December 2023

Corporate Presentation

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

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Corporate Overview

Global Fully Integrated Commercial Stage Biotech

Developing marine-inspired oncology drugs

3 Approved Oncology Products

Yondelis (trabectedin) · ZEPZELCA (lurbinectedin) · Aplidin (plitidepsin)

Established European oncology sales force

Revenue Generating & Profitable

Revenues in 2022	**€196.3m**
EBITDA 2022	**€51.4m**
Cash 3Q2023	**€185.5m**
Market cap	**~ €730mn[1]**

Discovery Platform Strengthening Oncology Pipeline

Diversified pipeline with late and early stage assets

(1) As of 30th November 2023

The Plan for growth

Continue delivering 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

- 1 Phase 2 trial for ecubectedin enrolling
- PM534 in PoC Phase I
- PM54 in PoC Phase I

Corporate development

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

Zepzelca: Transformative for PharmaMar

License agreement in the US/Canada

Jazz Pharmaceuticals

$200m
received upfront

$100m
received approval

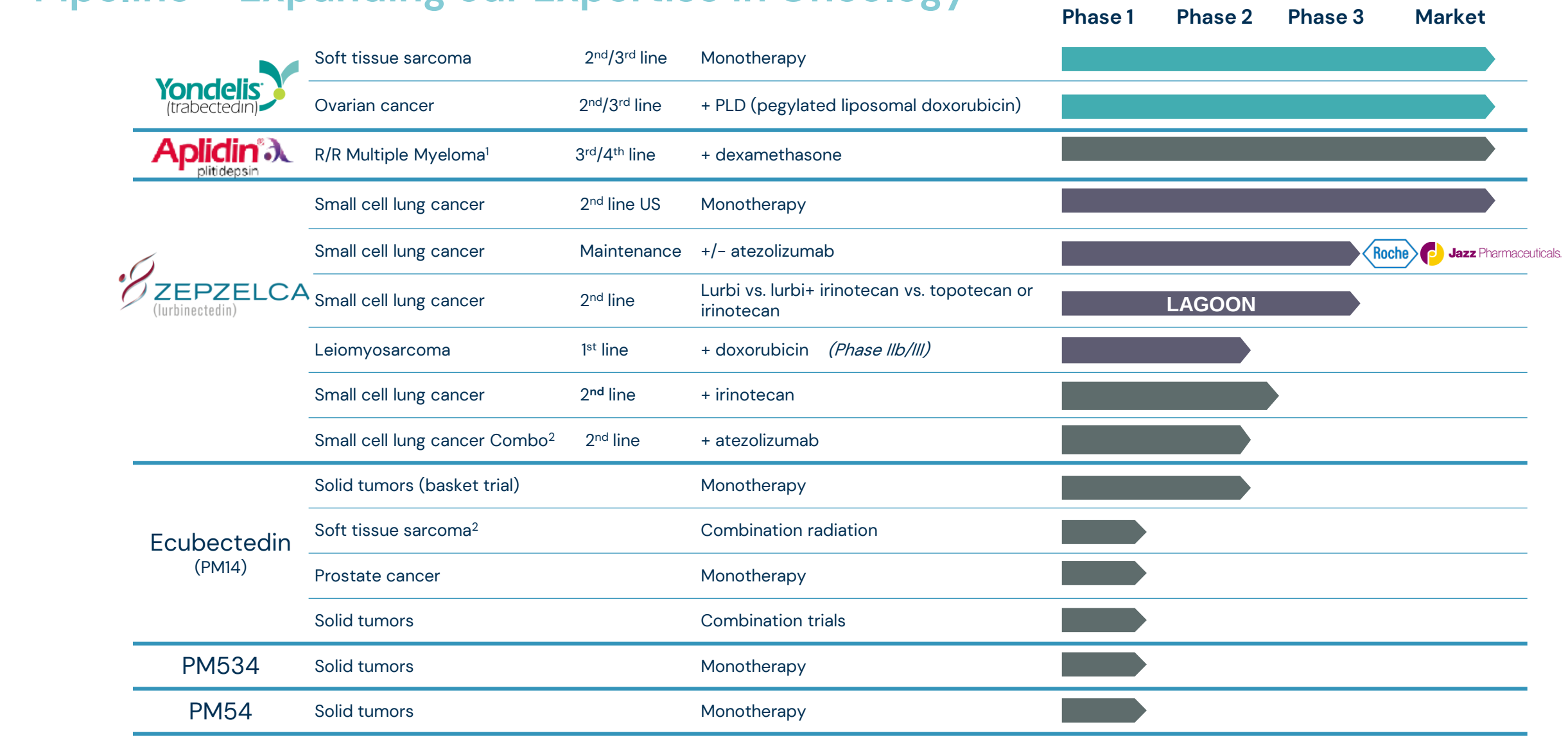
$25m
received commercial milestone

Potential up to $675m
in regulatory and commercial milestones

- High teens to **30% Royalties** on US/Canada sales
- Phase 3 in 1L maintenance ES-SCLC in combination with Tecentriq® in collaboration with Roche. **Top-line PFS readout expected end of 2024 / early 2025.**

PharmaMar

Pipeline – Expanding our Expertise in Oncology

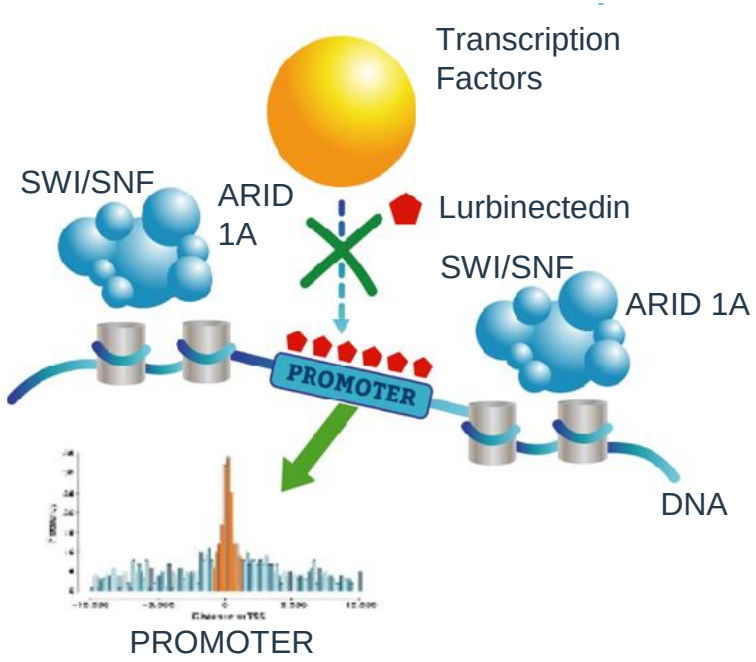


(1) Approved in Australia
(2) IST – Investigator Sponsored Trial

Zepzelca – A Transcription Inhibitor Leading to Tumour Inhibition

Primary Effect

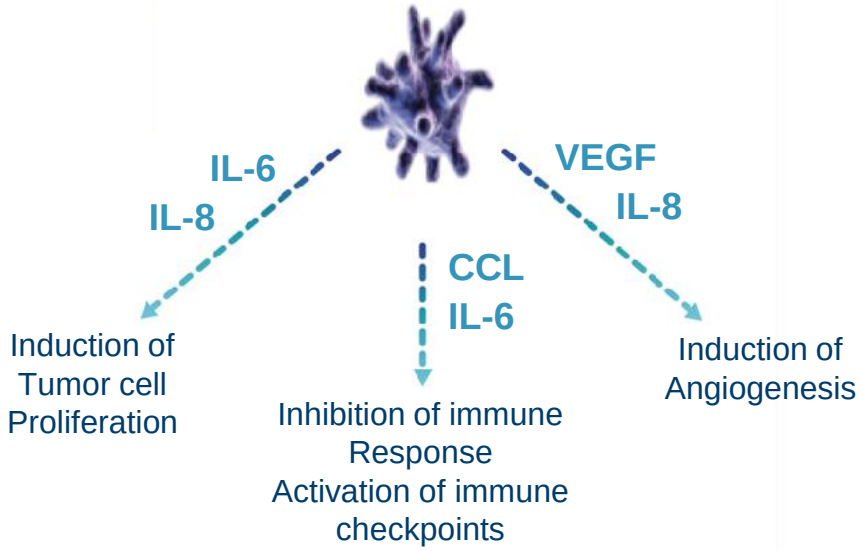
Cancer is frequently a transcriptional disease caused by deregulated oncogenic transcription factors



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)

Standard of Care in 2L SCLC in the US

Pharma Mar

Small Cell Lung Cancer (SCLC)

A high unmet medical need

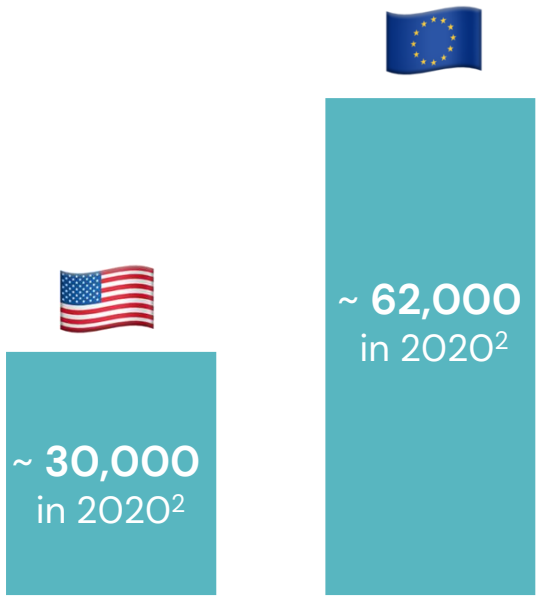
Among all Lung Cancers

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	Maintenance	2nd Line	3rd Line
FDA Approved	• Platinum/ etoposide + • Atezolizumab or durvalumab	----▸ ----▸	• **Zepzelca** • Topotecan (sensitive)	
			Subsequent Therapy	
NCCN Guidelines[1]			CTFI>6m • Re-challenge • Irinotecan	• **CTFI <6m** • Irinotecan • Re-challenge • Nivo/pembro • Taxane • Temozolomide • CAV • Gemcitabine

	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] Tartalamab	

1. NCCN guidelines v1.2024
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

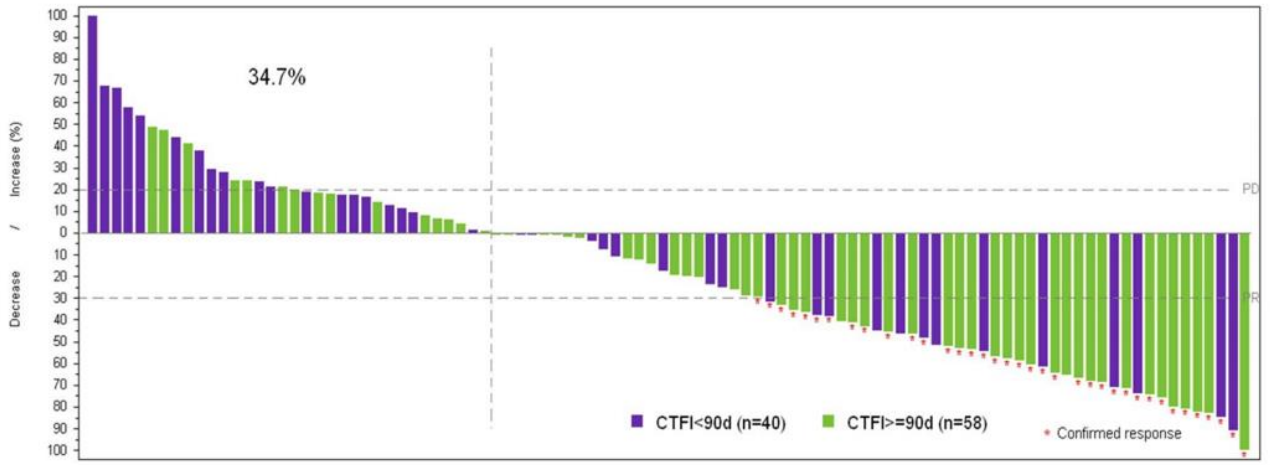
Zepzelca Demonstrated Efficacy in Sensitive and Resistant Small Cell Lung Cancer patients

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 (confirmed responses), median (95% c.i.)*	35.2% (26.2-45.2)	22.2% (11.2-37.1)	45.0% (32.1-58.4)
Duration of response (months), median (95% c.i.)	5.3 (4.1-6.4)	4.7 (2.6-5.6)	6.2 (3.5-7.3)
Disease Control Rate %**, (95% c.i.)	68.6 (58.8-77.3)		

* Tumour 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 leading to treatment discontinuation	2 (1.9)
Dose delays treatment related	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
# Based on 95 patients who received ≥2 cycles of treatment

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/m² every 3 weeks

Arm B

Lurbinectedin 2 mg/m² every 3 weeks
+ irinotecan 75 mg/m² D1,8 q3wks

Arm C - Physician's choice

Topotecan oral 2.3 mg/m² d1-5 q3wks
or
Topotecan IV 1.5 mg/m² d1-5 q3wks
or
Irinotecan 350 mg/m² 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 data sets.

- In **LAGOON, patients will have scans to confirm CNS mets are stable** at worst. In prior trial, we allowed stable brain mets, and this proved the worst subgroup, HR 1.2911.

- 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.

Efficacy & safety profile of lurbi-irino in patients with relapsed SCLC

Interim data from a Phase Ib-II trial

SCLC cohort, efficacy table (n=21)
WCLC 2020

Fully enrolled n=101
Data expected late 2023 or early 2024

	All patients (n=21)	CTFI		Setting	
		≥ 90 days (n=13)	<90 days (n=8)	2nd line (n=13)	3rd line (n=8)
Median number of cycles (range)	8+ (1-20)	10+ (6-20)	6+ (1-8)	8+ (3-21)	8+ (1-18)
Objective Response Rate (PR)	62%	69%	50%	77%	38%
Clinical Benefit Rate (PR+SD>4m)	81%	92.3%	62.5%	92.3%	62.5%
Disease Control Rate (PR+SD)	90%	100%	75%	100%	75%
Median DOR (m) (95% CI)	6.7+ (3.0-N.R)	7.5+ (3.0-N.R)	3.7+ (2.8-3.7)	6.7+ (3.0-N.R)	3.0+ (3.0-N.R)
Median PFS (m) (95% CI)	6.2+ (4.3-8.5)	8.1+ (4.3-N.R)	4.8+ (0.7-5.0)	8.5+ (4.8-N.R)	4.2+ (0.7-7.2)

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Ponce Aix S, *et al.* Lurbinectedin With irinotecan in relapsed Small Cell Lung Cancer. Results From the Expansion Stage of a Phase I-II Trial IASLC 2020 World Conference on Lung Cancer in Singapore (WCLC 2020).

Efficacy & safety profile of lurbi-irino in patients with relapsed SCLC

Interim data from a Phase Ib-II trial

SCLC cohort, safety profile table (n=21)

Adverse Events and Laboratory abnormalities		LUR 2mg/m2 D1 + IRI 75 mg/m2 D1 8 + G-CSF	
		Gr 1-2, (%)	Gr 3-4, (%)
Treatment-related adverse events	Fatigue	66.7	23.8*
	Nausea	57.1	-
	Vomiting	38.1	4.8
	Diarrhea	33.3	28.6**
	Constipation	19	-
	Abdominal pain	4.8	-
	Anorexia	52.4	-
	Febrile neutropenia	-	9.5
Non-Hematological AEs	Anemia	81	19
	Neutropenia	33.3	61.9***
	Thrombocytopenia	66.7	9.5
	ALT increase	57.1	4.8
	AST increase	61.9	4.8

Related AEs summary / dose modifications / supportive treatment	n (%)
Any AE	21 (100)
AE ≥ grade 3	16 (76.2)
SAEs	6 (28.5)
Related AEs leading to death	0 (0.0)
Related AEs leading to treatment discontinuation	0 (0.0)
Does delays treatment related	6 (28.6)
Dose reductions	11 (52.4)
Transfusions (red blood)	7 (33.3)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; IRI irinotecan; LUT, lurbinectedin
* 1 episode per patient (n=5 pts)
** All were grade 3, 1 episode per patient, except in 1 patient (2 episodes of 1 day of duration each
*** 6/21 patients (28.6%) neutropenia grade 4

Ponce Aix S, *et al.* Lurbinectedin With irinotecan in relapsed Small Cell Lung Cancer. Results From the Expansion Stage of a Phase I-II Trial IASLC 2020 World Conference on Lung Cancer in Singapore (WCLC 2020).

ZEPZELCA
(lurbinectedin)

1st line-Maintenance Study in SCLC

SITC 2021

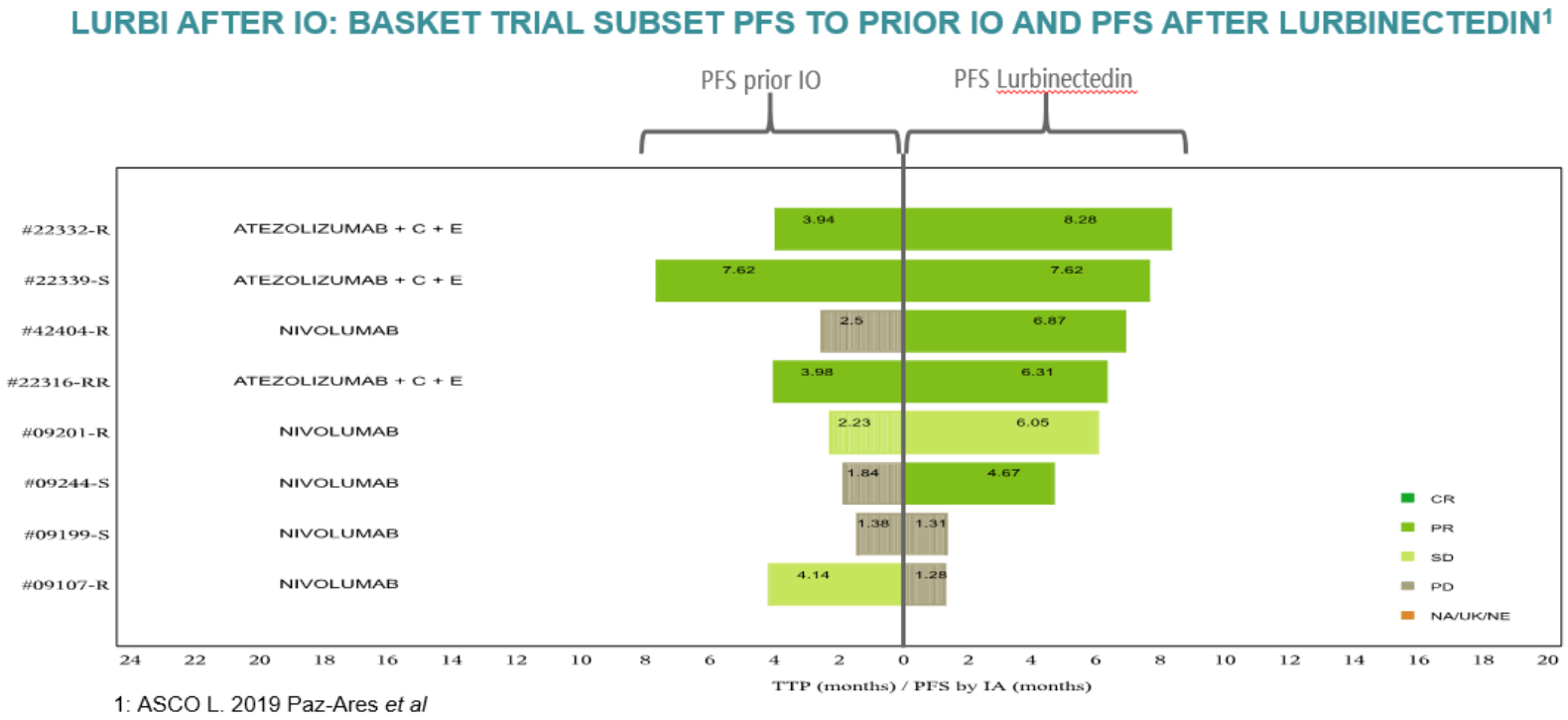
Combo with IO delivers efficacy not seen for either drug as single agent

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)

- Phase I open label dose ranging trial in pts who had progressed on platinum. ECOG 0-1
- Full dose atezo (1200 mg) + lurbi 2.5mg/m^2 (n=5) followed by lurbi 3.2mg/m^2 (n=21, full dose)

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



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

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

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 maintenance positioning

Phase 3 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/m²
q3wk

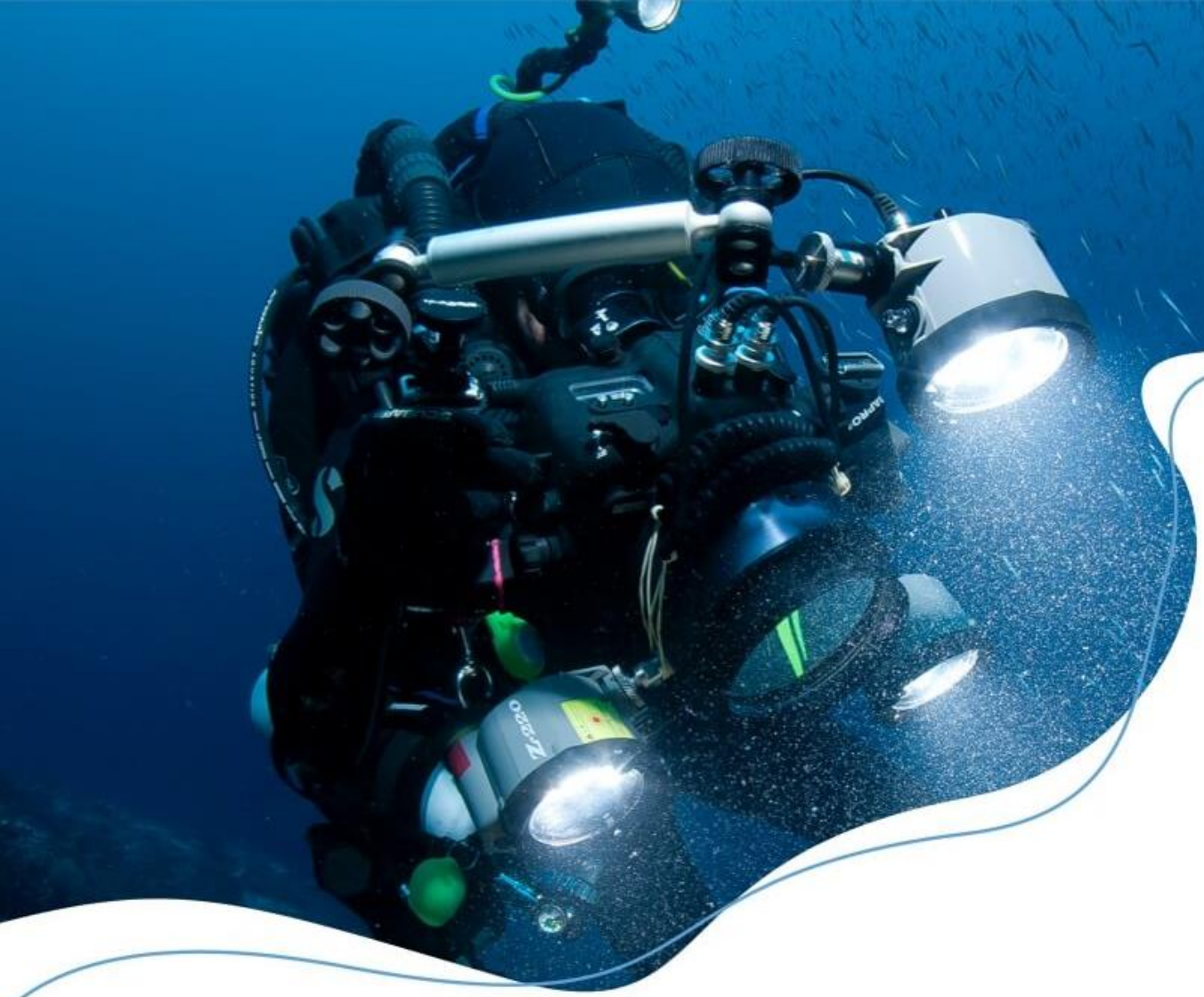
Endpoints:

Co-Primary:
IRC-assessed PFS, OS

Secondary:
PFS; ORR , DOR , etc.

Atezolizumab 1,200 mg q3wk

1. NCT05091567
2. IRC=Independent Review Committee



ZEPZELCA
(lurbinectedin)

Leiomyosarcoma

Leiomyosarcoma

Incidence and treatment paradigm

One of the most common soft tissue sarcoma (STS) accounting for ~ 10%-20% of all STS

Incidence ~2,100[1] in USA

	1st Line	2nd Line
FDA Approved	• Doxorubicin • Ifosfamide	• Trabectedin • Pazopanib
NCCN Guidelines		• Dacarbazine • Ifosfamide • Gemcitabine based regimen

Incidence and ~4,500[2] in Europe

	1st Line	2nd Line
EMA Approved	• Doxorubicin • Ifosfamide	• Trabectedin • Pazopanib
ESMO Guidelines		• Gemcitabine+ docetaxel • Dacarbazine-gemcitabine

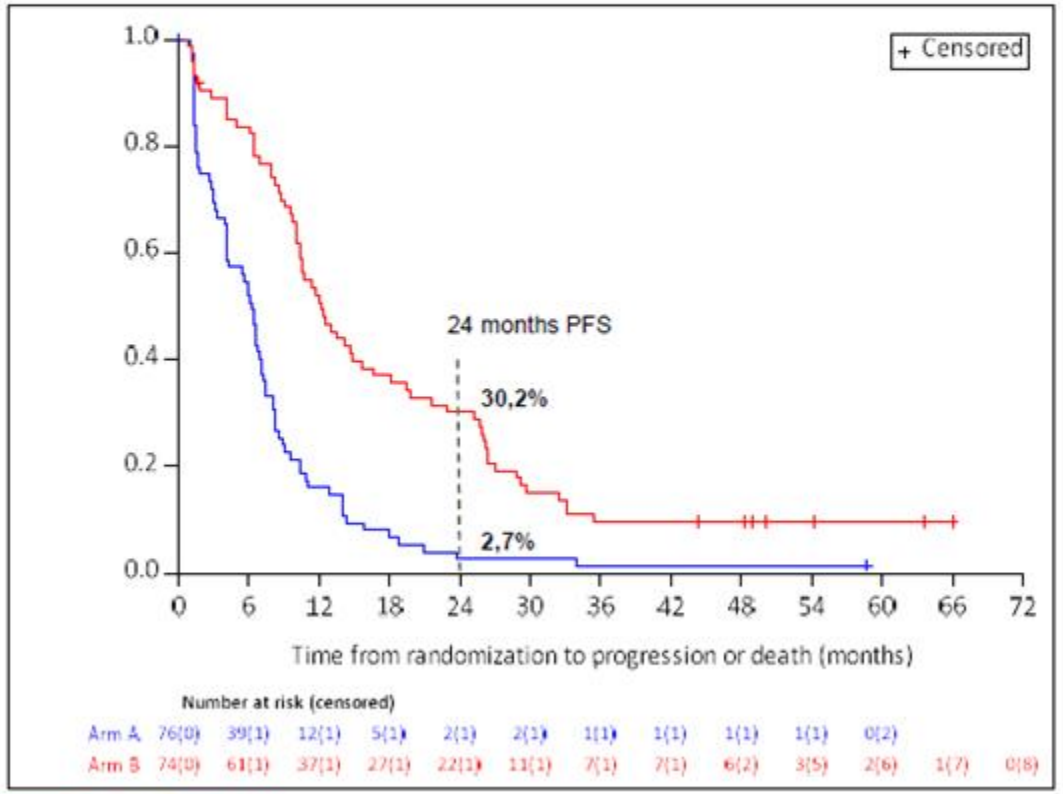
1. The American Cancer Society
2. ESMO Sarcoma guidelines 2021

Leiomyosarcoma

Randomized P3 comparing doxorubicin +/- trabectedin in 1L metastatic or unresectable LMS

Updated PFS-RECIST

LMS-04 study



Median follow-up : 55 months

	Arm A Doxorubicin (N = 76)	Arm B Doxorubicin + Trabectedin (N = 74)
Events, n (%)	74 (97.4%)	66 (89.2%)
Median PFS, months	**6.21**	**12.19**
2-year PFS rate, %	**2.7**	**30.2**

HR 0.37 [95%CI = 0.26-0.53]; ***P* = <0.0001**

63% reduction in risk of disease progression or death for Trabectedin + Doxorubicin *vs* Doxorubicin alone

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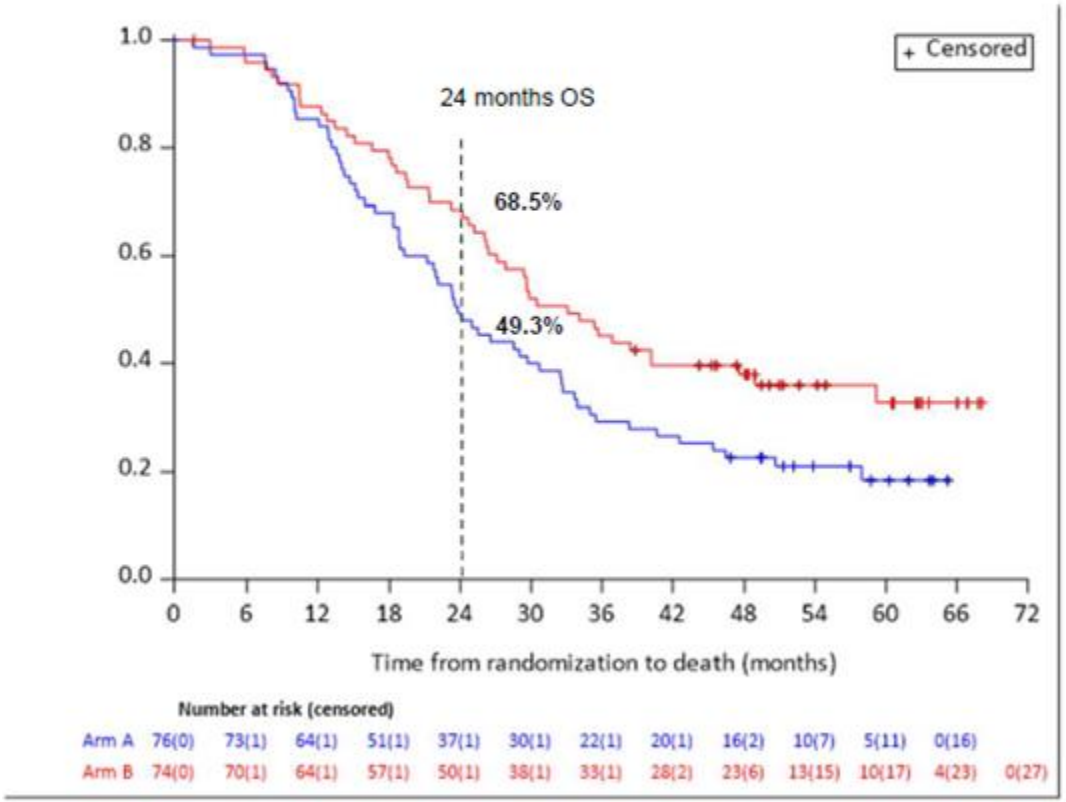
Patricia Pautier

Leiomyosarcoma

Randomized P3 comparing doxorubicin +/- trabectedin in 1L metastatic or unresectable LMS (BICR)

Overall Survival

LMS-04 study



Median Follow-up : 55 months

	Arm A Doxorubicin (N = 76)	Arm B Doxorubicin + Trabectedin (N = 74)
Events, n (%)	60 (78.9)	47 (63.5)
Median OS, months	**23.78**	**33.08**
2-year OS rate, %	**49.3**	**68.5**

HR 0.65 [95% CI = 0.44-0.95];
P = 0.0253

35% reduction in risk of death for Trabectedin + Doxorubicin *vs* Doxorubicin alone

MADRID 2023 ESMO congress

Patricia Pautier

Zepzelca (lurbinectedin)-Leiomyosarcoma

Phase IIb/III adaptive trial

- Metastatic Uterine/ST LMS
- No prior chemo
- ECOG 0-1

Stratification:
- Uterine vs ST
- Time from dx(< / >12m)
- Lung mets only yes/ no

Phase IIb

1:1:1(**)

- Doxo 50 mg/m^2 + Lurb 2.2 mg/m^2 + GCSF, D1 q3w
- Doxo 25 mg/m^2 + Lurb 3.2 mg/m^2 + GCSF, D1 q3w
- Doxo 75 mg/m^2 D1 q3w

IDMC Interim Efficacy analysis

Phase III

N based on Phase II data

- Selected combination*
- Doxo 75 mg/m2 D1 q3w

Primary endpoint: PFS by IRC

Powered for OS

(*) Treatment may continue until PD, tox or up to a maximum cumulative dose of doxo of 450mg/m^2 (continuing lurbi 3.2mg/m^2 D1 q3w in experimental arms)
(**) Cohort sizes to be finalized by IDMC as trial evolves

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

19 Regional Partners for Local Distribution

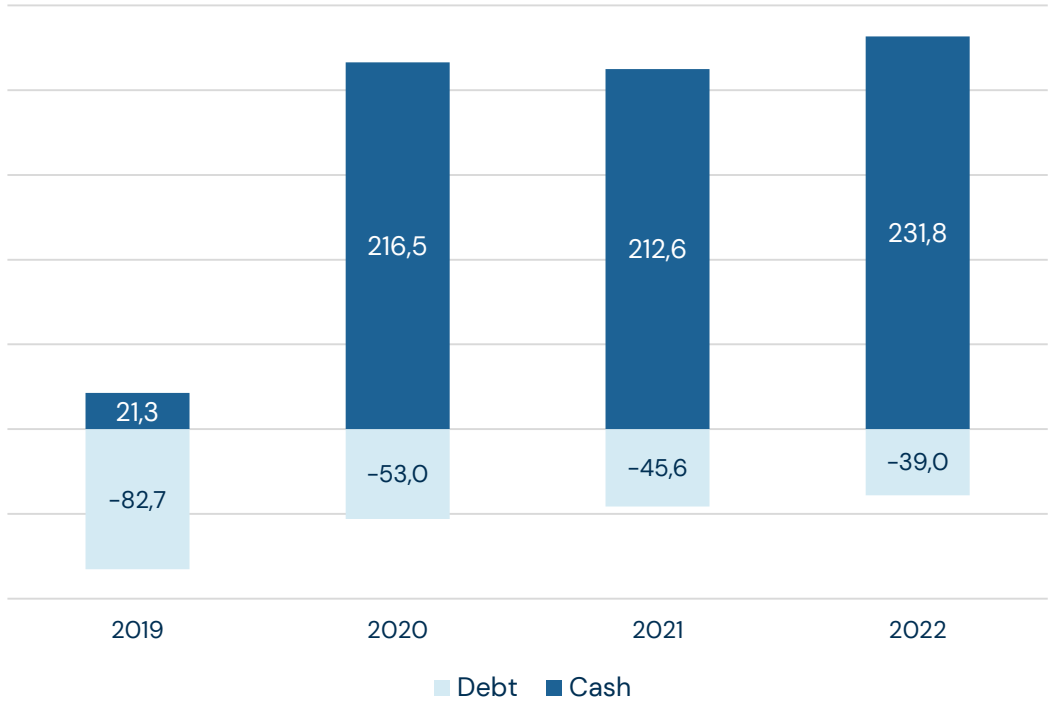
~100 Sales force infrastructure

Development and regulatory expertise

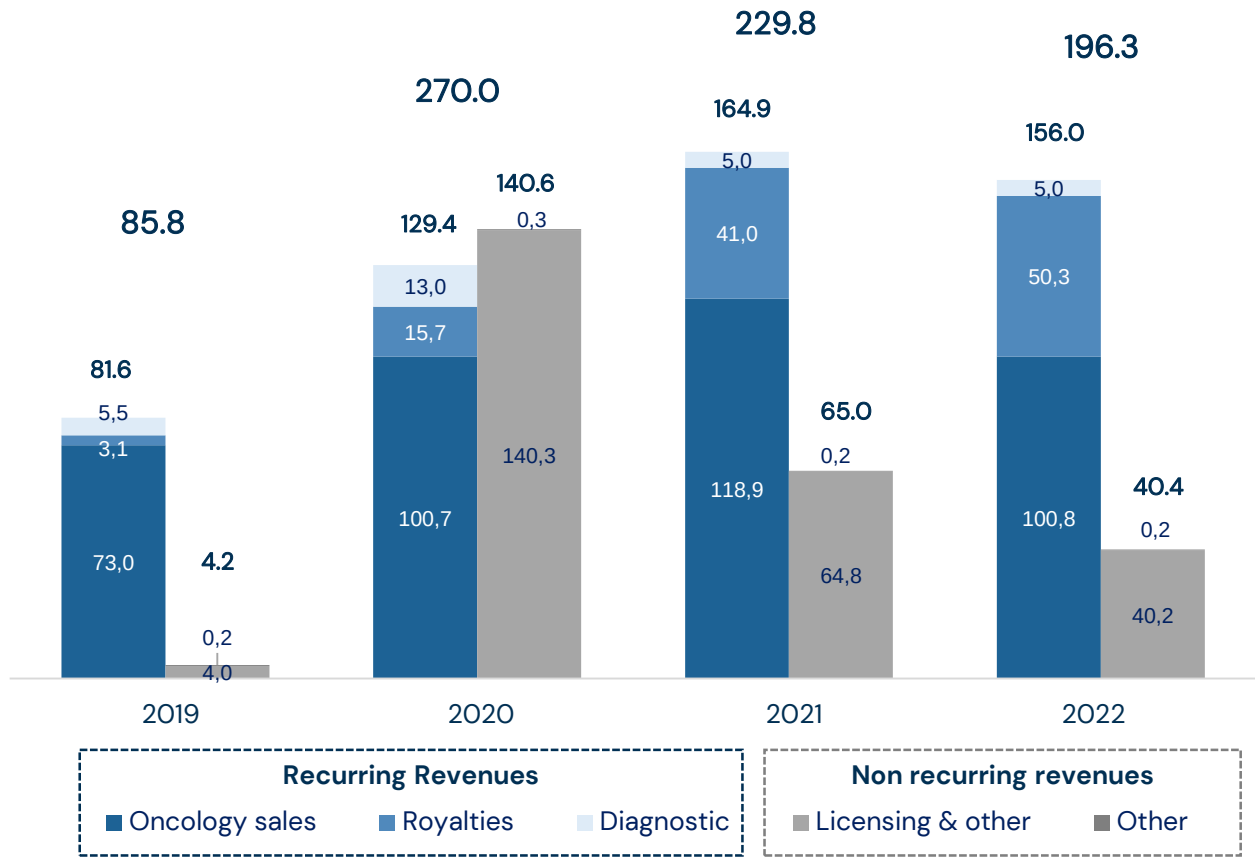
Financials

Profitable and solid and stable financial position

Robust cash position *(€ mn)*



Historical revenues evolution *(€ mn)*



Key Events
Catalyst Calendar

Zepzelca approved in Switzerland for SCLC	✓
Potential lurbinectedin approvals and launches in other countries	Ongoing
Lurbi + Irinotecan Phase 2 topline data	~YE2023
Potential in-licensing	Ongoing
Phase I new product	✓
First patient in Leiomyosarcoma Phase IIb-III	✓
IMForte PFS Data	~YE24/1Q25

Building the Next Phase of Growth

2021-2026

Profitable Biotech with **3 commercial assets** and cash to support growth

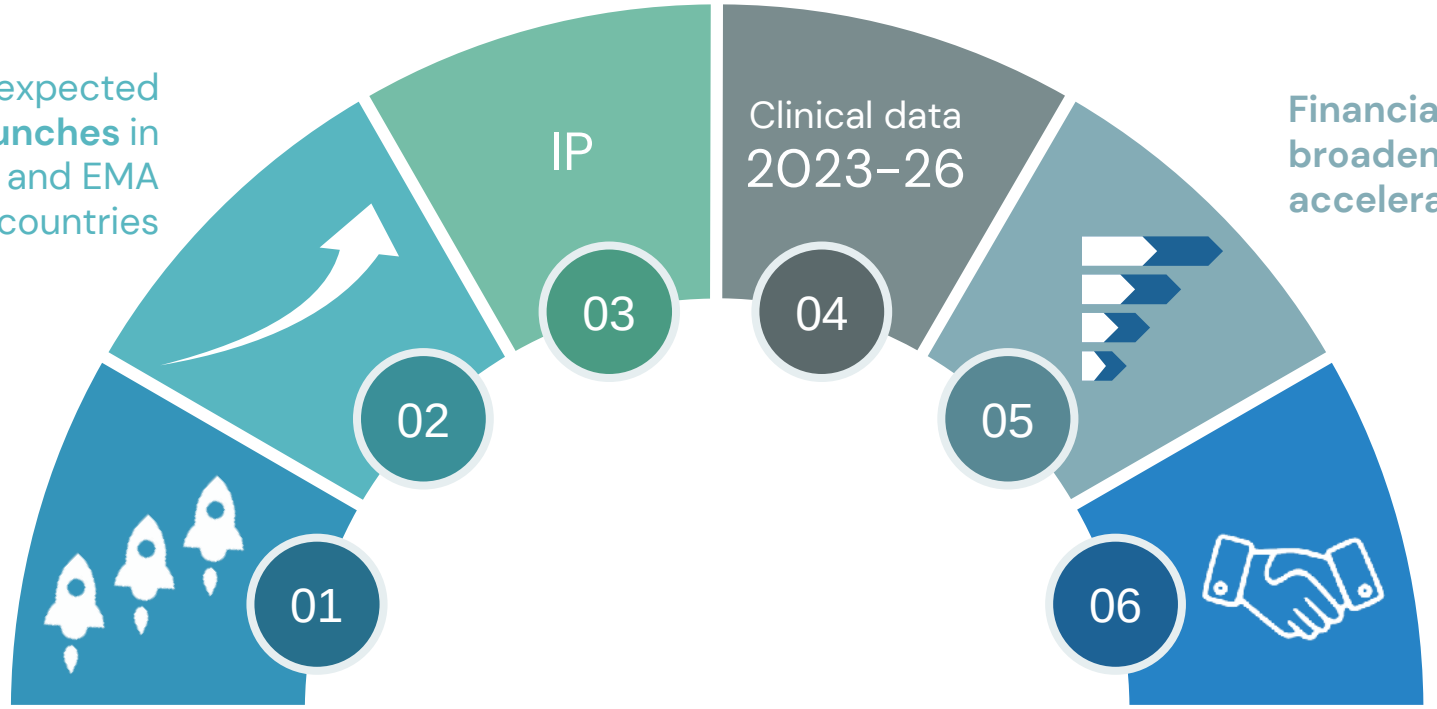
Zepzelca expected **approvals/launches** in non-EMA and EMA countries

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

www.pharmamar.com