67.348
<b>Royalties</b>		
Oncology Segment	<b>5.779</b>	<b>1.788</b>
<b>Licenses and co-development agreements</b>		
Oncology Segment	<b>11.129</b>	<b>29.034</b>
<b>Services Rendered</b>		
Not assigned	<b>5</b>	<b>1.003</b>
<b>TOTAL REVENUES</b>	<b>180.947</b>	<b>193.817</b>

	December 2016	December 2015
<b>EBITDA</b>		
Biopharmaceutical Area	-6.530	23.670
Consumer Chemicals Segment	5.308	5.122
Not assigned	-9.813	-9.452
<b>TOTAL EBITDA</b>	<b>-11.035</b>	<b>19.340</b>

(€'000)

### **Total Group revenues**

**Net sales** in the Biopharmaceutical segment amounted to €94.4 million, (€94.6 million in 2015). Of that figure, €88.2 million were in Oncology (PharmaMar) for Yondelis® sales, vs €88.44 million in 2015. It is worth mentioning that in 2015, Pharma Mar sold raw materials to its partners Janssen and Taiho for €7.8 million to enable them to build inventory of Yondelis®, which was approved in their territories in that year. Sales of raw materials to those partners amounted to €1.5 million in 2016. Thus, eliminating sales of raw materials to partners Janssen and Taiho, net commercial sales increased by 7.2% year-on-year in 2016. Sales in the Diagnostic segment (Genómica) totalled €6.2 million, the same as in 2015.

Sales by the Consumer Chemicals companies amounted to €69.7 million, a 3,5% increase year-on-year (€67.3 million in 2015).

**Royalty revenues** correspond to the Oncology segment. Royalties collected from Janssen and Taiho for sales of Yondelis® in the US, Japan and the rest of the world except the European Union increased to €5.8 million in 2016, from €1.8 million in 2015, after both companies obtained regulatory approval from their respective regulators to market Yondelis® in the fourth quarter of 2015.

**Revenues from licensing and other co-development agreements**, which correspond entirely to the Oncology segment, amounted to €11.1 million in 2016; €6.0 million were the recognition of a part of the upfront payment under the lurbinectedin (PM1183) licensing contract signed in December between PharmaMar and Chugai Pharmaceutical. The upfront payment, which totalled €30 million, will be recognised in revenues in line with the degree of progress with the clinical trials referred to in the contract. Also in 2016, PharmaMar recognised €4 million in revenues from Chugai Pharmaceutical for attainment of a regulatory milestone under the Aplidin® licence contract signed in 2014. Additionally, €1.1 million were collected for a number of licensing contracts for Aplidin® in certain Asian countries.

In 2015, Yondelis® was approved for commercialisation in the US and Japan, which triggered sizeable payments, and there was also the last payment under the Yondelis development plan (Coordination Agreement) signed with Janssen in 2011. Receipts under licensing agreements amounted to €29 million in 2015.

Consequently, **total revenues** amounted to €180.97 million in 2016, compared with €192.81 million in 2015 (-6.15%).

## EBITDA

Group EBITDA amounted to -€10.7 million in 2016 (vs. +€19.3 million in 2015).

This decrease is attributable to two factors: 1) revenues under licensing and other agreements (€11.1 million in 2016 vs. €29.0 million in 2015): this was also due to recognition of only €6 million of the total €30 million upfront payment on the Lurbinectedin (PM1183) licensing agreement as a result of the application of IFRS 15 for revenue recognition. As a result of this partial recognition, revenues from licences and other agreements were €17 million lower than in 2015, when revenues under those contracts were collected from Janssen and Taiho for attaining Yondelis® milestones; and 2) R&D expenditure increased by €18 million net in 2016, basically as a result of ongoing Phase III trials. The impact of these two items it is partly offset by the €5 million increase in net sales and royalties.

(EBITDA: earnings before interest, taxes, depreciation and amortisation).

## R&D expenditure

R&D expenditure increased by 25% year-on-year (+€16.2 million), from €63.5 million gross in 2015 to €79.8 million in 2016. R&D expenditure of the Oncology area was of €72.3 million in 2016 (€55.6 million in 2015), while the Diagnostics and RNA interference areas spent €7.3 million (€7.9 million in 2015). In 2016, Oncology capitalised €1.4 million of R&D expenses incurred (€3.3 million in 2015); accordingly, net investment increased by 30% in the year.

I + D	2016	2015	Dif <sup>a</sup>	Var.
Segmento Oncología	72.301	55.610	16.691	30%
Segmento Diagnóstico	2.426	2.218	208	9%
Segmento RNAi	4.890	5.687	-797	-14%
Segmento Química Gran Consumo	163	34	129	
	<b>79.780</b>	<b>63.549</b>	<b>16.231</b>	<b>25%</b>
- Capitalización I+D	-1.357	-3.258	1.901	-58%
<b>TOTAL I + D GRUPO</b>	<b>78.423</b>	<b>60.291</b>	<b>18.132</b>	<b>30%</b>

(Thousand euro)

Increased R&D in the oncology segment was mainly due to the considerable progress achieved in the clinical trials with Lurbinectedin in platinum resistant ovarian cancer and small-cell lung cancer, as well as a number of preclinical and clinical trials with that same compound.

## Marketing and commercial expenses

Marketing and commercial expenses of the Group amounted a total of €47.7 million in 2016 (€48.6 million in 2015) of which €29 million are attributable to the oncology business area (€29 million in 2015). The Consumer Chemical business accounted for €18.6 million of the total amount compared to 19.6 million spent in 2015.

## Income attributable to the parent company

Income attributable to the parent company amounted to a loss of -€24.24 million in 2016, compared with a profit of €6.6 million in 2015. This difference is mainly due to the year on year net increase of €18 million of the R&D expenditure, as well as a lower amount booked as revenues for licensing and other agreements due to the fact that under the IFRS 15, only a part of the total upfront payment of €30 million of the agreement signed with Chugai in December 2016, were recognised as revenues in 2016.

## Cash and Debt

Cash and cash equivalents plus current financial assets amounted to €33.5 million (€46.7 million at 31 December 2015). The Group's total debt (current and non-current) amounted to €95.5 million at the end of 2016 (€93.6 million at 31 December 2015). By December 31st, the Company had refinanced the total amount of maturities due in 2016 (€17.5 million) by means of two new long-term bank loans (5 and 6 years) as well as funding from governmental and supranational authorities (at 10 years).

The breakdown of total debt, at amortised cost, classified as current and non-current, together with current and non-current financial assets and cash and cash equivalents, is shown in the table below:

	2016	2015
<b>Deuda no corriente</b>	<b>67.583</b>	<b>64.973</b>
Entidades bancarias	25.351	20.651
Obligaciones y bonos	16.350	16.350
Organismos oficiales	25.882	27.972
<b>Deuda corriente</b>	<b>27.906</b>	<b>28.629</b>
Pólizas de crédito	10.958	10.558
Descuentos comerciales	1.238	2.148
Préstamos	10.685	11.585
Organismos oficiales	4.438	3.753
Intereses y otros	587	585
<b>Total deuda financiera</b>	<b>95.489</b>	<b>93.602</b>
<b>Efectivo y equivalentes más activos financieros corrientes y no corrientes</b>	<b>33.505</b>	<b>46.692</b>
<b>TOTAL DEUDA NETA</b>	<b>-61.984</b>	<b>-46.910</b>

*(Thousand euro)*

On 22 December 2016, PharmaMar signed a licensing, development and commercialization contract agreement for Lurbinectedin (PM1183) in Japan with Chugai Pharmaceutical. The contract provides for a non-refundable upfront payment of €30 million. That payment was collected in early January 2017 and, consequently, does not appear in the preceding table. The payment from Chugai is to be added to the cash and cash equivalents amount and enhanced the Group's financial position, though it is not reflected in the 2016 year-end figures.

## **BUSINESS PERFORMANCE.**

Below is an overview of the group companies' business performance through September 2016.

### **A) Biopharmaceutical area:**

#### **1. Oncology segment: PharmaMar**

##### **1.1. New licensing agreements:**

##### **1.1.1. Lurbinectedin (PM 1183)**

In December, PharmaMar and Chugai Pharmaceutical Co. Ltd. signed a licence, development and commercialisation agreement covering PM1183 (lurbinectedin) in Japan. Under the terms of the agreement, PharmaMar was to and did collect an upfront payment of €30 million 30 days after signature, in addition to double-digit stepped royalties on sales of PM1183 by Chugai if and when the drug is authorised for commercialisation in Japan. The agreement also provides for other payments by Chugai to PharmaMar upon attaining certain milestones relating to clinical development and product sales in Japan, potentially totalling over €100 million.

PharmaMar will handle clinical development of PM1183 in Japan for the first two indications (platinum-resistant ovarian cancer and 2<sup>nd</sup> line small-cell lung cancer) while Chugai will make payments when those clinical trials commence and will handle registration in that territory. Chugai will also be entitled to engage in clinical development of the drug in Japan for other indications and may contribute to the molecule's development worldwide. PharmaMar will retain exclusive rights to produce Lurbinectedin and will supply the active ingredient to Chugai.

##### **1.1.2. Aplidin® (plitidepsin)**

In February 2016, PharmaMar licensed Aplidin® to Specialised Therapeutics Asia Pte, Ltd. (STA), a Singapore-based company, for the treatment of haematological tumours in 12 Asian countries: Brunei, Cambodia, East Timor, Indonesia, Laos, Malaysia, Myanmar, Papua New Guinea, Philippines, Singapore, Thailand and Vietnam. PharmaMar collected an upfront payment (\$250,000) for signing the agreement, and will receive recurring payments in the future

for sales, and additional remuneration for the attainment of sales and regulatory milestones. PharmaMar will retain exclusive production rights and will supply the product to STA.

In October, PharmaMar signed a licensing agreement with Boryung Pharm to commercialise Aplidin® in South Korea. Under the terms of the agreement, at the date of this report PharmaMar had received an upfront payment and a regulatory milestone which together amount to close to €1 million. In the future, it will collect recurring revenues from sales as well as payments for regulatory milestones attained by Aplidin®. PharmaMar will retain exclusive production rights and will supply the product to Boryung for commercialisation.

## **1.2. Scientific conferences:**

Following the approval of Yondelis® in the United States and Japan, and the fact that it is now available virtually worldwide, PharmaMar held a symposium in Barcelona on 12 March to discuss the state of the art in soft tissue sarcoma with the world's leading researchers. A total of 250 European specialists attended the symposium.

PharmaMar also presented the latest progress with Yondelis®, Aplidin® and PM1183 at the 52nd annual meeting of the American Society of Clinical Oncology (ASCO), held in Chicago on 2-6 June, which was attended by over 30,000 oncologists from around the world. Papers were presented on these three molecules, which were discovered and are being developed by PharmaMar. They were selected for oral presentation poster discussion and a poster presentation. In this venue, PharmaMar presented the results of the Phase I trial with Aplidin® in combination with bortezomib and dexamethasone in patients with multiple myeloma.

On May 6th PharmaMar also organised the 5th Forum on Ovarian Cancer, at the Reina Sofía Hospital in Cordoba, with the aim of sharing experiences and the latest therapeutic trends in this disease and progressing with its clinical management.

PharmaMar presented the data from a number of clinical trials with its anti-tumour compounds of marine origin, Yondelis® and lurbinectedin, at the European Society for Medical Oncology (ESMO) 2016 Conference, held in Copenhagen on 7-11 October. PharmaMar participated with posters and oral presentations in which it reported on the latest progress with the clinical development of those molecules. It presented results on, among others, the Phase II trial with lurbinectedin (PM1183) in patients with BRCA 1/2 metastatic breast cancer. Additionally, the French Sarcoma Group presented data from a prospective Phase III trial being conducted in France (T-SAR) comparing trabectedin (Yondelis®) with the standard treatment for soft tissue sarcoma.

## **1.3. The current status of compounds in the clinical development pipeline is described below.**

### **a) Yondelis®:**

The post-authorisation trials (both observational and retrospective) with Yondelis® in the two approved indications (soft tissue sarcoma and platinum-sensitive ovarian cancer) continued satisfactorily in 2016.

At year-end, there were 26 open trials: 17 in soft tissue sarcoma and 9 in ovarian cancer. Research into Yondelis® generated a large number of abstracts and publications during the year that were presented at leading oncology meetings.

#### **Soft-tissue sarcoma**

A number of major international publications were presented in 2016, such as the T-SAR randomised Phase III trial with Yondelis® compared with best supportive care, being conducted in France by the French sarcoma group, and the ISG-STs 101-01 trial in neo-adjuvant treatment conducted by the Italian Sarcoma Group and the Spanish Sarcoma Research Group. Results from the TOMAS Phase I trial with Yondelis® in combination with olaparib in sarcoma were presented at the American Society of Clinical Oncology (ASCO) annual meeting in June 2016.

#### **Ovarian cancer**

Recruitment continues satisfactorily in the NIMES-ROC international prospective observational trial on the efficacy and safety of the Yondelis® + PLD

The INOVATYON Phase III trial comparing Yondelis® + PLD to carboplatin + PLD headed by Gruppo MaNGO (Mario Negri Gynecologic Oncology), continued recruiting very actively in eleven European countries in 2016

The MITO 23 Phase III trial comparing Yondelis® as monotherapy vs. investigator-choice chemotherapy in patients with a BRCA mutation or a BRCAness phenotype is being conducted in cooperation with the Italian MITO group.

Regarding combinations with other drugs for this indication, the IRFMN-OVA 6152 Phase II trial with Yondelis® + bevacizumab, with and without carboplatin, which is being promoted by the Mario Negri Institute in Milan, is ongoing; interim data from this trial were reported to the International Gynecologic Cancer Society meeting in Lisbon in 2016.

#### **Other indications**

Recruitment is continuing in the ATREUS Phase II trial promoted by the Mario Negri Institute for Pharmacological Research (IRCCS) in cooperation with the Department of Medical Oncology at San Gerardo Hospital (Monza, Italy) to evaluate the activity and safety of Yondelis® in malignant pleural mesothelioma (MPM).

Recruitment is also continuing satisfactorily in the EORTC 1320-BTG trial, conducted in cooperation with the European Organization for Research and Treatment of Cancer (EORTC); this Phase II randomised trial with Yondelis® in patients with highly recurrent meningioma seeks to assess the drug's efficacy and safety in comparison with the standard treatment.

#### **b) Aplidin®**

##### **Multiple Myeloma**

In September, PharmaMar filed an application with the European Medicines Agency (EMA) for authorisation to market Aplidin® (plitidepsin) in combination with dexamethasone for treating relapsed or refractory multiple myeloma.

That application was made using data from the ADMYRE Phase III trial, which assessed Aplidin® (plitidepsin) in combination with dexamethasone vs. dexamethasone as monotherapy in patients with relapsed or refractory multiple myeloma. That trial, which concluded in the first quarter of the year, disclosed a statistically significant 35% reduction in the risk of progression or death vs. the comparator, thereby achieving the primary endpoint.

The Phase II trial with Aplidin® in combination with bortezomib and dexamethasone in patients with double refractory multiple myeloma has commenced, having opened centers in Spain, Italy and France.

The Phase I trial with Aplidin® in combination with bortezomib in patients with relapsed or refractory multiple myeloma continues recruiting in the expansion phase. Between 15 and 20 new evaluable patients are expected to be added in this stage.

A new Phase I trial has been designed with Aplidin® in combination with bortezomib, pomalidomide and dexamethasone in patients with multiple myeloma exposed to proteasome inhibitors who are refractory to lenalidomide. This trial will be conducted at centers in Spain and the Czech Republic. We are currently awaiting approval from the ethics committees and the regulators before opening the trial for recruitment.

##### **T-cell lymphoma**

The registration trial with Aplidin® as monotherapy in patients with angioimmunoblastic T-cell lymphoma has commenced recruitment and opened new centers in Spain, the Czech Republic, Italy and the US. The trial will include 60 patients at approximately 25 centers in Europe and the US.

## **c) Lurbinectedin (PM1183)**

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

The CORAIL Phase III pivotal trial with Lurbinectedin as monotherapy vs. topotecan or pegylated liposomal doxorubicin in patients with platinum-resistant ovarian cancer completed recruitment in October 2016. A total of 443 patients were enrolled.

In August, PharmaMar received the green light from the Independent Data Monitoring Committee (IDMC) to continue with this trial. This decision was based on a futility analysis conducted with the first 210 patients (50% of the total) which assessed the safety and efficacy of Lurbinectedin in this indication.

The trial's primary endpoint is to assess progression free survival; secondary endpoints are overall survival, the objective response rate and patient quality of life variables. Patients are currently being monitored to determine progression-free survival and secondary variables.

### **Advanced breast cancer**

The clinical data obtained from analysing the Phase II A arm (breast cancer patients with a BRCA 1 or 2 mutation) were selected for an oral presentation at the European Society for Medical Oncology (ESMO) 2016 Conference, held in Copenhagen from 7 to 11 October 2016. In the Phase II clinical trial in advanced breast cancer, recruitment is ongoing in the A1 arm, consisting of breast cancer patients with BRCA 1 or 2 mutations who had been pre-treated with PARP inhibitors.

The registration strategy for Lurbinectedin in breast cancer patients with the BRCA gene mutation was discussed and agreed upon with the FDA at a meeting in Washington in December 2016.

### **Small-cell lung cancer**

In August, PharmaMar commenced the ATLANTIS Phase III trial, which compares the activity and safety of the combination of Lurbinectedin, a drug of marine origin, plus doxorubicin with topotecan or CAV (cyclophosphamide, adriamycin and vincristine) for treating patients with small-cell lung cancer who have relapsed after a first round of platinum treatment. Topotecan is the only drug approved in the US and Europe for this indication. FDA approval to commence the trial had been obtained in February.

ATLANTIS is an open label, randomized controlled multicenters Phase III trial that will enrol 600 patients in over 150 centers throughout the world. The trial's primary endpoint is to demonstrate an increase in progression free survival in the experimental arm, as assessed by an IDMC using the RECIST 1.1 criteria. Secondary endpoints include overall survival, response duration, quality of life variables, response rates in accordance with RECIST 1.1, and the correlation between pharmacokinetics and pharmacodynamics.

### **Combination trials**

As regards Phase I combination trials, recruitment was completed for the combinations of Lurbinectedin with either doxorubicin, cisplatin, capecitabine and paclitaxel with or without bevacizumab. The latter two trials produced promising preliminary results in a range of breast cancer types, among others; consequently, the next stages of development for this indication are currently being assessed. These results were presented as a poster at the European Society for Medical Oncology (ESMO) 2016 Conference, which was held in Copenhagen from 7 to 11 October this year. The results of the combination trial with cisplatin were presented at the European Cancer Organisation (ECCO) Congress, which was held in Amsterdam on 27-30 January 2017,

Recruitment continues on schedule for the Phase I trial in combination with irinotecan.

### **Basket trial in advanced solid tumours**

Recruitment is continuing for the Phase II trial with Lurbinectedin as monotherapy in indications chosen on the basis of the drug's mechanism of action or on the basis of its activity as observed previously in combination cancer trials. Those indications are small cell lung, neuroendocrine tumors, head and neck, germ cell cancer, endometrial, bile duct ,



cancer of unknown primary origin (CUP), and Ewing's sarcoma. Recruitment is continuing in the cohorts of endometrial cancer, small-cell lung cancer, germ cell cancer and Ewing's sarcoma. The trial is being conducted in Belgium, France, Germany, Italy, Spain, Switzerland, the United Kingdom and the United States.

#### **d) PM060184**

The Phase I dose escalation trial assessing the combination of PM184 with gemcitabine is recruiting on schedule. It is being conducted at two centers, one in Spain and one in the US. There are plans to include patients with specific diseases in which clinical benefit has been observed, such as non-small-cell lung cancer, breast cancer and tumors of the head and neck.

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

## **2. Diagnostics Genómica**

Genómica's revenues were €6.43 million in 2016, i.e. 1% more than in 2015 (€6.35 million).

Clinical diagnostics is the main area of activity, accounting for 94% of revenues.

The domestic market in diagnostics expanded by 4%, with revenues totalling €3.05 million in 2016 compared with €2.92 million in 2015.

Exports accounted for 46% of revenues and amounted to €2.98 million in 2016 (€3.21 million in 2015). Exports to Europe declined, while exports to Latin America increased by 22% to €1.37 million in 2016 (€1.13 million in 2015).

Continuing with efforts at international expansion, three new distribution deals were signed in and Asia in 2016: for India (ICS Incorporation Ltd.), South Korea (AG Bio Diagnostics Co.) and Malaysia (INTERSCIENCE Sdn Bhd), which are expected to be fruitful in future years.

There was considerable R&D activity in 2016 that saw a total of 36% of revenues spent there

In the area of infectious diseases, an enhanced version of the CLART® PneumoVir kit was launched which focuses on detecting respiratory viruses; CLART® PneumoVir2 allows for the faster detection of more targets than its predecessor, including coronavirus OC43, coronavirus NL63 and influenza A H7N9. Also, a new version of CLART® HPV2 was released. This is an accelerated freeze-dried product that can be transported and stored at room temperature, which is a comparative competitive advantage by avoiding the drawbacks of shipping a frozen product to distant countries, and we believe should open up new sales opportunities.

As for oncology, the CLART® EGFR BL kit for detection in blood of 39 mutations of the EGFR gene which are significant in lung cancer was released. This kit makes it possible to track and monitor an oncological patient without requiring a solid biopsy.

Additionally, the CLART®CMA ALK-ROS1 kit, launched in 2016, detects and provides genetic identification of the main chromosome translocations in the ALK and ROS1 genes in patients with lung cancer.

At the end of the year, the company had 11 families of patents, each comprising the outcome of registering a given invention in different territories (Spain and internationally).

Genómica holds 31 patents (in the EU, China, Israel, Mexico, Russia and Canada) and 20 patent applications that are pending (in the EU, international patent applications under PCT, the USA, Brazil, Canada, India, Mexico and China).

### **3. RNA interference: Sylentis**

The Phase IIb clinical trial with Bamosiran (SYL040012) in glaucoma and ocular hypertension to determine the optimal dose and the efficacy vs. a comparator (timolol) has concluded. In view of the results, Sylentis is exploring the possibility of trials combining Bamosiran with other treatments on the market. Consequently, Sylentis is awaiting progress with these negotiations before proceeding with clinical development of this product.

Sylentis completed the second Phase II trial with SYL1001 in Dry eye syndrome in March 2016. Both of the Phase II trials were multi-center randomized parallel group double-blind, placebo controlled, and they took place at eight centers in two European countries: Spain and Estonia. The results of the Phase II trials evidenced SYL1001's efficacy in improving the 'signs and symptoms' of Dry eye syndrome in patients, as well as determining the most effective dose.

In June, Sylentis presented the Phase II results and the clinical strategy for subsequent stages to the FDA. The protocol for Phase III clinical development was defined subsequently, and the centers for the next trial with SYL1001 were selected; the regulatory documentation has been drafted and a CRO has been engaged to perform the trial. All the documentation was presented to the Estonian State Agency of Medicines to obtain approval for this clinical trial in Estonia. The documentation will be presented in the other participating countries early in 2017.

Additionally, a new line of research is being pursued to develop RNAi candidates for treating diseases of the retina.

### **B) Consumer chemicals:**

#### **1. Xylazel (varnishes and paints for protecting wood and metal)**

In 2016, Xylazel increased revenues by 16% to €19.2 million (€16.6 million in 2015).

As a result, it has achieved 30% compound annual growth in revenues over the last three years.

Exports also increased notably and now account for close to 12% of total revenues.

Average raw material prices continued to be beneficial for raw materials and packaging: there was a decline in prices, particularly of petroleum derivatives.

EBITDA amounted to €1.9 million in 2016, a 40% increase with respect to 2015 (€1.4 million).

This growth was driven by actions focused on the interior decoration niche, into which Xylazel first made inroads in 2015; sales of Rust Oleum-Xylazel co-branded chalky finish paint for furniture made a notable contribution. Xylazel continues to address this niche very effectively with novel marketing approaches to end users, such as on-site workshops and interactions in social media.

#### **2. ZelnovaZeltia and Copyr (household insecticides, air fresheners and other household cleaning products)**

In 2016, combined sales by Zelnova-Copyr increased by €660 thousand (+1.3%) with respect to 2015. This performance was due broadly to Copyr's product lines: Hygiene Systems, Home & Gardening and Ecological Agriculture (in the latter case, because of Europe-wide expansion of its line of ecological products based on natural pyrethrins). This trend confirms the prospects for natural pyrethrin, Copyr's leading product for ecological farming.

The increase in Copyr sales and the recovery by geographies (France, Switzerland, Portugal and several African countries) offset less positive performance in the domestic market. Insecticide sales (Casa Jardin, ZZ Paff and Kill Paff) declined in Spain as a result of adverse weather conditions. The other business lines (household cleaning and private labels) increased sales year-on-year.

The table below shows the breakdown of sales by geographic market, Sales outside Spain exceeded domestic sales for the first time and now account for 51% of the total. This situation, which is positive for the Company's future growth, is the result of several years of efforts in foreign markets (61 countries in 2016, up from 55 in 2016).

(thousand euro)	2015	2016	Change	
Sales in Spain	26,493	25,130	-1,363	-5.1%
Sales in other countries	24,444	26,467	+2,023	+8.3%
Total net sales	50,937	51,597	+660	+1.3%

As for costs, raw material prices were broadly stable in the first half, while the euro/dollar exchange rate had a positive impact on Copyr's purchases of pyrethrum extracts in dollars. However, the price of petroleum derivatives rose moderately towards the end of the year.

<b>BALANCE SHEET</b> <i>(Thousand euro)</i>	<b>12/31/2016</b>	<b>12/31/2015</b>
<b>ASSETS</b>		
<b>Non-current assets</b>	<b>100.145</b>	<b>99.804</b>
Property, plant & equipment	31.141	30.624
Investment properties	6.119	6.157
Intangible assets	24.900	26.829
Goodwill	2.548	2.548
Long-term financial assets	1.138	1.067
Deferred tax assets	34.299	32.579
<b>Current assets</b>	<b>120.992</b>	<b>112.135</b>
Inventories	22.158	22.990
Customer and other receivables	62.652	40.200
Current financial assets	18.077	37.996
Other current assets	3.815	3.320
Cash & cash equivalents	14.290	7.629
<b>TOTAL ASSETS</b>	<b>221.137</b>	<b>211.939</b>

<b>BALANCE SHEET</b> <i>(Thousand euro)</i>	<b>12/31/2016</b>	<b>12/31/2015</b>
<b>EQUITY</b>		
<b>Shareholders' equity</b>	<b>52.358</b>	<b>76.874</b>
Share capital	11.110	11.110
Share premium	69.189	69.189
Treasury shares	(3.247)	(2.944)
Revaluation and other reserves	11	8
Retained earnings and other reserves	(24.705)	(489)
<b>Minority interest</b>	<b>(3.863)</b>	<b>(3.838)</b>
<b>TOTAL EQUITY</b>	<b>48.495</b>	<b>73.036</b>
<b>LIABILITIES</b>		
<b>Non-current liabilities</b>	<b>85.478</b>	<b>68.280</b>
Financial debt	67.583	64.973
Non-current deferred revenues	16.790	2.709
Other non-current liabilities	1.105	598
<b>Current liabilities</b>	<b>87.164</b>	<b>70.623</b>
Supplier and other accounts payables	39.175	31.959
Financial debt	27.906	28.629
Derivatives	0	14
Provisions for other liabilities & expenses	6.988	6.306
Current deferred revenues	10.012	54
Other current liabilities	3.083	3.661
<b>TOTAL LIABILITIES</b>	<b>172.642</b>	<b>138.903</b>
<b>TOTAL LIABILITIES AND EQUITY</b>	<b>221.137</b>	<b>211.939</b>

<b>INCOME STATEMENT</b>		
<i>Thousand euro</i>	<b>12/31/2016</b>	<b>06/30/2015</b>
Revenues:		
Product Sales	164.035	161.992
Co-development	11.129	29.034
Licensing agreements	5.779	1.788
Other income	5	1.003
	<b>180.948</b>	<b>193.817</b>
Cost of sales	(43.971)	(45.705)
Other operating revenues	1.533	3.824
Marketing & commercial organisation expenses	(47.688)	(48.614)
General and administration expenses	(20.328)	(19.984)
Research & development expenses	(78.423)	(60.291)
Other operating expenses	(10.777)	(11.750)
<b>Net operating profit (loss) (EBIT)</b>	<b>(18.706)</b>	<b>11.297</b>
Net financial results	(5.993)	(5.388)
<b>Result from continuing operations</b>	<b>(24.699)</b>	<b>5.909</b>
Corporate income tax in the period	592	654
<b>Profit (Loss) for the year</b>	<b>(24.107)</b>	<b>6.563</b>
Profit for the year	(24.107)	6.563
<b>Attributable to owners of the parent</b>	<b>(24.082)</b>	<b>6.588</b>
Attributable to minority interest	(25)	(25)

<b>Net operating profit (loss) (EBIT)</b>	(18.706)	11.297
<b>Amortisation and depreciation</b>	7.672	8.011
<b>EBITDA</b>	<b>(11.034)</b>	<b>19.308</b>

**CONSOLIDATED OF CASH FLOW**

<b>INTERIM CONDENSED CONSOLIDATED STATEMENT OF CASH FLOW (Thousand euro)</b>	<b>2016</b>	<b>2015</b>
<b>Cash flows from operating activities</b>		
<b>Income before taxes:</b>	<b>(24.699)</b>	<b>5.909</b>
<b>Adjustments for:</b>	<b>13.677</b>	<b>12.594</b>
Depreciation and amortization	7.243	6.281
Provision for impairment of accounts receivable	258	(44)
Impairment losses of property, plant and equipment and investment property	171	1.774
Fair value loss/(gain) on financial assets	(14)	(26)
Finance income	(256)	(258)
Finance costs	5.214	5.509
Share based payments	303	308
Deferred income - grants	76	(1.036)
Provisions	682	86
<b>Changes in working capital:</b>	<b>7.981</b>	<b>(1.755)</b>
Inventories	832	1.414
Trade and other receivables	1.290	(3.167)
Other assets and liabilities	(1.357)	(3.251)
Trade and other accounts payable	7.216	3.249
<b>Other cash flows from operations:</b>	<b>(5.374)</b>	<b>(5.664)</b>
Interest paid	(5.241)	(5.529)
Interest received	241	230
Income tax paid	(374)	(365)
<b>Net cash inflow from operating activities</b>	<b>(8.415)</b>	<b>11.084</b>
<b>Cash flows from investing activities</b>		
<b>Acquisitions:</b>	<b>(47.674)</b>	<b>(63.632)</b>
Property, plant and equipment, intangible assets and investment property	(6.093)	(9.288)
Other financial assets	(41.581)	(54.344)
<b>Proceeds from:</b>	<b>61.558</b>	<b>35.378</b>
Property, plant and equipment, intangible assets and investment property	129	70
Other assets		0
Other financial assets	61.429	35.308
<b>Other investing cash flow:</b>	<b>(105)</b>	<b>(74)</b>
Other investment receipts/(payments)	(105)	(74)
<b>Net cash (outflow) from investing activities</b>	<b>13.779</b>	<b>(28.328)</b>
<b>Cash flows from financing activities</b>		
<b>Receipts and (payments) in connection with equity instruments:</b>	<b>(632)</b>	<b>6.169</b>
Purchase of treasury shares	(4.165)	(4.684)
Proceeds from shares issued	3.533	10.853
<b>Receipts and (payments) in connection with financial liabilities:</b>	<b>1.926</b>	<b>(23)</b>
Proceeds from borrowings	20.140	34.867
Repayment of borrowings	(18.214)	(34.890)
<b>Other financing cash flow</b>	<b>2</b>	<b>2.176</b>
Other financing receipts/(payments)	2	2.176
<b>Net cash (outflow) from financing activities</b>	<b>1.296</b>	<b>8.322</b>
<b>Net increase (decrease) in cash and cash equivalents</b>	<b>6.660</b>	<b>(8.922)</b>
Cash and cash equivalents at beginning of the year	7.629	16.551
<b>Cash and cash equivalents at period ended September 30</b>	<b>14.289</b>	<b>7.629</b>