Pharma Mar

February 2023

Corporate Presentation

World leader in the development and commercialization of anticancer drugs of marine origin

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Management Team

We are inspired by the sea, driven by science, and motivated to improve the lives of cancer patients by delivering novel medicines. We intend to continue to be the world leader in marine medicinal discovery, development and innovation.

D. José María Fernández, Ph.D

Chief Executive Officer and Chairman of the Board

Luis Mora

Managing director

Pascal Besman

Vice President – Strategic Development

José Luis Moreno

Director Capital Markets and Investor Relations

Corporate Overview

Global Fully Integrated Commercial Stage Biotech

Developing marine-inspired oncology drugs

3 Approved Oncology Products

Yondelis (trabectedin)

Aplidin plitidepsin

ZEPZELCA (lurbinectedin)

Established European oncology sales force

Revenue Generating & Profitable

Revenues in 2021	€230m
EBITDA 2021	€97.7m
Cash 9M22	€241m
Market cap	€1.1Bn[1]

Discovery Platform Strengthening Oncology Pipeline

Diversified pipeline with late and early stage assets

(1) As of 31st January 2023

The Plan for growth

On track to deliver value to shareholders

Lurbinectedin development

- Phase 3 trials with Lurbinectedin in SCLC for EU approval and confirmatory US
- Phase 3 trial with Lurbinectedin in other indications
- Potential Lurbinectedin approvals in other countries

Other drugs development

- 2 Phase 2 trials for Ecubectedin enrolling
- PM534 in PoC Phase I
- 1 new compound to enter Phase 1 in 2023

Corporate development

- Looking for in-licensing products to market in EU
- Profitable with robust cash position

Zepzelca: Transformative for PharmaMar

License agreement in the US/Canada

Jazz Pharmaceuticals

$200m
received upfront

$100m
received approval

$25m
received commercial milestone

Potential up to $675m
in regulatory and commercial milestones

- 2021 sales = $46m royalties for PharmaMar
- High teens to 30% Royalties on US/Canada sales
- Initiated Phase 3 in 1L maintenance ES-SCLC in combination with Tecentriq® in collaboration with Roche

PharmaMar

Pipeline – Expanding our Expertise in Oncology

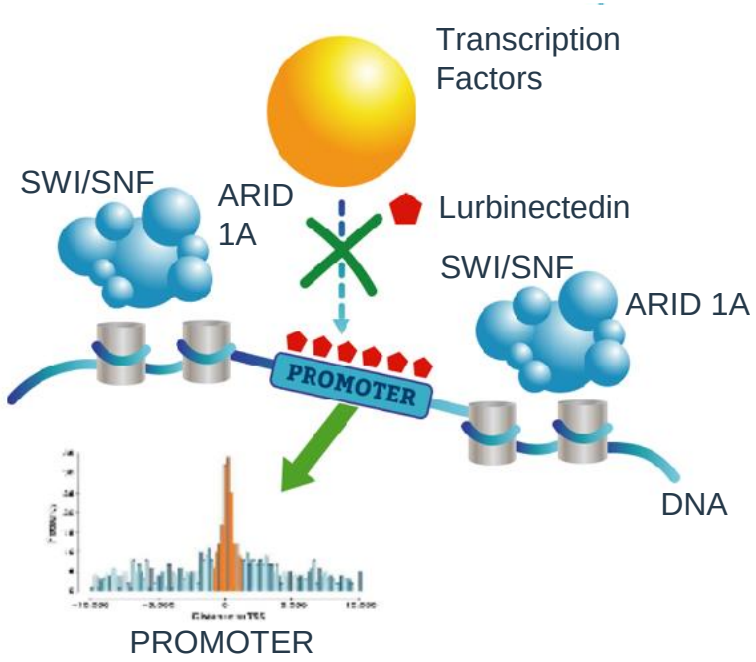
				Phase 1	Phase 2	Phase 3	Market
Yondelis (trabectedin)	Soft tissue sarcoma	2nd/3rd line	Monotherapy				
	Ovarian cancer	2nd/3rd line	+ Doxil (PLD)				
Aplidin plitidepsin	R/R Multiple Myeloma[1]	3rd/4th line	+ dexamethasone				
ZEPZELCA (lurbinectedin) (Lurbinectedin)	Small cell lung cancer	2nd line US	Monotherapy				
	Small cell lung cancer Maintenance		+ Atezolizumab			IMforte (Roche, Jazz Pharmaceuticals)	
	Small cell lung cancer 2nd line		Lurbi vs. Lurbi+ Irinotecan vs. Topotecan or Irinotecan			LAGOON	
	Mesothelioma	≥2nd line	+ IO			SEALIGHT	
	Small cell lung cancer	2nd line	+ Irinotecan				
	SCLC 2nd line Combo[2]		+ Atezolizumab				
Ecubectedin (PM14)	Solid tumors (basket trial)		Monotherapy				
	Soft tissue sarcoma[2]		Combination radiation				
	Prostate cancer		Monotherapy				
	Solid tumors		Combination trials				
PM534	Solid tumors		Monotherapy				

(1) Approved in Australia
(2) IST – Investigator Sponsored Trial

Zepzelca – A Transcription Inhibitor Leading to Tumor Inhibition

Primary Effect

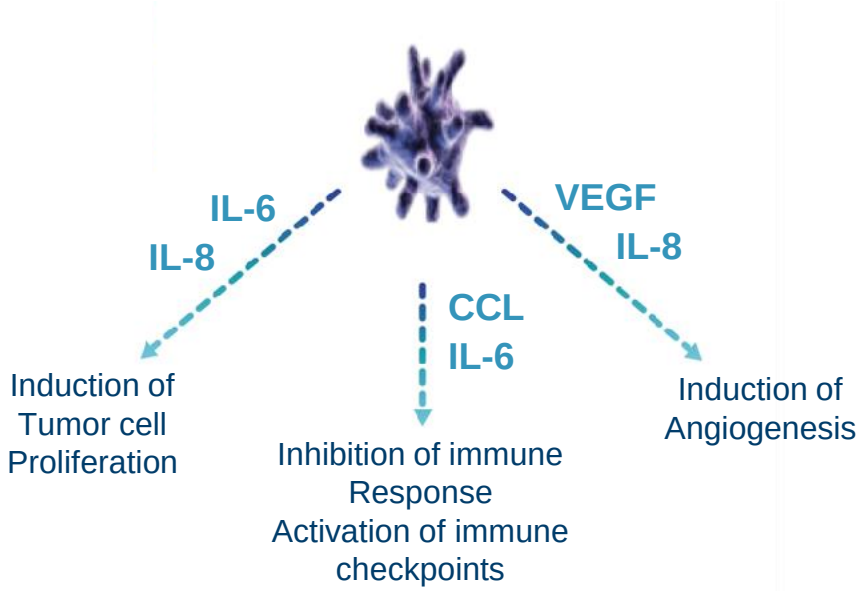
Cancer is frequently a transcriptional disease caused by deregulated oncogenic transcription factors



Selectively inhibits active transcription of protein-coding genes through binding to promoters and irreversibly stalling elongating RNA polymerase II on the DNA template, thereby leading to double-stranded DNA breaks and apoptosis

Secondary Effect

Marked effect on the tumour microenvironment by inhibiting the transcription and secretion of tumour-growth promoting cytokines by Tumour Associated Macrophages (TAMs)[1]



1. Dumoulin et al, 2022, Eu J of Cancer 172; 357-366

ZEPZELCA
(lurbinectedin)

1st FDA approved drug in over 24 years for Relapsed Small Cell Lung Cancer (SCLC)

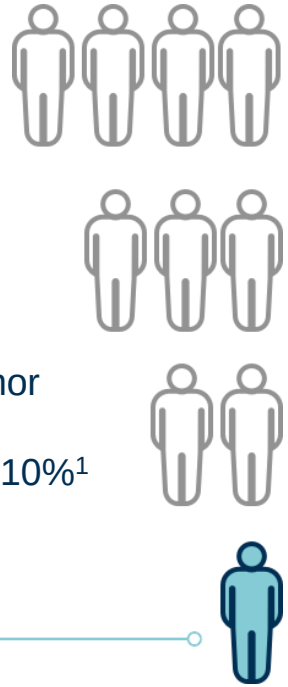
New **Standard of Care** in 2L SCLC in the US

Small Cell Lung Cancer (SCLC)
An high unmet medical need

Among all Lung Cancers

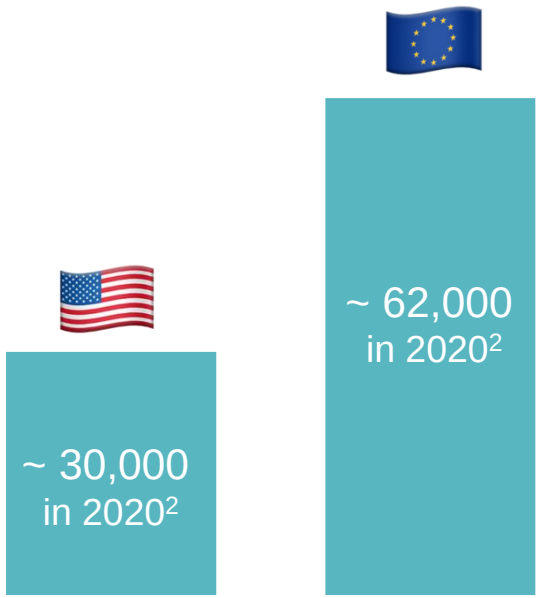
SCLC
~15%

Low survival rate at 5 years



- Highly aggressive tumor
- 5-year survival rate 5-10%[1]

Limited treatment options in both the US and Europe



Newly diagnosed
patients each year

1. http://www.cancer.gov/types/lung/hp/small-cell-lung-treatment-pdq
2. Data Monitor: Small Cell Lung Cancer (SCLC) Globocan 2020. All ages, both genders

Small Cell Lung Cancer (SCLC)

Development lagging behind NSCLC; FDA approvals

Zepzelca (Lurbinectedin) – The SCLC Treatment Paradigm

Strong positioning opportunity

	1st Line	2nd Line	3rd Line
FDA Approved	• Platinum/ Etoposide + • Atezolizumab or Durvalumab	• Zepzelca • Topotecan (sensitive)	
Subsequent Therapy			
NCCN Guidelines*[1]		• Bendamustine • CAV[3] • Docetaxel • Gemcitabine • Irinotecan • Nivo	• Oral etoposide • Paclitaxel • Pembro • Rechallenge • Temozolomide • Vinorelbine

	1st Line	2nd Line	3rd Line
EMA Approved	• Platinum/ Etoposide + • Atezolizumab or Durvalumab	• Topotecan	
Subsequent Therapy			
ESMO Guidelines*[2]		• Lurbinectedin • CAV[3] • Re-challenge	

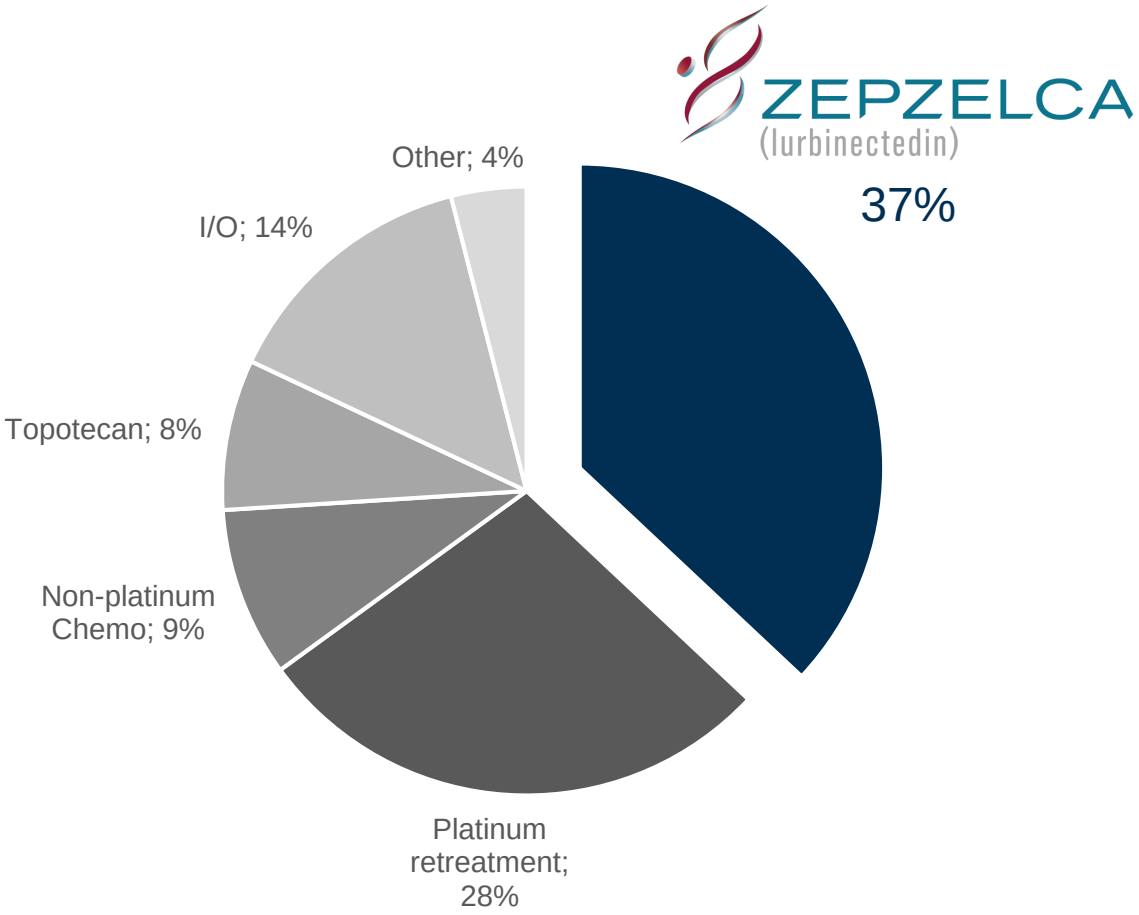
	1st Line	Maintenance	2nd Line	3rd Line
Phase 3 Trials		Zepzelca + atezolizumab[4]	LAGOON[5]	RRx-001

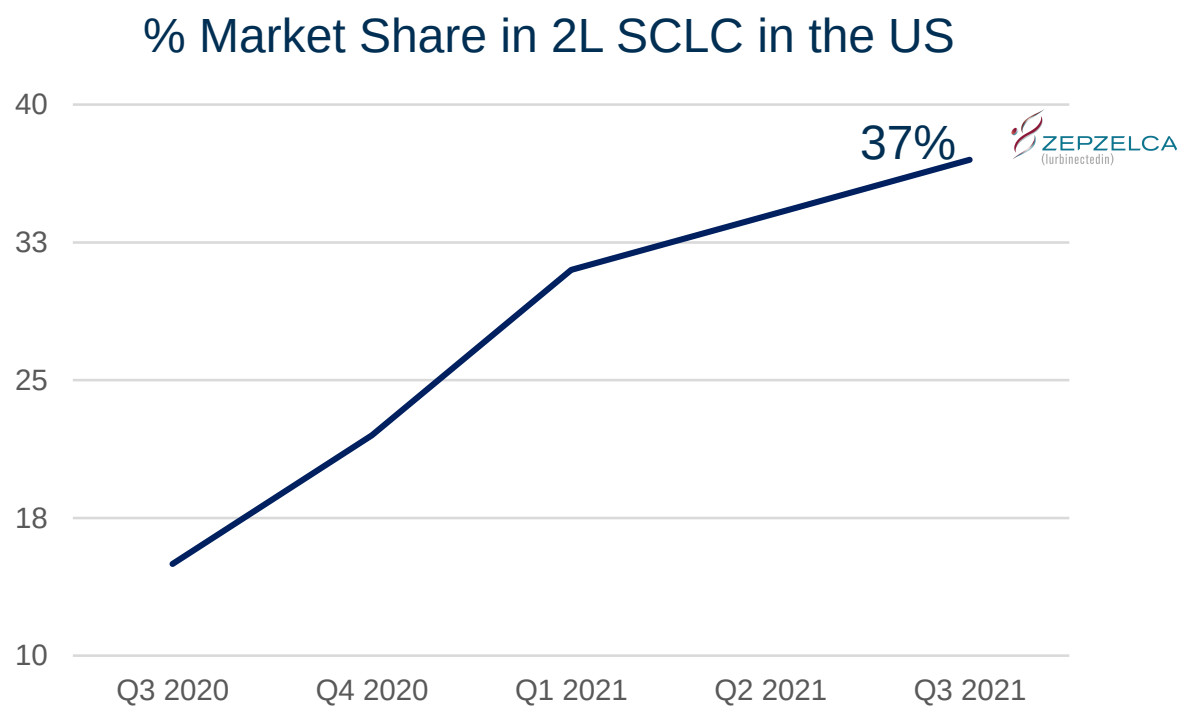
- Investigational drugs or not approved for this indication/line

1. NCCN guidelines v3.2023
2. ESMO guidelines Apr 13 2021
3. CAV: cyclophosphamide, adriamycin and vincristine
4. https://clinicaltrials.gov/ct2/show/NCT05091567
5. https://clinicaltrials.gov/ct2/show/NCT05153239

Zepzelca Already Treatment of Choice in 2L SCLC

Opportunities for future growth





1. Adapted from Jazz Pharmaceuticals Q3 2021 presentation

Zepzelca Already Treatment of Choice in 2L SCLC

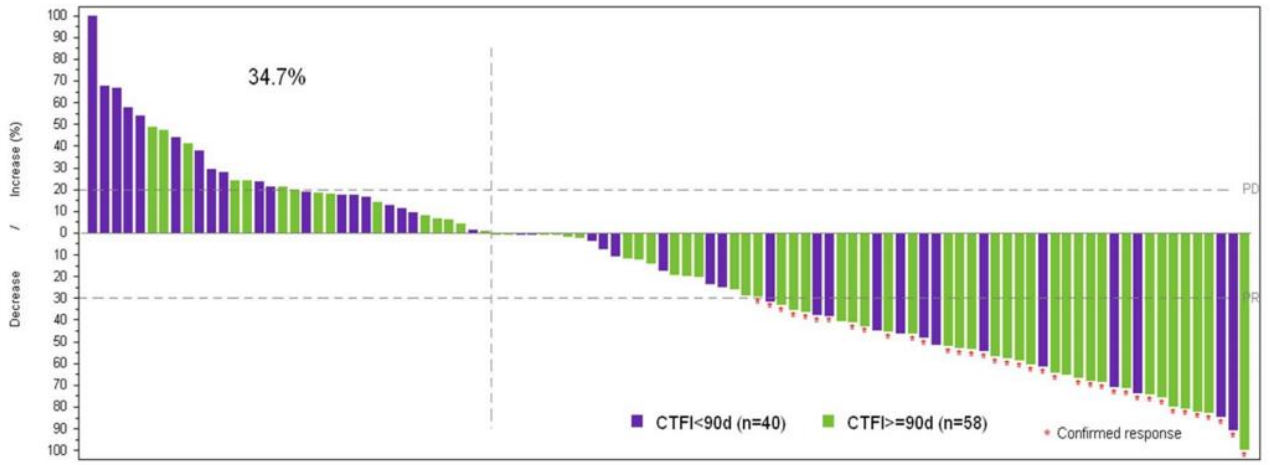
Zepzelca Demonstrated Efficacy in Sensitive and Resistant Small Cell Lung Cancer patients

In relapsed SCLC as monotherapy under accelerated approval based on Phase 2 monotherapy data[1]

	Overall (n=105)	Resistant CTFI< 90 days (n=45)	Sensitive CTFI= 90 days (n=60)
ORR (95% CI) (confirmed responses) ^	35.2% (26.2-45.2)	22.2% (11.2-37.1)	45.0% (32.1-58.4)
Duration of response (months), median (95% CI)	5.3 (4.1-6.4)	4.7 (2.6-5.6)	6.2 (3.5-7.3)
Disease Control Rate *, % (95% CI)	68.6 (58.8-77.3)		

^ Tumor assessments performed every 2 cycles until cycle 6 and every 3 cycles thereafter
• Disease Control Rate: Response or SD
CFTI – Cancer Therapy-Free Interval

Decrease in tumor size in 65% patients[2]



1. Trigo J. et V. Subbiah et al - Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial; Lancet Oncology 2020
2. Adapted from Luis Paz-Ares Presentation – ASCO 2019

Zepzelca Already Treatment of Choice in 2L SCLC

Low rate of AEs and manageable hematological safety profile despite low use of G-CSF [1,2]

Safety: Related or Unknown Adverse Events

Overall (n=105)	n (%)
AEs	89 (84.8)
- Grade ≥3	36 (34.3)
SAEs	11 (10.5)
AEs leading to death	0 (0.0)
AEs	2 (1.9)
- Grade ≥3	21 (22.1*)
Dose reductions #	25 (26.3*)
G-CSF	23 (21.9)
Transfusions (red blood cells and/or platelets)	10 (9.5)

* Per protocol: dose had to be reduced in case of grade 4 neutropenia

Treatment Related (or Unknown) Adverse Events (AEs) (>5% or Gr 3-4)

	Overall (n=105)	Gr 1-2 n (%)	Gr 3-4 n (%)
Hematological AEs *	Neutropenia	6 (5.7)	24 (22.9)
	Anemia	2 (1.9)	7 (6.7)
	Thrombocytopenia	2 (1.9)	5 (4.8)
Non-Hematological AEs	Febrile neutropenia	–	5 (4.8)
	Fatigue	54 (51.4)	7 (6.7)
	Nausea	34 (32.4)	–
	Decreased appetite	22 (21.0)	–
	Vomiting	19 (18.1)	–
	Diarrhea	13 (12.4)	1 (1.0)
	Constipation	10 (9.5)	.
	Pneumonia	–	2 (1.9)
	Alanine aminotransferase increased *	–	2 (1.9)
	Skin ulcer	–	1 (1.0)

* Lab abnormalities associated with a specific treatment, were considered a SAE, or were reasons for dose reduction or treatment delay

1. J. Trigo et V. Subbiah et al - Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial – Lancet Oncology 2020
2. ASCO 2019, Paz-Ares et al.

Zepzelca: Pathway to 2nd line in SCLC by EMA and Full Approval by FDA

Phase 3 (LAGOON) randomized trial

- Relapsed SCLC
- One prior platinum containing regimen
- CTFI ≥30 days
- ECOG 0-2

Stratification Factors

- CTFI (≥ 90 days, <90 days)
- Prior PD-L1/PD-1 (Y/N)
- LDH (> ULN or ≤ ULN)
- CNS involvement (Y/N)
- Investigator´s preference of the control arm

Randomization
1:1:1
705 patients

Arm A

Lurbinectedin 3.2 mg/m^2 every 3 weeks

Arm B

Lurbinectedin 2 mg/m^2 every 3 weeks
+ Irinotecan 75 mg/m^2 D1,8 q3wks

Arm C - Physician's choice

Topotecan oral 2.3 mg/m^2 d1-5 q3wks
or
Topotecan IV 1.5 mg/m^2 d1-5 q3wks
or
Irinotecan 350 mg/m^2 d1 q3wks

Primary Endpoint:
Overall Survival
Arm A vs. C
90% powered to deliver
HR 0.81

Positioning LAGOON for success

- 70% of patients to have had prior IO. There is no evidence of additive or synergistic benefit for control arm. For lurbinectedin, there are three pieces of data.
- Prior mandatory use of G-CSF in all patients serves to make control arm more tolerable. In LAGOON, no mandatory G-CSF, except in exploratory Arm B.
- In prior trial, we allowed stable brain mets. Partly due to protocol violations this proved the worst subgroup, HR 1.291[1]. In LAGOON, patients will have scans to confirm CNS mets are stable at worst.
- Topotecan is a difficult to tolerate drug with inconvenient iv dosing of 5 days out of 7 which introduces patient selection biases. In LAGOON, the allowance of oral topotecan is expected to allow for recruitment of worse PS patients, where lurbinectedin has been shown to be efficacious and well tolerated.

1. Source: Paz-Ares, L. *et al,* WCLC 2021, Lurbinectedin/doxorubicin *versus* CAV or topotecan in relapsed SCLC patients: Phase III randomized ATLANTIS trial , SCLC 2021

ZEPZELCA
(lurbinectedin)

1st line-Maintenance Study in SCLC

SITC 2021

Combo with IO delivers efficacy not seen for either drug as single agent

- Phase I open label dose ranging trial in pts who had progressed on platinum. ECOG 0-1
- Full dose Atezo (1200 mg) + L2.5mg/m^2 (n=5) followed by L3.2mg/m^2 (n=21, full dose)

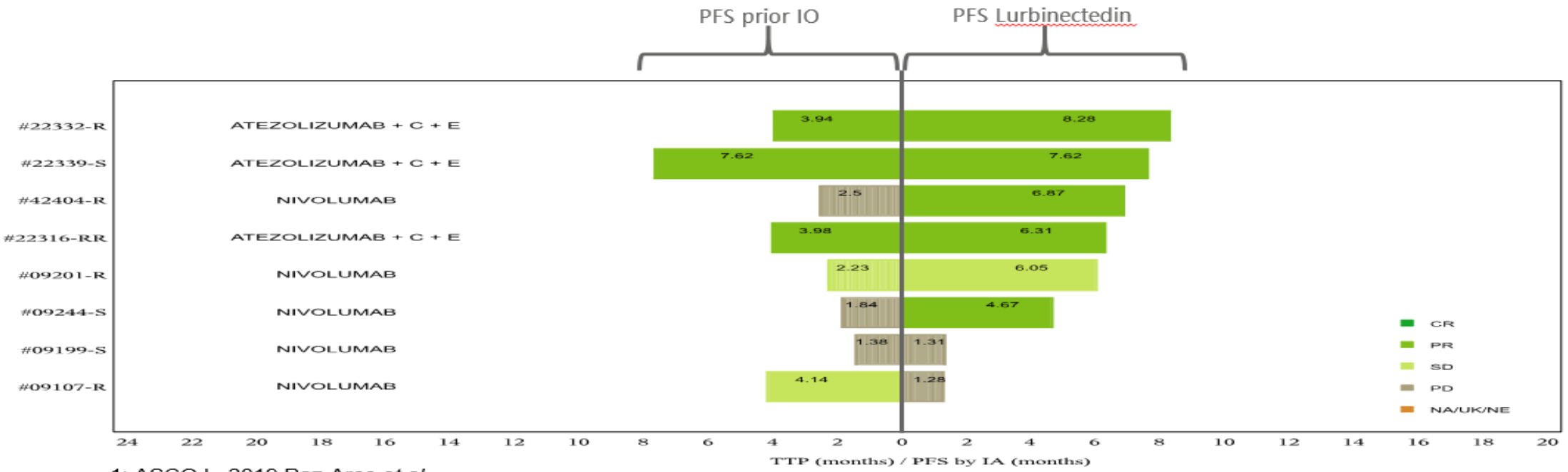
Response	N=26
CR	7.7% (2)
PR	50% (13)
ORR	57.7% (15)
SD	26.9% (6)
DCR	84.6%
PD	11.5% (3)
mPFS (8 censored)	4.93m (3.37-7.47m)

Ponce Aix et al; 2SMALL phase I Lurbinectedin in combination with Atezolizumab for second line Extensive Stage Small Cell Lung Cancer pts; **SITC 2021**

Lurbinectedin: evidences of additive/synergistic benefit with or post IO

Basket trial: 6 of 8 had lurbi PFS ≥ PFS with prior IO including 5 CRs, 2 of which happened in 2L post PD

LURBI AFTER IO: BASKET TRIAL SUBSET PFS TO PRIOR IO AND PFS AFTER LURBINECTEDIN[1]



1: ASCO L. 2019 Paz-Ares *et al*

Source: Paz-Ares, L *et al.* Efficacy and safety profile of lurbinectedin in 2nd-line SCLC patients: Results from a phase II single-agent trial. ASCO 2019

Lurbinectedin: First line positioning

Phase 3 IMforte trial for first line-maintenance SCLC

Induction Phase

- Extensive-stage SCLC (ES-SCLC)

Atezolizumab + Carboplatin + Etoposide

Randomization
1:1
690 patients

Maintenance Phase

Atezolizumab 1,200 mg q3wk
+
Lurbinectedin 3.2 mg/m^2 q3wk

Endpoints:

- Co-Primary:
  IRC-assessed PFS, OS
- Secondary:
  PFS; ORR , DOR , etc.

Atezolizumab 1,200 mg q3wk

1. NCT05091567
2. IRC=Independent Review Committee

Strategic importance of Zepzelca Phase 3s in SCLC

Potential treatment landscape after Phase 3s

	1st Line	1st Line-Mantenance	2nd Line
FDA	✦ Platinum/ Etoposide + ✦ Atezolizumab or Durvalumab	✦ Zepzelca + Atezolizumab	✦ Zepzelca ✦ Topotecan (sensitive)

	1st Line	1st Line-Mantenance	2nd Line
EMA	✦ Platinum/ Etoposide + ✦ Atezolizumab or Durvalumab	✦ Zepzelca + Atezolizumab	• Zepzelca • Topotecan (sensitive)

MPM

ZEPZELCA
(lurbinectedin)

Malignant Pleural Mesothelioma

Trial start 2023

Pharma Mar

Zepzelca (Lurbinectedin) – Relapsed Malignant Pleural Mesothelioma

A rare disease with limited available therapeutic options

Aggressively growing tumor
~ 80% of cases related to asbestos exposure

Incidence ~3,500[1] patients diagnosed in the US per year

	1st Line	2nd Line
FDA Approved	• Nivo + Ipi • Pemetrexed + Plat • Gemcitabine + Cis	
NCCN[3] Guidelines	• Pemetrexed + plati+bev[4]	• Pemetrexed[4] (IO naïve) • Ramucirumab[4] • Vinorelbine • Gemz + Cis

Incidence and ~13,700[1] in Europe[2]

	1st Line	2nd Line
EMA Approved	• Pemetrexed + Plat • Nivol + Ipi	
ESMO[5] Guidelines	• Pembro, Nivo +/-Ipi[6] • Pemetrexed +/- Plat • Gemz +/-ramu • Vinorelbine	

Phase 3 Trials	Atezolizumab[5]	Durvalumab[5]	Pembrolizumab[5]

1. Data Monitor: Globocan 2020. All ages, both genders
2. Contributors – UpToDate
3. NCCN Guidelines v1.2022; All recommendations category 2A except where stated
4. Not approved in this indication
5. ESMO guidelines Nov 2021
6. Only in IO naive patients

Zepzelca (Lurbinectedin) – Phase III trial starting 2023

A Phase3 schema[1]

- 42 patients progression on 1 prior platinum based therapy
- Lurbinectedin at 3.2 mg/m^2 every 3 weeks until progression/toxicity, prior (I/O allowed)

- Primary endpoint PFS at 12 weeks:
  - Primary endpoint met (p=0.015)
- mPFS 4.1 months
- mOS 11.5 months[2]
- Grade 3-4 AEs (>10%):
- Neutropenia 24%
- Fatigue 17%
- Febrile neutropenia 12%

Phase 3

Lurbi

Vs.
Lurbi + Atezo.

Vs.
Gemz/Vin

N=750
OS
1 prior platinum

1. https://pubmed.ncbi.nlm.nih.gov/32085891/
2. Mark, M., Long-term benefit of lurbinectedin as palliative chemo in progressive MPM: final efficacy and translational data of the SAKK 17/16 study; ESMO Open 2022; v7, i3

Leveraging Commercial Infrastructure in Europe

PharmaMar positioned as a partner of choice in Europe

European experience:

- Strong KOL connections in solid tumors
- Navigation of EU, UK and CH regulators
- Logistics in place for distribution
- Expertise in multi-language labelling
- Broad knowledge in reimbursement procedures, market access and negotiations in key European countries
- Engaged in multiple negotiations for oncology assets in EU

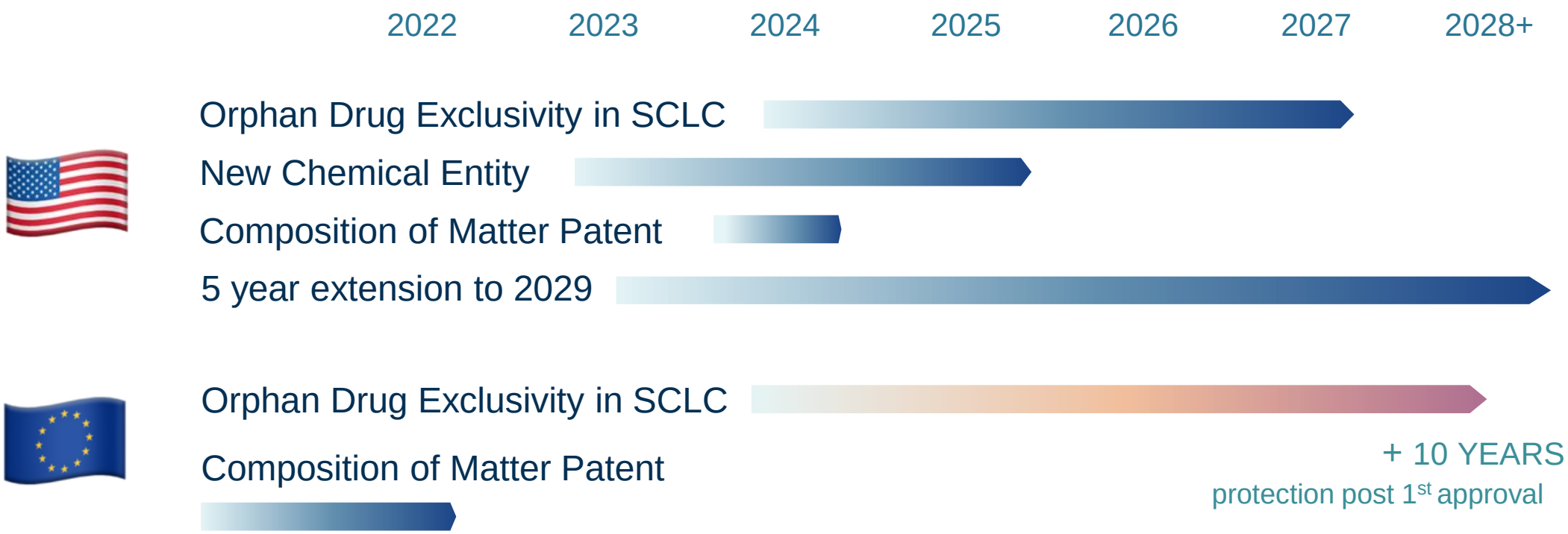
18 Regional Partners for Local Distribution

~100 Sales force infrastructure

Development and regulatory expertise

Zepzelca (Lurbinectedin) – Intellectual property

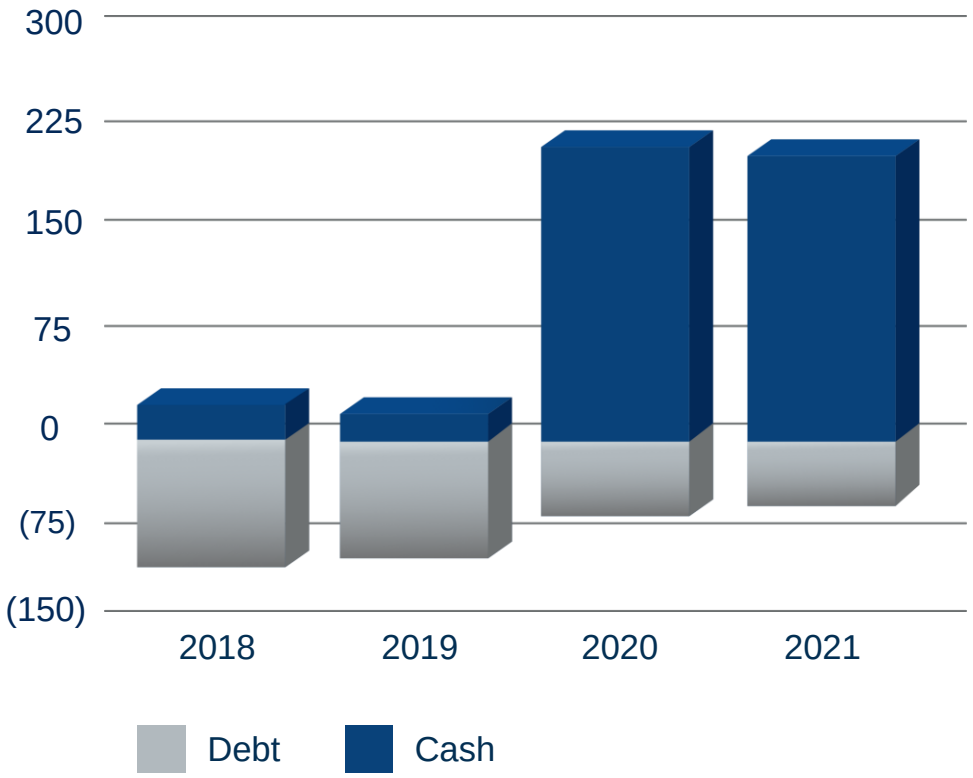
Life cycle management plans under way



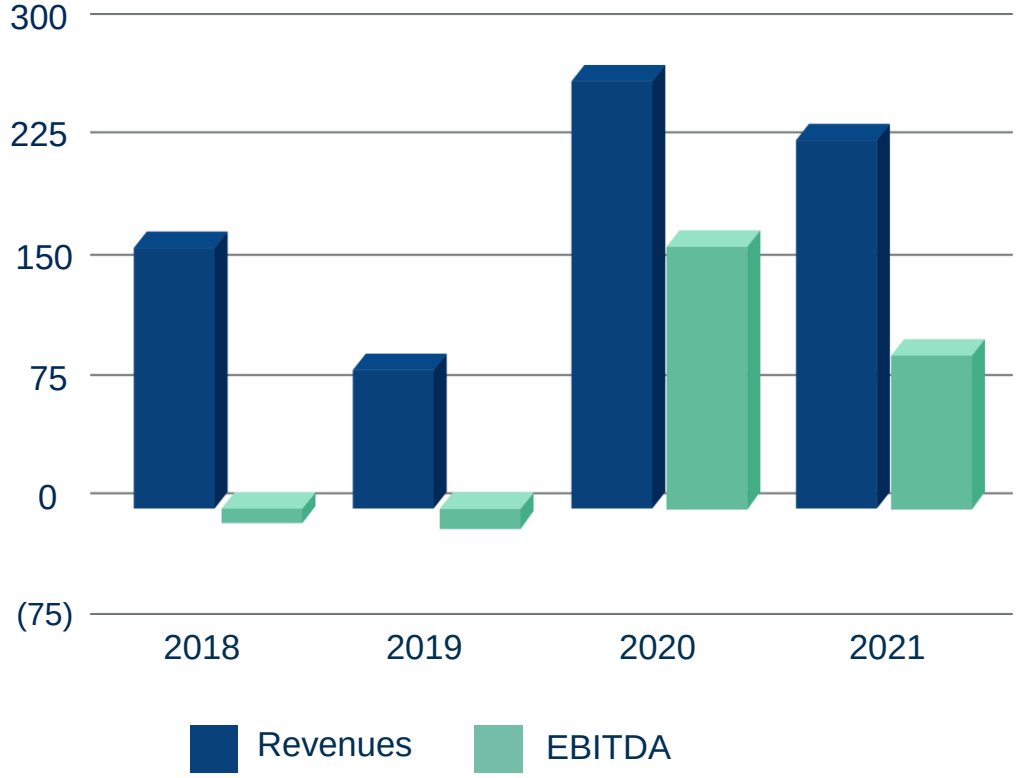
Financials

Well financed to support next stages of development

Robust Cash Position (€m)



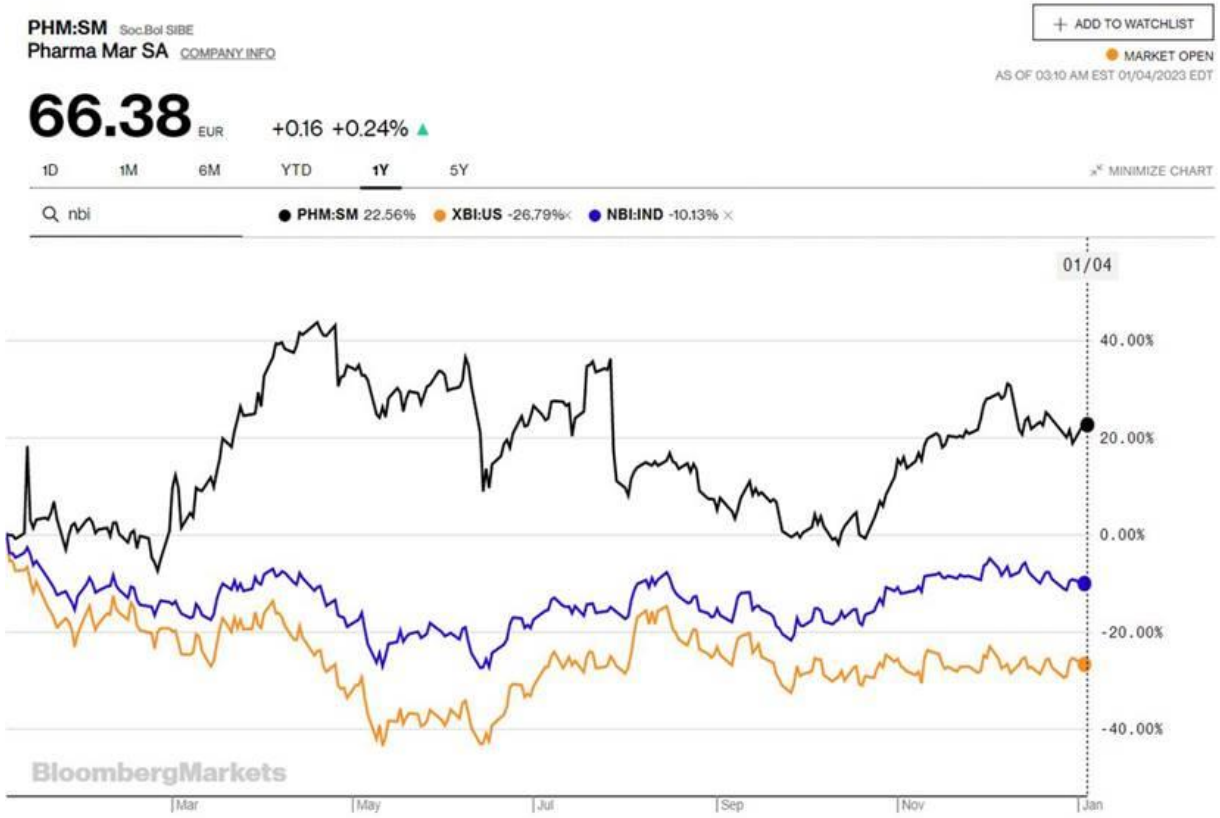
Profitable (€m)



Key Events
Catalyst Calendar

Potential lurbinectedin approvals and launches in other countries	Ongoing
Lurbi + Irinotecan Phase 2 update	2023
Phase I new product in pipeline	2023
Potential in-licensing	Ongoing
First patient in Mesothelioma	Mid 2023
IMforte last patient in	2023

Value Proposition



PHM Profile

- Profitable
- €240mm cash
- Zepzelca further country approvals expected
- Continuing growth/market share gain in USA
- Confirmatory/Registrational Phase III ongoing
- Phase III trial in maintenance setting accruing
- Registrational Phase 3 in mesothelioma start 2023
- Pipeline: one PII,1 NCE entering clinical trials 2023
- BDL talks ongoing for multiple assets for EU market

What we don't have:

- Binary event in 2023
- Crowded long of usual suspects
- Large short interest
- Need to raise capital

Building the Next Phase of Growth

2021-2026

Profitable Biotech with 3 commercial assets and cash to support growth

Zepzelca expected approvals/launches in non-EMA countries

Strong Zepzelca I.P

Leveraging proven oncology platform in new indications

Financial strength allows broadening and accelerating R&D engine

Fuel leading EU sales force with in-licensing

2021 – 2026 Objectives

- Lurbinectedin in 4 Phase 3 trials; potentially all four filed for approval
- Potential approvals of lurbinectedin in 1L maintenance and 2L (US, EMA)
- 2 in-licensed assets adding to revenue in Europe
- Ecubectedin in Phase 2/3 trials
- 2 new assets in the clinic

www.pharmamar.com