

#### **REPORT AT 30 SEPTEMBER 2018**

Madrid, 30 October 2018

#### 9 month MILESTONES 2018

# Corporate

- Group revenues amounted to €133.4 million in the first nine months of 2018, compared with €123.9 million in the same period of 2017.
- EBITDA from continuing operations amounted to €2.3 million (€6.2 million in the same period of 2017).
- On 20 September, PharmaMar completed the sale of subsidiary Xylazel, which manufactures, supplies and distributes products for wood and metal treatment, protection and decoration, special paints and other similar and related products, as well as other products for construction and related products.

The buyer, Akzo Nobel Coatings, S.L., acquired 100% of the shares of Xylazel for a cash price of €21.8 million.

The consolidated income statement of September 2017 has been restated taking into account the discontinued operation due to the sale of Xylazel, so that it is comparable to the one corresponding to September 2018.

# Oncology

- PharmaMar completed enrolment for the ATLANTIS registration trial with lurbinectedin in relapsed small cell lung cancer. Patients were recruited in 160 centers in 20 countries.
- The FDA has designated lurbinectedin as an orphan drug for the treatment of small cell lung cancer.

# **Diagnostics**

• The CLART® PneumoVir 2 and Pneumo CLART bacteria® diagnostic kits (both lyophilized) were released onto the market in September.

# RNAi

• In October, the HELIX Phase III trial being conducted with Sylentis for treating the signs and symptoms of dry eye syndrome achieved the 300 patients planned for the trial.

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#### 1. FIGURES TO SEPTEMBER 2018

	09/30/18	09/30/2017 (*)	Var.
Net Sales	57,425	64,603	-11.1%
Comercial sales	57,360	62,103	-7.6%
API sales	65	2,500	-97.4%
Royalties	2,582	3,887	-33.6%
License agreements	24,396	7,104	243.4%
ONCOLOGY TOTAL REVENUES	84,403	75,594	11.7%
DIAGNOSTICS REVENUES	4,381	4,400	-0.4%
CONSUMER CHEMICAL REVENUES	44,621	43,873	1.7%
GROUP TOTAL REVENUES	133,405	123,867	7.7%

(Thousand euro)

#### **Total Group revenues**

(\*) To make the two periods comparable, the revenues through September 2017 have been adjusted by classifying Xylazel as a discontinued operation as a result of the sale referred to on page 1 of this report.

Net revenues in the Oncology segment amounted to €57.4 million in the first nine months of 2018 (€64.6 million in the same period of 2017). The inter-year difference is attributable to a number of factors: the first is that sales of the raw material to Yondelis partners Janssen Products and Taiho Pharmaceutical amounted to €2.5 million in 2017 but to just €0.06 million in 2018; additionally, there was price erosion in some European countries and new competitors have appeared in both soft tissue sarcoma and relapsed platinum-sensitive ovarian cancer. Diagnostics sales (€4.4 million in 9M18 vs. €4.4 million in 9M17) reflect a setback in sales in Latin America which was almost fully offset by higher sales in the Middle East and Asia.

Revenues in the Consumer Chemicals division amounted to €44.6 million in the first 9 months of 2018, i.e. 1.7% more than in the same period of 2017 (€43.9 million). The decline in sales in the first half of the year was recovered in the third quarter.

**Royalty revenues**, which arise in the Oncology segment from partners Janssen Products and Taiho Pharmaceutical Co for sales of Yondelis in the United States, Japan and the rest of the world except the European Union, amounted to €2.6 million in the first 9 months of 2018 (€3.9 million in the same period in 2017); this reduction is due to commercialization of new products in the United States that compete with Yondelis®.

Revenues from licensing and other co-development agreements, which also correspond entirely to the Oncology segment, amounted to €24.4 million in the first 9 months of 2018, compared with €7.1 million in the same period in 2017.

Firstly, as a result of the early termination by Chugai Pharmaceutical Co. of the licensing agreement for Zepsyre for the Japan territory that was signed with PharmaMar in December 2016, the Group recognized €15.1 million in profit and loss statement as the part of the upfront payment collected upon signature of that agreement that had been deferred as a function of the progress with the clinical trials that the Group had undertaken to perform. PharmaMar also collected €3 million in additional revenues as a result of the early termination of the licensing agreement.

In the first quarter of 2018, the company signed a licensing agreement with Seattle Genetics Inc. under which the latter received exclusive worldwide rights over certain molecules and conjugated antibodies (ADCs) owned by Pharma Mar, S.A. for the development, production and commercialization of the conjugated antibodies. The Company received an upfront payment of \$5 million (€4.1 million).

PharmaMar also collected €2 million as a result of a marketing agreement with Impilo Pharma, a member of the IMMEDICA group, for the promotion and distribution of Yondelis® in certain European countries.

Consequently, **total revenues** amounted to €133.4 million in the first nine months of 2018, compared with €123.9 million in the same period of 2017 (+7.7%).

# **Gross margin and EBITDA**

The Group's gross margin was 72.5% of total revenues in the first nine months of 2018 (74% in the same period of 2017). (Calculated with respect to sales only, not including royalties or licensing revenues).

Group EBITDA from continuing operations as of September 2018 amounted to €2.3 million.

	09/30/2018	09/30/2017(*)
Net Result of continuing		
operations	(5.701)	(16.119)
Income Tax	(1.045)	220
Net Financial Income	3.405	3.718
Depreciation and Amortization	3.438	5.135
Severances	2.179	850
EBITDA	2.276	(6.196)
(Thousand euro)		

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

The EBITDA contribution by the business segments is as follows:

	09/30/2018	09/30/2017(*)
Oncology	12.012	830
Diagnostic	(3.343)	(711)
RNAI	(3.867)	(3.794)
QGC	3.884	3.735
Not asigned	(6.410)	(6.256)
EBITDA	2.276	(6.196)

(Thousand euro)

# **R&D** expenditure

R&D expenditure increased from €55.7 million net in the first nine months of 2017 to €57 million in the same period of 2018.

R&D	09/30/2018	09/30/2017	Difª	Var.
Oncology Segment	(49.801)	(51.443)	1.642	-3%
Diagnostic Segment	(3.139)	(1.172)	(1.967)	168%
RNAi Segment	(3.938)	(3.700)	(238)	6%
Consumer Chemicals Segment	(147)	(137)	(10)	7%
	(57.025)	(56.452)	(573)	1%
- Capitalization R&D	0	785	(497)	
TOTAL R&D	(57.025)	(55.667)	(1.070)	2%

(Thousand euro)

Capital expenditure in the Oncology segment focused basically on the clinical trials with Zepsyre: The ATLANTIS trial, Basket trial, and Phase I trial in Japan. The increase in the diagnostics area was due to investment in point-of-care diagnostics by Genómica.

<sup>(\*)</sup> To make the two periods comparable, results through September 2017 have been adjusted by classifying Xylazel as a discontinued operation as a result of the sale referred to on page 1 of this report.

# Other operating expenses

Other operating expenses, i.e. marketing and commercialization expenses, general and administration expenses, and other operating expenses (mainly corporate expenses), were stable overall with respect to the same period of 2017, amounting to \$51.2 million; commercialization expenses increased by \$0.9 million while administration, general and other operating expenses decreased by \$1.3 million.

#### **Cash and Debt**

As of 30 September 2018, the balance of cash, cash equivalents and current financial assets amounted to €30.4 million (vs. €31.8 million as of 2017 year-end). Including non-current financial assets, the total was €31.3 million as of 30 September 2018 (vs. €32.7 million as of 2017 year-end).

For the purpose of comparing the balance sheet figures, the Group's total net interest-bearing debt at amortized cost is detailed below:

	09/30/18	12/31/2017
Long term debt	65,560	73,607
Bank debt	26,780	33,394
Obligations and bonds	16,489	16,350
Govt. agencies: R&D funding	22,291	23,863
Short term debt	33,140	26,395
Credit facilities	14,620	9,974
Effects and certifications	2,185	2,203
Bank loan	10,619	8,676
Govt. agencies: R&D funding	4,895	4,730
Interest and others	821	812
Total financial debt	98,700	100,002
Cash & cash equivalents + no		
current and current financial		
investments	31,314	32,736
TOTAL NET DEBT	-67,386	-67,266
(Thousand euro)	07,300	07,200

The Group's long-term interest-bearing debt was reduced by €8 million, while current interest-bearing debt increased by €6.7 million, mainly due to more intensive use of credit lines. Total interest-bearing debt amounted to €98.7 million, compared with €100 million as of 31 December 2017.

The balance of cash and cash equivalents plus financial assets is similar to that at 2017 year-end.

# 2. BUSINESS PERFORMANCE.

Below is an overview of the group companies' business performance through September 2018.

# 1.- Oncology segment: PharmaMar

## a) Yondelis (Trabectedin)

#### Sarcoma

During the third quarter of 2018, a total of 22 clinical trials in soft tissue sarcoma were under way, fifteen of which were actively recruiting.

#### **Ovarian cancer**

There are currently nine post-authorization trials under way in this indication, seven of which are actively recruiting.

## Other indications

The analysis of the results of 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), is currently ongoing.

## b) ZEPSYRE® (Lurbinectedin)

The FDA Office of Orphan Products Development (OOPD) grants "orphan drug" status as means of supporting the development of medicines for the diagnosis, prevention or safe and effective treatment of diseases that affect less than 200,000 people in the United States. Orphan drug status offers a number of benefits, including a 7-year period of exclusivity in the market if the drug is finally approved, tax credits for clinical trials and exemption from fees on applications to the FDA for marketing approval.

## Small-cell lung cancer

Recruitment concluded in August for the ATLANTIS pivotal Phase III trial that compares the activity and safety of the combination of Zepsyre® (lurbinectedin, a drug of marine origin) plus doxorubicin, against 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. The trial has a primary endpoint of overall survival and data is expected around year end 2019. A total of 613 patients were enrolled. In the comparison arm, 42% of the patients were treated with topotecan and the other 58% with CAV.

#### Basket trial in advanced solid tumors

Recruitment is continuing for the Phase II basket trial with Zepsyre® as monotherapy in indications chosen on the basis of the drug's action mechanism or on the basis of its activity as observed in previous combination trials. Those indications are small cell lung cancer, neuroendocrine tumors, carcinoma of the head and neck, germ cell cancer, endometrial cancer, bile duct cancer, cancer of unknown primary, Ewing's sarcoma and breast cancer with BRCA 1/2 mutation.

Recruitment is ongoing for the small cell lung cancer cohort and the breast cancer BRCA 1/2 mutation cohort. The trial is being conducted in Spain, France, Belgium, the United States, Germany, Italy, Switzerland and the United Kingdom.

## **Combination trials**

As regards Phase I combination trials, recruitment was completed for the combinations with doxorubicin, cisplatin, capecitabine and paclitaxel with or without bevacizumab.

The updated survival data for the subgroup of patients with small cell lung cancer treated with the combination involving doxorubicin was presented at the International Association for the Study of Lung Cancer (IASLC) conference in Toronto in September 2018.

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

## Phase I trial in Japan

This trial, designed to ascertain the dosage for Zepsyre™ in Japanese patients, is still recruiting patients.

#### c) PM184

The Phase I dose escalation trial assessing the combination of PM184 with gemcitabine continues recruitment on schedule. This trial is being conducted at two centers: one in Spain and the other in the United States. Enrollment will be focused on specific diseases where clinical benefit has been observed, such as non-small cell lung cancer, breast cancer, and head and neck tumors.

#### Colorectal cancer

This Phase II trial in colorectal cancer enrolled its first patient in February 2018 and has enrolled 32 patients to date.

## d) PM14

The main endpoint of the Phase I trial is to identify the optimal dose for administration of PM14 in patients with advanced solid tumors, and to define the compound's safety profile and assess its pharmacokinetics and pharmacogenetics in treated patients. The trial, being conducted at Vall d'Hebron hospital (Barcelona), Doce de Octubre hospital (Madrid) and Institut Gustave Roussy (Paris), is expected to enroll approximately 50 patients with a confirmed diagnosis of advanced solid tumor for which there is no standard treatment available.

## e) APLIDIN®

After the rejection of the European Commission related to the approval of Aplidin®, on October 21st Pharma Mar AG presented a request for the withdrawal of the authorization for the commercialization of Aplidin® in Switzerland.

# 2.- Diagnostics Genómica

Genómica ended the third quarter of 2018 with €4.4 million in revenues, compared with €4.4 million in the same period of 2017.

In Spain, adjusting for the effect of the Castilla-La Mancha Regional Government's campaign for prevention and early detection of cervical cancer, revenues increased by 11% to €2.04 million (€1.84 million at the end of the third quarter of 2017). If the revenues from that program are included, revenues increased by 2%. However, the company expects that the larger budget allocation to this program in 2018 will enable revenues at year-end to be in line with the growth projections made at the beginning of the year.

Exports increased by 2% in the period (€1.84 million in 2018, vs. €1.81 million in 2017), including growth in the Middle East and Asia where, following registration by the distributors in those regions, sales of Autoclart® plus reader equipment amounted to €331,000 (€227,000 in 2017).

Exports accounted for 41% of revenues in the period.

The company's strategic focus on Point-of-care testing within the R&D area is advancing as expected.

## 3.- RNA interference: Sylentis

During the third quarter of 2018, research and development continued on new lines of RNA interference (RNAi) for topical treatment of diseases of the retina, such as age-related macular degeneration and diabetic retinopathy.

Regarding the Helix Phase III trial with Tivanisiran for treating dry eye syndrome, a total of 322 patients enrolled at the end of September 2018, and 277 of them had been randomized (92% of the total patients required to conclude the trial). The Helix trial is being conducted in six European countries: Spain, Germany, Italy, Estonia, Slovakia and Portugal. Clinical development of Bamosiran for treating glaucoma in combination with commercial drug Latanoprost is ongoing.

Preclinical toxicology trials with SYL1801, a compound for treating age-related macular degeneration (AMD), have commenced in order to assess product safety.

During the period, research and development continued on existing lines of RNA interference (RNAi), and new lines of research are being pursued in topical treatment of diseases of the retina, such as age-related macular degeneration and diabetic retinopathy.

Enrollment continues for the HELIX Phase III trial with Sylentis product Tivanisiran for treating dry-eye syndrome; the trial is designed for 300 patients and is being conducted in six European countries: Spain, Germany, Italy, Estonia,

Slovakia and Portugal. A total of 241 patients (i.e. 80% of the planned total) had been enrolled in the participating countries at the end of the period.

Clinical development of Bamosiran for treating glaucoma continued in combination with commercial drug Latanoprost.

# 4) Consumer chemicals:

## ZelnovaZeltia and Copyr (household insecticides, air fresheners and other household products)

Combined sales by Zelnova-Copyr increased by 1.7% year-on-year in the first nine months of 2018. This was achieved despite unusual weather conditions in the spring which negatively affected the onset of the insecticide season. The new line of OTC pharmaceutical products, launched at the beginning of the year, achieved 70% growth in sales. This line of business has been enhanced by expanding the portfolio and restyling the ZZ brand image. The air freshener segment also performed well: +6% year over year.

Copyr increased revenues by 3.0% year-over-year. Organizational and business changes made at this subsidiary resulted in a significant increase in sales, particularly in the Ecological Agriculture division, both in Italy and in the rest of Europe: sales amounted to €3.5 million (+11% year-on-year).

The table below shows the breakdown of sales by geographic market:

(Million euro)	Sept. 2017	Sept. 2018	
Sales in Spain	21,7	22,4	+ 3.2%
Sales in other countries	22,2	22,2	+ 0.2%
Total net sales	43,9	44,6	+ 1.7%

Prices of the main raw materials (butane, solvents, metal) show slightly rising trends. The Company is actively seeking more competitive sources worldwide, and productivity improvements in all areas have made it possible to keep costs in line with previous years.

The Company is confident that the new "A tu Aire" line of air fresheners will boost sales in this segment in the final months of the year so that it should broadly attain its revenue and earnings targets by year-end.

No major risks are observed for the remainder of the year since the sale of insecticides in this period is not material in comparison with the rest of the year.

BALANCE SHEET (Thousand euro)	09/30/18	12/31/2017
(Triousariu euro)	09/30/18	12/31/2017
ASSETS		
Non-current assets	86,578	94,543
Property, plant & equipment	27,059	31,207
Investment properties	6,071	6,119
Intangible assets	17,443	20,212
Goodwill	2,548	2,548
Long-term financial assets	885	977
Deferred tax assets	32,572	33,482
Current assets	88,272	93,178
Inventories	19,873	23,904
Customer and other receivables	32,844	31,388
Current financial assets	4,265	7,671
Other current assets	5,127	6,126
Cash & cash equivalents	26,164	24,089
TOTAL ASSETS	174,850	187,721

BALANCE SHEET		
(Thousand euro)	09/30/18	12/31/2017
EQUITY		
Shareholders' equity	32,135	26,866
Share capital	11,132	11,132
Share premium	71,278	71,278
Treasury shares	(2,533)	(4,470)
Revaluation and other reserves	13	13
Retained earnings and other reserves	(47,756)	(51,087)
Minority interest	(3,895)	(3,881)
TOTAL EQUITY	28,240	22,985
LIABILITIES		
Non-current liabilities	68,128	81,626
Financial debt	65,560	73,607
Non-current deferred revenues	1,806	7,234
Other non-current liabilities	761	785
Current liabilities	78,483	83,111
Supplier and other accounts payables	35,731	37,436
Financial debt	33,140	26,395
Provisions for other liabilities & expenses	7,136	6,232
Current deferred revenues	0	10,221
Other current liabilities	2,475	2,826
TOTAL LIABILITIES	146,610	164,736
TOTAL LIABILITIES AND EQUITY	174,850	187,721

INCOME STATEMENT			
Thousand euro	09/30/18	09/30/17	Chg. (%)
Revenues:			
Product Sales	106,199	112,863	
Co-development	24,396	7,104	
Licensing agreements	2,582	3,887	
Other income	228	13	
	133,405	123,867	7.7%
Cost of sales	(29,286)	(29,249)	
Marketing & commercial organisation expenses	(31,608)	(30,667)	
General and administration expenses	(12,901)	(13,270)	
Research & development expenses	(57,025)	(55,668)	
Other operating expenses	(6,731)	(7,623)	
Other operating revenues	805	429	
Net operating profit (loss) (EBIT)	(3,341)	(12,181)	-72.6%
Net financial results	(3,405)	(3,718)	
Result before income tax	(6,746)	(15,899)	-57.6%
Corporate income tax in the period	1,045	(220)	
Result from continuing operations	(5,701)	(16,119)	-64.6%
Result from discontinued operation	10,709	1,638	553.8%
Attributable to equity holders	10,709	1,638	
Profit for the year	5,008	(14,481)	-134.6%
Attributable to owners of the parent	5,022	(14,467)	-134.7%
Attributable to minority interest	(14)	(14)	

<sup>(\*)</sup> To make the two periods comparable, the Income Statement as of September 2017 have been adjusted by classifying Xylazel as a discontinued operation as a result of the sale referred to on page 1 of this report.

CONSOLIDATED CASH FLOW STATEMENT	09/30/18
TOTAL NET OPERATING CASH FLOW	(20,061)
Income before taxes	(6,746)
Profit before tax from continuing operations	(6,746)
Adjustments for:	8,815
Amortisation and depreciation	4,875
Other adjustements	3,940
Changes in working capital:	(21,608)
Other cash flow from operations:	(522)
Financial expenses	· 56
Financial revenues	(3,497)
Income tax received	2,919
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TOTAL NET INVESTING CASH FLOW	23,415
Investments payments:	(1,893)
Group companies, associates and business units	(16)
Purchases of property, plant & equipment and intangible assets	(1,872)
Other financial assets	(4)
Disvestment receipts:	25,308
Group companies, associates and business units	21,826
Purchases of property, plant & equipment and intangible assets	197
Other financial assets	3,285
TOTAL NET FINANCING CASH FLOW	(1,279)
Collections and (payments) in connection with equity instruments:	(400)
Acquisition	(2,072)
Disposal	1,672
Collections and (payments) in connection with financial liabilities:	(6,483)
Issue	3,098
Refund and amortization	(9,582)
Other financing cash flow:	5,604
Other financing receipts / (payments)	5,604
TOTAL NET CASH FLOW	2,075
Net increase / (decrease) in cash and cash equivalents	2,075
Beginning balance of cash and cash equivalents	24,089
ENDING BALANCE OF CASH AND CAHS EQUIVALENTS	26,164