REPORT AT 30 JUNE 2021

29 July 2021

MILESTONES IN 2021

Corporate

- Group net sales amounted to €65.0 million, 24% more than in the first half of 2020 (€52.6 million).
- Royalties from sales of Yondelis and Lurbinectedin by our partners in their respective territories amounted to €17.4 million, up from €1.4 million in the same period of 2020.
- Recurring revenues (sales plus royalties) increased by 53% with respect to the same period of 2020.
- Licensing revenues totaled €16.3 million, from the licensing agreement for Zepzelca signed with Jazz Pharmaceuticals in 2019 (€115.0 million in the same period of 2020).
- Total Group revenues amounted to €98.7 million (€169.1 million in 1H20).
- Operating cash flow totaled €13.3 million in the first half of 2021.
- Total debt and net cash were unchanged with respect to December 2020.

Oncology

- At ASCO 2021, PharmaMar presented data from the Phase Ib/II trial with Zepzelca in combination with irinotecan for treating small cell lung cancer.
- The NEPTUNO Phase III trial with plitidepsin for treating COVID-19 commenced.
- The Therapeutic Goods Administration (TGA), which is the Australian regulator, approved Yondelis for treating patients with liposarcoma or leiomyosarcoma.

Diagnostics

- Forthcoming launch of the new Fast Clart PneumoVir kit; in addition to simultaneously detecting and identifying 20 viruses associated with respiratory infections, it can now detect coronavirus and has a shorter processing time.
- Genómica's qCOVID-19 Respiratory COMBO kit has been validated for use with direct saliva samples.

RNAi

- The first patients were enrolled in a Phase III trial with SYL1001 in dry eye disease associated with Sjögren's syndrome.

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FIGURES TO JUNE 2021

	06/30/2021	06/30/2020	Var.
Oncology Sales	62.517	46.950	33%
Commercial Sales	*55.003*	*44.334*	24%
API sales	*7.514*	*2.616*	187%
Diagnostics Sales	2.465	5.639	-56%
Sales	**64.982**	**52.589**	**24%**
Royalties	**17.383**	**1.420**	**1124%**
Licences	**16.280**	**114.966**	
Other	**47**	**135**	
TOTAL REVENUES	**98.692**	**169.110**	**-42%**

(Thousand euro)

Group revenues:

Group net revenues amounted to €65.0 million in the first half of 2021, up 24% on the same period of 2020 (€52.6 million). This increase was due to good performance by oncology sales. Sales of Zepzelca under the Temporary Authorisation for Use (TAU) in Europe amounted to €15.8 million, a 169% increase on the €5.6 million reported in the same period of 2020. Yondelis sales in European were stable year-on-year at €36.7 million (vs. €36.9 million in the same period of 2020). Sales of Yondelis and Zepzelca raw materials to partners rose from €2.6 million in the first half of 2020 to €7.5 million this year (+187%). Diagnostics sales fell €3.1 million year-on-year, impacted by lower demand and the drastic decline in the price of COVID-19 diagnostics tests.

Royalties revenues amounted to €17.4 million in the first half of 2021, up from €1.4 million in the same period last year. That figure includes royalties from Yondelis sales by our partners in the United States and Japan (€1.4 million) and from Zepzelca sales by our US partner Jazz Pharmaceuticals (€16 million). Royalties for the second quarter of 2021 are an estimate since the figures for sales by Jazz in that period were not available at the date of publishing this report.

Recurring revenue, i.e. net sales plus royalties from partners, increased by 53% year-on-year to €82.4 million in the first half of 2021 (from €54.0 million).

Licensing revenues amounted to €16.3 million in the first half of 2021, compared with €115.0 million in the same period of 2020. In both cases, those figures relate to the recognition, on the basis of progress with the contractual commitments, of amounts collected in 2020 as a result of the licensing agreement for Zepzelca with Jazz Pharmaceuticals.

R&D

Group **R&D** spending increased by 19.2% year-on-year to €28.9 million in the first half of 2021 (€24.3 million in the same period of 2020).

Oncology invested €24.4 million in the first half of 2021, including €5.5 million of costs incurred in clinical trials to develop plitidepsin (Aplidin) for the treatment of COVID-19.In the first half of 2021, the Oncology area made progress with trials of lurbinectedin in combination with other therapeutic agents, and in the design of new Phase III trials for small cell lung cancer and other indications, as well as in preparing new candidates for clinical development.

The interference RNA segment increased R&D spending to €3.9 million in the reporting period, reflecting commencement of the first of two Phase III trials in the US with tivanisiran in dry eye disease associated with Sjögren's syndrome, as well as the necessary preparatory work to commence the Phase I trial in Spain with SYL18001 in macular degeneration.

The breakdown of R&D expenditure is shown in the next table:

	06/30/21	06/30/20	Difª	
R&D expenses	**28.903**	**24.252**	**4.651**	**19,2%**
Oncology	24.410	22.687	1.723	7,6%
Diagnostics	572	279	293	105,0%
RNAi	3.921	1.286	2.635	204,9%

(Thousand euro)

Other operating expenses

Other operating, commercial, administrative and corporate expenses amounted to €25.0 million in the first half of 2021, a reduction of 4.7% with respect to the same period of 2020 (€26.2 million). This decline was due mainly to expenditure in 2020 as a result of the licensing agreement.

	06/30/21	06/30/20	Difª	
Other operating expense	**25.000**	**26.238**	**-1.238**	**-4,7%**
Marketing expenses	10.736	11.495	-759	-6,6%
General and Administrative	8.582	8.439	143	1,7%
Other operating expense (Corporate)	5.682	6.304	-622	-9,9%

(Thousand euro)

EBITDA

Group EBITDA amounted to €40.6 million in the first half of 2021 (€118.8 million in same period of 2020).

	06/30/21	06/30/20
Net result	**43.205**	**113.789**
Income tax	(3.925)	1.501
Net financial income	(1.328)	(265)
Depreciation and amortization	2.619	3.739
EBITDA	**40.571**	**118.764**

(Thousand euro)

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

The variation in EBITDA, from €118.8 million in the first half of 2020 to €40.6 million in the same period this year, reflects the lower amount of revenues recognized under the licensing agreement signed with Jazz Pharmaceuticals in December 2019 (€98.7 million less than in the first half of 2020), which was partly offset by higher sales and royalties (an increase of €28.4 million year-on-year). Overall, operating expenses (including R&D) increased by €3.4 million as a result of higher R&D expenditure.

Cash and Debt

As of 30 June 2021, cash and cash equivalents plus current and non-current financial assets amounted to €217.7 million (vs. €216.5 million as of 31 December 2020).

In the first six months of 2021, loans from banks and official agencies amounting to €6.3 million were repaid and new (mainly bank) loans in the amount of €5.4 million were arranged; as a result, total interest-bearing debt was similar to the December 2020 level.

For the purpose of comparing balance sheet figures, the Group's total net financial position at amortized cost is detailed below:

	06/30/2021	12/31/2020
Non current debt	**37.160**	**37.732**
Bank debt	5.790	3.561
Obligations and bonds	16.626	16.600
Govt. Agencies: R&D funding	14.744	17.571
Current debt	**16.152**	**15.313**
Credit facilities	5.217	4.771
Bank loan	5.318	5.487
Govt. Agencies: R&D funding	4.766	4.621
Interest and others	851	434
Total financial debt	**53.312**	**53.045**
Cash&cash equivalents + non current and current financial investment	**217.660**	**216.504**
TOTAL NET CASH / (DEBT)	**164.348**	**163.459**

(Thousand euro)

BUSINESS PERFORMANCE.

Below is an overview of research and development activities in the first half of 2021.

1.- Oncology segment: PharmaMar

Compounds:

A) Trabectedin (YONDELIS)

Soft tissue sarcoma

In the first half of 2021, 21 post-authorization trials were under way, 15 of them active (8 enrolling new patients). The other trials were in the process of closing and data analysis or were pending the presentation of results. Four additional trials are scheduled to commence in the coming months.

The preliminary results from the cohort of non-L soft-tissue sarcoma patients in the NiTraSarc Phase II trial to assess the efficacy of the combination of nivolumab with trabectedin, which showed that this is a viable combination, were presented at the ASCO 2021 meeting, which was held online on 4-8 June 2021. The results of the L-sarcoma cohort are expected to be presented at the CTOS 2021 meeting.

Also notable were the following publications in connection with two trials with Yondelis that have concluded: Publication in *Annals of Oncology* of the results of the T-SAR Phase III trial comparing trabectedin with best supportive care, which was sponsored by the French Sarcoma Group; the results confirmed that Yondelis offers superior disease control to supportive care without limiting quality of life in soft tissue sarcoma patients. And publication in *Cancers* of the results of the TroBs retrospective real-life trial involving 512 patients, sponsored by the Italian Sarcoma Group, which confirmed that Yondelis® offers clinical benefit to advanced sarcoma patients with multiple histologies.

Ovarian cancer
During the first half of 2021, there were 13 trials being managed in this indication: six of them were active (4 actively enrolling and 2 in the activation phase).

Other indications
Enrolment continued for the TOP-ART trial, which combines trabectedin and olaparib in treating solid tumors with DNA repair defects.

B) Lurbinectedin (ZEPZELCA)

Small-cell lung cancer
With regard to lurbinectedin, after discussion with the FDA, PharmaMar plans to initiate a confirmatory trial in relapsed second-line Small-Cell Lung Cancer (SCLC) later this year. This is expected to be a 3-arm trial, comparing lurbinectedin as either monotherapy or in combination with irinotecan vs. investigators' choice of irinotecan or topotecan. If positive, this trial could serve to confirm the benefit of lurbinectedin in the treatment of SCLC when patients progress following first-line treatment with a platinum-based regimen.

The registration dossier for Zepzelca in this indication is advancing in several countries.

Combination trials with Zepzelca (lurbinectedin)
Recruitment continues on schedule for the Phase I trial in combination with irinotecan, pembrolizumab and atezolizumab.

PharmaMar presented new data from the trial with Zepzelca in combination with irinotecan in patients with endometrial cancer at the ASCO 2021 Virtual Meeting, held on 4-8 June 2021. The data showed that the combination of lurbinectedin with irinotecan is effective in patients with advanced endometrial cancer after failure of more than one line of therapy. Data were presented from a total of 21 evaluable patients with advanced endometrial cancer, 75% of whom had received at least two previous lines of treatment. The Objective Response Rate (ORR) was 19%, with 6-month Progression-Free Survival (PFS) at 42%. The combination was found to have a manageable safety profile.

Phase I trial in China
The Phase I trial being conducted by our partner Luye and designed to ascertain the dose of Zepsyre® in Chinese patients is recruiting satisfactorily.

C) PM14

The main endpoint of the Phase I trial with PM14 is to identify the optimal dose for administration in patients with advanced solid tumors, to define the compound's safety profile, and assess its pharmacokinetics and pharmacogenetics in treated patients. The expansion phase in selected tumors continues to enroll patients.

The results of the dose-escalation phase were presented as a poster at the ASCO 2021 Meeting, on 4-8 June.

Phase I/II trials with this compound in combination with others are being designed and are expected to commence this year.

D) Virology Unit: Plitidepsin (APLIDIN®)

Aplidin (plitidepsin)

The APLICOV-PC trial in adult patients with COVID-19 requiring hospital admission attained its primary endpoint, safety; notably 74% of patients with moderate disease were able to be discharged in the first week of treatment. The NEPTUNO Phase III trial to determine plitidepsin's efficacy for treating patients hospitalized with moderate COVID-19 commenced in the data base of the former trial. This randomized, controlled Phase III clinical trial to determine the efficacy and safety of two dosages of plitidepsin versus control in adult patients requiring hospitalization for the treatment of moderate COVID-19 infection has already begun to enroll patients.

2.- Diagnostics Genómica

Genómica ended 1H21 with €2.5 million in net revenues (€5.8 million in the same period of 2020). That 57% decrease was due to lower sales of COVID-19 tests (PCR, antigen and antibody), mainly as a result of increased competition and a sharp decline in prices. Sales of non-COVID diagnostics tests (papillomavirus, herpes virus, respiratory infections, STDs, etc.) are recovering towards pre-pandemic levels, with the exception of the tests for respiratory diseases as the widespread use of masks eliminated demand for them this year. Exports are recovering, but much more slowly. Nevertheless, we expect exports and sales of the main non-COVID-19 kits to pick up in the second half as a result of improving pandemic figures.

Net sales in the first half of 2021 and 2020 are shown in the next table:

	06/30/21	06/30/20	
COVID-19 Tests	499	3.904	-87%
HPV and other Tests	1.793	1.678	7%
Other income	196	194	1%
Total	**2.487**	**5.776**	**-57%**

Thousand euro

In January, Genómica validated its qCOVID-19 Respiratory COMBO kit for use with direct saliva samples. This kit can detect SARS-CoV-2 in saliva samples.

The R&D Department is working on validation of a new kit that improves on the existing Clart® PneumoVir by including coronavirus detection and also shortening process times. It is expected to be launched in November 2021.

The international market accounts for 20% of revenues.

3.- RNA interference: Sylentis

Clinical development of tivanisiran for treating dry eye disease continued in the second quarter of 2021. In March 2021, the US Food and Drug Administration (FDA) authorized the SYL1001 V Phase III trial in treating dry eye disease associated with Sjögren's syndrome. A total of 31 hospitals in the US are participating and the trial plans to recruit 200 patients. This is a randomized, double-masked, placebo-controlled trial whose primary and secondary end-points are, respectively, the efficacy (signs and symptoms) and safety of tivanisiran in patients with dry eye disease associated with Sjögren's syndrome. The first patients was enrolled on 25 May 2021.

Additionally, the Spanish Agency of Medicines and Medical Devices (AEMPS) has authorized a Phase I trial with SYL1801 for the treatment and/or prevention of choroid neovascularization associated with pathologies such as age-related macular degeneration (AMD) and diabetic retinopathy. This Phase I trial involving 36 healthy volunteers is being conducted at Hospital Universitario Ramón y Cajal in Madrid. The trial will assess the safety of several doses of SYL1801 and the product's pharmacokinetics. Treatment of 21 volunteers was completed in the first half of 2021.

CONDENSED CONSOLIDATED STATEMENTS OF FINANCIAL POSITION (Thousand euro)	June 30, 2021	December,30 2020
ASSETS		
Non-current assets		
Property, plant and equipment	23.344	21.947
Investment property	845	845
Intangible assets	3.490	3.860
Right-of-use assets	3.836	3.552
Non-current financial assets	928	20.988
Deferred tax assets	33.416	33.416
	65.859	**84.608**
Current assets		
Inventories	10.744	11.933
Trade and other receivables	27.997	24.054
Financial assets at amortised cost	87.145	99.306
Other assets	21.210	14.148
Cash and cash equivalents	129.587	96.210
	276.683	**245.651**
TOTAL ASSETS	**342.542**	**330.259**

CONDENSED CONSOLIDATED STATEMENTS OF FINANCIAL POSITION (Thousand euro)	June 30, 2021	December,30 2020
EQUITY		
Share capital	11.013	11.013
Share premium	71.278	71.278
Treasury shares	(22.345)	(21.453)
Revaluation reserves	16	14
Retained earnings and other reserves	74.892	41.870
Total capital and reserves attributable to equity holders of the parent company	**134.854**	**102.722**
TOTAL EQUITY	**134.854**	**102.722**
LIABILITIES		
Non-current liabilities		
Borrowings	37.160	37.732
Lease liabilities	2.121	2.150
Non-current deferred income	90.895	92.560
Other non-current liabilities	178	176
	130.354	**132.618**
Current liabilities		
Trade and other payables	15.752	23.220
Borrowings	16.152	15.313
Lease liabilities	1.798	1.470
Outstanding remunerations	4.984	6.411
Current deferred income	31.140	43.603
Other current liabilities	7.508	4.902
	77.334	**94.919**
TOTAL LIABILITIES	**207.688**	**227.537**
TOTAL EQUITY AND LIABILITIES	**342.542**	**330.259**

CONDENSED CONSOLIDATED STATEMENTS OF PROFIT OR LOSS		
(Thousand euro)	**June 30, 2021**	**June 30, 2020**
Revenue:		
Revenue from contracts with customers	64.982	52.589
Revenue from licensing and development agreements (excluding royalties)	16.280	114.966
Royalties	17.383	1.420
Other	47	135
	98.692	**169.110**
Cost of sales	(7.620)	(3.854)
Gross profit	**91.072**	**165.256**
Marketing expenses	(10.736)	(11.495)
General and administrative expenses	(8.582)	(8.439)
Research and development expenses	(28.903)	(24.252)
Net impairment on financial assets	168	(167)
Other operating expenses	(5.682)	(6.304)
Other results	615	426
Operating loss	**37.952**	**115.025**
Finance costs	(5.116)	(2.372)
Finance income	6.444	2.637
Finance costs - net	**1.328**	**265**
Result of the period before income taxes	**39.280**	**115.290**
Income tax benefit / (expense)	3.925	(1.501)
Result for the period	43.205	113.789
Result is attributable to:		
Equity holders of the parent company	43.205	113.808
Non-controlling interests	0	(19)

CONSOLIDATED CASH FLOW STATEMENT	EUR (Thousand)
	06/30/2021
TOTAL NET OPERATING CASH FLOW	**13.328**
Income before taxes	**39.281**
Profit before tax from continuing operations	*39.281*
Adjustments for:	**1.315**
Depreciation and amortization	2.725
Provision for impairment of accounts receivable	(105)
Finance income	(240)
Finance costs	1.457
Results on disposals of tangible/intangible assets	4
Share based payments	154
Deferred income - grants	(147)
Effects of exchange rate changes	(2.533)
Changes in working capital:	**(31.051)**
Inventories	1.188
Trade and other receivables	(3.838)
Other assets and liabilities	(5.526)
Trade and other accounts payable	(8.895)
Deferred or accrual items	(13.980)
Other cash flow from operations:	**3.783**
Financial expenses	(1.457)
Financial revenues	240
Income tax (collections/payments)	5.000
TOTAL NET INVESTING CASH FLOW	**31.478**
Investment payments:	**(2.786)**
Purchases of property, plant & equipment and intangible assets	(2.786)
Disvestment receipts:	**34.264**
Other financial assets	34.264
TOTAL NET FINANCING CASH FLOW	**(11.877)**
Collections and (payments) in connection with equity instruments:	**(316)**
Acquisition	(15.550)
Disposal	15.234
Collections and (payments) in connection with financial liabilities:	**(1.867)**
Loans received	5.379
Refund and amortization	(6.288)
IFRS16 Payment	(957)
Dividends paid to company's shareholders	**(10.872)**
Other financing cash flow:	**1.177**
Other financing receipts / (payments)	1.177
EFFECTS OF EXCHANGE RATE CHANGES ON CASH AND CASH EQUIVALENTS	**449**
TOTAL NET CASH FLOW	**33.378**
Beginning balance of cash and cash equivalents	96.210
ENDING BALANCE OF CASH AND CAHS EQUIVALENTS	**129.587**