



## REPORT AT 31 MARCH 2023

26 April 2023

### MILESTONES

#### **Corporate**

- Group revenue in the first quarter of 2023 amounted to €34.0 million (vs. 53.2 in the same period of 2022), reflecting the impact of the release of generic trabectedin.
- Royalties from sales of Yondelis and Zepzelca by our partners in their respective territories amounted to €11.1 million (vs. 11.0 in the year-ago quarter).
- Operating cash flow amounted to €7.7 million in the first quarter of 2023 (vs. €35.8 million in 1Q22).
- As of 31 March 2023, the net cash balance, after deducting net interest-bearing debt, amounted to €191.4 million (vs. 192.8 million as of 31 December 2022).

#### **Oncology**

- In March, PharmaMar received temporary authorization from the Swiss Agency for Therapeutic Products (Swissmedic) to market Zepzelca® (lurbinectedin) for the treatment of adult patients with small-cell lung cancer.
- In January 2023, PharmaMar partner Adium Pharma received full approval from the Mexican Federal Commission for Protection against Health Risks (COFEPRIS) to market Zepzelca® (lurbinectedin) for the treatment of adult patients with small cell lung cancer.
- Also in January, PharmaMar partner Megapharm Ltd. received conditional approval from the Israeli Ministry of Health to market Zepzelca® (lurbinectedin) for treating adult patients with small-cell lung cancer.

#### **Virology**

- The first patient was enrolled in the Nereida Phase II clinical trial in April. This trial's goal is to evaluate the efficacy of plitidepsin in pre-specified groups of immunosuppressed patients with symptomatic COVID-19 requiring hospitalization.

M<sup>a</sup> Luisa de Francia  
CFO  
PHARMA MAR, S.A.  
Plaza Descubridor Diego de Ordás, 3  
Madrid  
Telephone 91.444.45.00

José Luis Moreno  
Head of Capital Markets and Investor Relations  
PHARMA MAR, S.A.  
Plaza Descubridor Diego de Ordás, 3  
Madrid  
Telephone 91.444.45.00

## FIGURES TO MARCH 2023

	03/31/2023	03/31/2022	Var.
<b>RECURRING REVENUE</b>	<b>27,445</b>	<b>45,942</b>	<b>-40%</b>
Oncology sales	15,219	33,560	-55%
Diagnostics sales	1,152	1,378	-16%
Royalties	11,074	11,004	1%
<b>NON RECURRING REVENUE</b>	<b>6,534</b>	<b>7,244</b>	<b>-10%</b>
License Agreements	6,515	7,194	-9%
Other	19	50	-62%
<b>TOTAL REVENUES</b>	<b>33,979</b>	<b>53,186</b>	<b>-36%</b>

(Thousand euro)

### Group revenue:

Group revenue totaled €34.0 million in 1Q23, compared with €53.2 million in the same period of 2022. The breakdown of that figure is as follows:

**Recurring revenues** are the sum of the Group's net sales and royalties from sales by our partners. This item went from €45.9 million in 1Q22 to €27.4 million in 1Q23. This 40% variation with respect to the previous year is due mainly to the decrease in oncology sales.

Net revenue in the oncology segment amounted to €15.2 million in the first quarter of 2023, down 55% on the year-ago quarter (€33.6 million). The breakdown of net revenue is as follows:

- i) Net sales of Yondelis in the European market. This item amounted to €8.1 million in 1Q23 (vs. €17.5 million in 1Q22). This variation is a consequence of the release of generic trabectedin on the market in the last quarter of 2022, resulting in significant pressure on prices. In terms of sales by milligram, the decline was 9% year-on-year. Yondelis received its first marketing authorization in 2007, so it has been on the market for more than fifteen years.
- ii) Zepzelca revenue in Europe, mainly in France under early access programs. This revenue amounted to €5.6 million in the first quarter of 2023 (vs. €8.7 million in the year-ago quarter). The difference is due to the entry into force in France of a regulation imposing significant discounts on the prices of drugs made available in the compassionate use program under which Zepzelca is distributed in that territory. The figures for 1Q22 did not reflect an impact from that regulation. Unit sales were similar to the previous year.
- iii) Sales of raw materials, both Yondelis and Zepzelca, to our partners. This item amounted to €1.5 million in the first quarter of 2023, compared with €7.4 million in the year-ago quarter. This difference is temporary as our partners stocked up in previous quarters and there is a lag in purchase orders, so that this item is expected to rebound in the coming months.

**Royalties** revenue amounted to €11.1 million in the first quarter of 2023, compared with €11.0 million in the year-ago quarter. That figure includes royalties from Zepzelca sales by our US partner, Jazz Pharmaceuticals, amounting to €10.2 million in the first quarter (10.2 in the year-ago quarter). Royalties in both quarters are an

estimate since Jazz's sales figures in that period were not available at the date of publishing this report; deviations are corrected in the subsequent quarter. Royalties increased by 7% year-on-year in real terms, but this is not reflected here as royalties were overestimated in 1Q22.

In addition, royalties were also received for sales of Yondelis by our partners in the United States and Japan in the amount of €0.9 million in the first quarter of 2023 (vs. €0.8 million in the year-ago quarter).

**Non-recurring revenue**, mainly from out-licensing agreements, amounted to €6.5 million in 1Q23, compared with €7.2 million in 1Q22.

Revenue under this heading in the first quarter of 2023 and 2022 was entirely from licensing agreements for Zepzelca. In the first quarter of 2023, €6.0 million in revenue were recognized out of the USD 300 million received in 2020 under the Zepzelca license agreement to Jazz Pharmaceuticals, and €0.5 million were recognized for attaining milestones under various agreements with other partners. Almost all the revenue under this heading in the first quarter of 2022 was under the agreement with Jazz Pharmaceuticals (€7.2 million).

## R&D

**R&D** spending increased by 11% year-on-year to €21.1 million in the first quarter of 2023, from €19.0 million in the year-ago quarter.

Oncology spent €17.8 million on R&D in the first quarter, including €2.1 million on clinical trials to develop plitidepsin as an antiviral, which are recognized in this segment. Expenditure directly on oncology in the period was related mainly to the LAGOON confirmatory Phase III trial with lurbinectedin in small cell lung cancer, in which enrolment is proceeding, as well the commencement of two other Phase III trials with lurbinectedin: one in relapsed mesothelioma and one in front line leiomyosarcoma. Also noteworthy was spending on the clinical trial of ecubectedin in solid tumors, and progress with clinical trials in humans with PM534 for treating solid tumors, which commenced in the second half of 2022. Progress continues to be made in preparing new candidates for clinical development, as well as in researching new compounds in earlier phases and in preclinical trials to bring new molecules to the clinical pipeline.

The main R&D spending in the RNA interference segment relates to Phase III clinical trials with tivanisiran in dry eye associated with Sjögren's syndrome. A Phase II trial with SYL1801 for treating and/or preventing choroid neovascularization, a common cause of retinal diseases such as age-related macular degeneration (AMD) and diabetic retinopathy, has commenced.

	03/31/2023	03/31/2022	Dif <sup>a</sup>	
<b>R&amp;D expenses</b>	<b>21,056</b>	<b>19,028</b>	<b>2,028</b>	<b>11%</b>
Oncology	17,751	16,089	1,662	10%
Diagnostics	0	528	-528	-100%
RNAi	3,305	2,411	894	37%

(Thousand euro)

## Other operating expenses

Operating expenses: the Group spent €13.3 million on marketing and commercial, general and administrative expenses in the first quarter of 2023, a 4.5% decrease year-on-year (€13.9 million in 2022). The decrease in administrative and general expenses is mainly due to expenses incurred in 2022 in connection with the transfer of technology for the production of lurbinectedin intermediates. The other operating expenses account mainly includes expenses incurred in corporate activities (not allocated to any segment), amounting to €3.4 million

(€2.7 million in the year-ago quarter); the increase between years is due mainly to the contribution to the PharmaMar Foundation.

	03/31/2023	03/31/2022	Dif <sup>a</sup>	
<b>Other operating expense</b>	<b>13,275</b>	<b>13,897</b>	<b>-622</b>	<b>-4.5%</b>
Marketing expenses	6,036	6,019	17	0.3%
General and Administrative	3,799	5,183	-1,384	-26.7%
Other operating expense (Corporate)	3,440	2,695	745	27.6%

(Thousand euro)

## EBITDA

Group EBITDA amounted to (€1.3 million) in 1Q23 and €20.6 million in 1Q22, calculated as follows:

	03/31/23	03/31/22
<b>Net result</b>	<b>1,411</b>	<b>21,975</b>
Income tax	(4,628)	(1,352)
Net financial income	645	(1,609)
Depreciation and amortization	1,314	1,615
<b>EBITDA</b>	<b>(1,258)</b>	<b>20,629</b>

(Thousand euro)

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

The variation in EBITDA is due mainly to the increase in R&D expenses (€2.0 million) between the two periods and the reduction in revenue (€19.2 million).

## Cash and Debt

As of March 31, 2023, total debt had increased by €0.8 million compared to December 31, 2022. This was due to repayment of loans to banks and official agencies in the amount of €2.1 million. New loans arranged in the first quarter of 2023 were from official agencies and amounted to €2.5 million (no new official funding or bank loans were arranged in the year-ago quarter).

The Group ended the first quarter of 2023 with a positive net cash position of €191.4 million (vs. €192.8 at 2022 year-end). This level of net cash will enable the Group to undertake the planned development and R&D work without cash stresses.

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

	03/31/2023	03/31/2022	Var.
<b>Non current debt</b>	<b>26,562</b>	<b>25,883</b>	<b>679</b>
Bank debt	174	231	-57
Obligations and bonds	16,724	16,709	15
Govt. Agencies: R&D funding	9,664	8,943	721
<b>Current debt</b>	<b>13,213</b>	<b>13,125</b>	<b>88</b>
Credit facilities	4,645	3,506	1,139
Bank loan	4,133	4,430	-297
Govt. Agencies: R&D funding	3,651	3,791	-140
Interest and others	784	1,398	-614
<b>Total financial debt</b>	<b>39,775</b>	<b>39,008</b>	<b>767</b>
<b>Cash&amp;cash equivalents + non current and current financial investment</b>	<b>231,138</b>	<b>231,818</b>	<b>-680</b>
<b>TOTAL NET CASH / (DEBT)</b>	<b>191,363</b>	<b>192,810</b>	<b>-1,447</b>

(Thousand euro)

## RESEARCH AND DEVELOPMENT

Below is an overview of research and development activities.

### 1.- Oncology segment: Pharma Mar. Compounds:

#### A) Lurbinectedin (ZEPZELCA)

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

The LAGOON pivotal Phase III trial as treatment for relapsed small cell lung cancer that had been agreed upon with the FDA continues enrolling patients. This is a three-arm trial comparing lurbinectedin as monotherapy or in combination with irinotecan against investigator's choice of irinotecan or topotecan.

If the outcome is positive, the trial could confirm the benefits of lurbinectedin for treating small cell lung cancer when patients have experienced progression after first-line treatment with platinum in the USA, and would serve as a registration trial for territories outside the USA.

Recruitment continues for the Phase III trial that our partner Jazz Pharmaceuticals and Hoffmann-La Roche are conducting with Zepzelca® in combination with Atezolizumab, a PD-L1 inhibitor, for first-line maintenance treatment of small cell lung cancer. This trial, which is sponsored by Hoffmann-La Roche and co-financed by Jazz, will measure progression-free survival and general survival with Zepzelca® in combination with atezolizumab as compared with atezolizumab as sole agent. This study will provide information on a novel first-line treatment option for small cell lung cancer. Our partner estimates that enrolment for this trial will conclude in 2023.

We continue to await the analysis of the data collected in the retrospective study in France, which included patients who received lurbinectedin as part of the "ATU nominative" (named-patient authorization) program, also called "French Early Access Program", to describe the clinical and demographic characteristics of these patients by assessing overall survival, real-world progression-free survival, etc. This study is headed by

*Intergroupe Francophone de Cancérologie Thoracique and Groupe Français de Pneumo-Cancérologie*, and the principal investigator is Professor Nicolas Girard of Institut Curie (Paris).

### **Combination trials with Zepzelca (Irbinitectin)**

Recruitment continues on schedule for the Phase I trials in combination with irinotecan and with atezolizumab.

Specifically, the combination trial with irinotecan continued in the expansion phase in small cell lung cancer, synovial sarcoma and neuroendocrine tumors, as planned.

Patient enrolment for the combination trial with pembrolizumab has concluded and the trial is in the monitoring phase.

### **B) Ecubectedin (PM14)**

The first Phase I/II trial with ecubectedin attained the optimal dose in patients with advanced solid tumors. An expansion Phase II basket trial with a number of tumor types is currently enrolling patients.

### **Combination trials**

Recruitment for the Phase I/II trial with this compound in combination with irinotecan is progressing satisfactorily. The Phase Ib trial in combination with atezolizumab is also recruiting satisfactorily.

### **C) PM54**

The regulators have approved for this new compound to enter in clinical trials and we expect patient enrolment to commence this year.

### **D) PM534**

A new Phase I trial commenced in December 2022 with PM534, a new antitumor compound of marine origin arising from the company's solid tumor research program. The endpoints of this first trial are to find the recommended dose and assess the safety and efficacy profile. The trial will be conducted in patients with advanced solid tumors, who will receive the drug intravenously.

### **E) Virology: Plitidepsin**

#### **COVID-19: Phase III**

PharmaMar decided to end the NEPTUNO trial ahead of schedule as a result of the evolution of the pandemic and its impact on patient numbers. Although the patient sample is insufficient, a preliminary analysis suggests a positive trend demonstrating the drug's potency. PharmaMar continues to analyze the trial data for presentation and publication.

#### **COVID-19: Phase II**

The NEREIDA clinical trial has been approved to proceed by the regulatory authorities in Spain, France, Greece, Hungary, Italy, Portugal and Poland, and the first patient was enrolled in the trial in April. This is a Phase II, multicenter open randomized controlled basket and pragmatic transactional clinical trial to determine the efficacy and safety of plitidepsin compared to control in immunocompromised adult patients with symptomatic COVID-19 requiring hospitalization.

## **2.- RNA interference: Sylentis**

In the first quarter of 2023, progress was made with enrolling patients for the Phase III clinical trials in the United States of tivanisiran for treating dry eye disease associated with Sjögren's syndrome. The PIVO 1 trial involves more than 30 hospitals in the United States and will enroll 200 patients. This is a randomized trial to assess the efficacy (signs and symptoms) and safety of tivanisiran in patients with dry eye disease associated with Sjögren's syndrome. The other Phase III trial (FYDES) is a multicenter (26 centers in the USA), randomized, double-blind study in which 300 patients with mild to severe dry eye will receive tivanisiran or the ophthalmic vehicle solution for 360 consecutive days. The main endpoint is to assess safety for ocular and non-ocular adverse events. The trial completed patient enrollment in October 2022 and treatment will continue until the last patient reaches 360 days.

Additionally, a Phase I trial in healthy volunteers with SYL1801 for the treatment and/or prevention of choroid neovascularization associated with pathologies such as age-related macular degeneration (AMD) and diabetic retinopathy concluded, showing an excellent safety and ocular tolerance profile. A Phase II trial has commenced with this compound, SYL1801, in three European countries (Czech Republic, Poland and Slovakia) in 90 patients with AMD. This is a multicenter, randomized, double-blind trial to compare the safety, tolerability and effect of different doses of SYL1801 in previously untreated patients with neovascular AMD. The first patient was enrolled in December 2022.

The company continues using Sylentis's proprietary SirFINDER 2.0 software to find new RNAi-based candidates for topical treatment of rare retinal diseases. Those new candidates' efficacy continues to be assessed using preclinical models of a number of retinal pathologies.

<b>CONDENSED CONSOLIDATED STATEMENTS OF FINANCIAL POSITION</b>	<b>March 31, 2023</b>	<b>December,31 2022</b>
<i>(Thousand euro)</i>		
<b>ASSETS</b>		
<b>Non-current assets</b>		
Property, plant and equipment	30,584	31,163
Investment property	845	845
Intangible assets	2,403	2,589
Right-of-use assets	3,564	3,552
Non-current financial assets	48,039	49,398
Deferred tax assets	30,807	30,529
	<b>116,242</b>	<b>118,076</b>
<b>Current assets</b>		
Inventories	32,618	27,746
Trade and other receivables	24,447	29,328
Financial assets at amortised cost	63,416	32,607
Other assets	17,283	35,689
Cash and cash equivalents	119,711	149,813
	<b>257,475</b>	<b>275,183</b>
<b>TOTAL ASSETS</b>	<b>373,717</b>	<b>393,259</b>

<b>CONDENSED CONSOLIDATED STATEMENTS OF FINANCIAL POSITION</b>	<b>March 31, 2023</b>	<b>December,31 2022</b>
<i>(Thousand euro)</i>		
<b>EQUITY</b>		
Share capital	11,013	11,013
Share premium	71,278	71,278
Treasury shares	(22,706)	(15,865)
Revaluation reserves	15	19
Retained earnings and other reserves	157,331	156,512
<b>Total capital and reserves attributable to equity holders of the parent company</b>	<b>216,931</b>	<b>222,957</b>
<b>TOTAL EQUITY</b>	<b>216,931</b>	<b>222,957</b>
<b>LIABILITIES</b>		
<b>Non-current liabilities</b>		
Borrowings	26,562	25,883
Lease liabilities	1,972	2,014
Non-current deferred income	39,034	44,899
Other non-current liabilities	189	186
	<b>67,757</b>	<b>72,982</b>
<b>Current liabilities</b>		
Trade and other payables	21,075	29,959
Borrowings	13,213	13,125
Lease liabilities	1,641	1,608
Outstanding remunerations	5,344	8,603
Current deferred income	24,569	24,666
Other current liabilities	23,187	19,359
	<b>89,029</b>	<b>97,320</b>
<b>TOTAL LIABILITIES</b>	<b>156,786</b>	<b>170,302</b>
<b>TOTAL EQUITY AND LIABILITIES</b>	<b>373,717</b>	<b>393,259</b>



**CONDENSED CONSOLIDATED STATEMENTS OF PROFIT OR LOSS**

<i>(Thousand euro)</i>	March 31, 2023	March 31, 2022
Revenue:		
Revenue from contracts with customers	16,371	34,938
Revenue from licensing and development agreements	6,515	7,194
Royalties	11,074	11,004
Other	19	50
	<b>33,979</b>	<b>53,186</b>
Cost of sales	(2,129)	(3,789)
<b>Gross Result</b>	<b>31,850</b>	<b>49,397</b>
Marketing expenses	(6,036)	(6,019)
General and administrative expenses	(3,799)	(5,183)
Research and development expenses	(21,056)	(19,028)
Net impairment on financial assets	80	(53)
Other operating expenses	(3,440)	(2,695)
Other results	(171)	2,595
<b>Operating Result</b>	<b>(2,572)</b>	<b>19,014</b>
<b>Finance costs - net</b>	<b>(645)</b>	<b>1,609</b>
<b>Result of the period before income taxes</b>	<b>(3,217)</b>	<b>20,623</b>
Income tax benefit / (expense)	4,628	1,352
<b>Result for the period</b>	<b>1,411</b>	<b>21,975</b>

<b>CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOW</b> (Thousand euro)	<b>March</b> <b>31,2023</b>
<b>Result before taxes:</b>	<b>(3,219)</b>
<b>Adjustments for:</b>	<b>2,345</b>
Depreciation and amortization	1,333
Variation of provisions	(64)
Finance income	(854)
Finance costs	665
Results on disposals of intangible assets	170
Share based payments	101
Deferred income - grants	203
Exchange differences on translation of foreign operations	820
Other adjustments to profit or loss	(29)
<b>Changes in working capital:</b>	<b>(8,239)</b>
Inventories	(4,874)
Trade and other receivables	4,900
Other assets and liabilities	9,999
Trade and other accounts payable	(12,099)
Deferred or accrual items	(6,165)
<b>Other cash flows from operations:</b>	<b>16,779</b>
Interest paid	(665)
Interest received	854
Income taxes paid	16,590
<b>NET CASH INFLOW (OUTFLOW) FROM OPERATING ACTIVITIES</b>	<b>7,666</b>
<b>Acquisitions:</b>	<b>(179,266)</b>
Property, plant and equipment, intangible assets and investment property	(272)
Other financial assets	(178,994)
<b>Proceeds from:</b>	<b>148,722</b>
Other financial assets	148,722
<b>NET CASH INFLOW (OUTFLOW) FROM INVESTING ACTIVITIES</b>	<b>(30,544)</b>
<b>Receipts and (payments) in connection with equity instruments:</b>	<b>(7,547)</b>
Purchase of treasury shares	(17,517)
Proceeds from shares issued	9,970
<b>Receipts and (payments) in connection with financial liabilities:</b>	<b>308</b>
Proceeds from borrowings	2,854
Repayment of borrowings	(2,546)
<b>NET CASH INFLOW (OUTFLOW) FROM FINANCING ACTIVITIES</b>	<b>(7,239)</b>
<b>EFFECTS OF EXCHANGE RATE CHANGES ON CASH AND CASH EQUIVALENTS</b>	<b>15</b>
<b>NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS</b>	<b>(30,102)</b>
Cash and cash equivalents at beginning of the period	149,813
<b>CASH AND CASH EQUIVALENTS AT END OF THE PERIOD</b>	<b>119,711</b>

## ANNEX I: Alternative performance metrics

In preparing the financial information, Pharma Mar's Board of Directors adopted a series of Alternative Performance Metrics ("APM") in order to gain a better understanding of business performance.

The APM are important indicators for users of the information, and for the Company's operational and strategic decision-making. Their purpose is to measure the Company's financial performance, cash flows and/or financial position in comparison with previous periods.

### EBITDA (Earnings Before Interest, Taxes, Depreciation and Amortization)

EBITDA means earnings before interest, taxes, depreciation and amortization. It is calculated from the balances of each of those items in the income statement.

The components and the basis of calculation of this APM are the following items in the income statement: Profit or loss - Income tax - Net financial income + Depreciation and amortization.

This APM reflects the Company's operating profitability, as it measures operating profit before interest, taxes, impairment and depreciation.

### Net cash/(debt) position

Net cash is the amount of cash, both current and non-current, that would be available to the Company after deducting total current and non-current interest-bearing debt.

The components and calculation basis of this APM are the following balance sheet items: Cash and cash equivalents + Financial assets at amortized cost (current) + Financial assets (non-current) - Interest-bearing debt (non-current) - Interest-bearing debt (current); the calculation is based on the balances of each of those items in the balance sheet.

This APM helps to determine:

- (i) Net cash position: indicates the Company's liquidity after deducting financial obligations. It reflects the portion of cash available for use in the Company's activities, i.e. the liquidity buffer;
- (ii) Net debt position: indicates the Company's level of indebtedness after deducting available cash and cash equivalents; therefore, it reflects the part of the Company's activity that is financed with external funds.

## ANNEX II: Glossary

In order to improve reporting quality and ensure better and proper understanding on the part of the user of such information, below we define a number of terms used by the Company.

### Revenue

Refers to consolidated net revenue. It is calculated as the sum of:

- (i) recurring revenue (net sales by the oncology segment, plus oncology royalties),
- (ii) non-recurring revenue (oncology out-licensing agreements, etc.).

### Recurring revenue

This item includes:

- (i) net sales by the oncology segment, after deducting returns, discounts and sales rebates
- (ii) royalties collected on sales by our partners in their respective territories.

### Non-recurring revenue

This item includes revenue from licensing agreements, mainly in oncology, which is received or recognized as revenue in the income statement on an irregular basis over time, such as upfront payments and payments for attaining a milestone (clinical, regulatory or commercial), as set out in the agreement.

### Sales by the oncology segment

Recurring revenue, which includes:

- (i) Net sales of finished products by PharmaMar (both commercial sales and compassionate use/early access sales).
- (ii) net sales of raw materials.

### Royalties

Recurring revenue includes royalties on the sale of:

- (i) Yondelis by our partners outside the territories in which Pharma Mar has its own sales network
- (ii) Zepzelca by our partners outside the territories in which Pharma Mar has its own sales network