



May 2024

# Corporate Presentation

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





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## Our vision

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.



# Corporate Overview

## Global Fully Integrated Commercial Stage Biotech

Developing marine-inspired oncology drugs

## Revenue Generating & Profitable

Revenues in 2023 **€158.2m**

EBITDA 2023 **€2.1m**

Cash 1Q 2024 **€164.5m**

Market cap **~ €570mn<sup>1</sup>**



(1) As of 2<sup>nd</sup> May 2024



## 3 Approved Oncology Products



Established European oncology sales force

## Discovery Platform Strengthening Oncology Pipeline

Diversified pipeline with late and early stage assets

# The Plan for growth

Continue delivering value to shareholders

## Lurbinectedin development

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- ✦ Phase 3 trials with lurbinectedin in SCLC for EU approval and confirmatory US
- ✦ Phase 2/3 trial with lurbinectedin in other indication
- ✦ Potential lurbinectedin approvals in other countries

## Other drugs development

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

## Corporate development

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

# Zepzelca: Transformative for PharmaMar

## License agreement in the US/Canada



**\$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.**

# Pipeline – Expanding our Expertise in Oncology

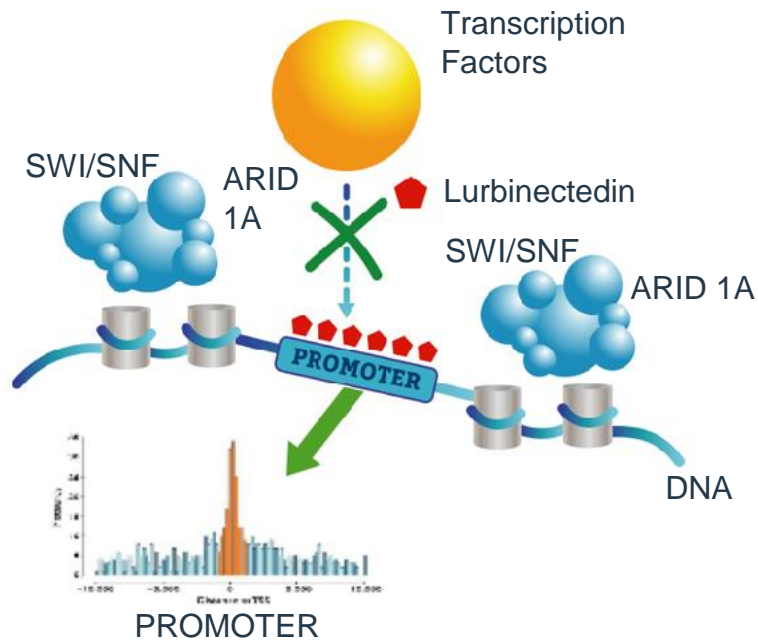
			Phase 1	Phase 2	Phase 3	Market	
	Soft tissue Sarcoma	Monotherapy	2 <sup>nd</sup> /3 <sup>rd</sup> line				
	Ovarian cancer	+ PLD (pegylated liposomal doxorubicin)	2 <sup>nd</sup> /3 <sup>rd</sup> line				
	R/R Multiple Myeloma <sup>1</sup>	+ dexamethasone	3 <sup>rd</sup> /4 <sup>th</sup> line				
	Small cell lung cancer	Monotherapy	2 <sup>nd</sup> line US / other countries				
	Small cell lung cancer maintenance	+ atezolizumab	1 <sup>st</sup> line maintenance			 	
	Small cell lung cancer	Lurbi vs. lurbi+ irinotecan vs. topotecan or irinotecan	2 <sup>nd</sup> line		LAGOON		
	Leiomyosarcoma	+ doxorubicin	1 <sup>st</sup> line	Phase IIb/III			
	Small cell lung cancer	+ irinotecan	2 <sup>nd</sup> line				
	Small cell lung cancer combo <sup>2</sup>	+ atezolizumab	2 <sup>nd</sup> line				
	Solid tumours (basket trial)	Monotherapy					
		Soft tissue sarcoma <sup>2</sup>	Combination radiation				
		Prostate cancer	Monotherapy				
Solid tumours		Combination trials					
		PM534	Solid tumours				
	PM54	Solid tumours					

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

# Zepzelca – A Transcription Inhibitor Leading to Tumour Inhibition

## Primary Effect

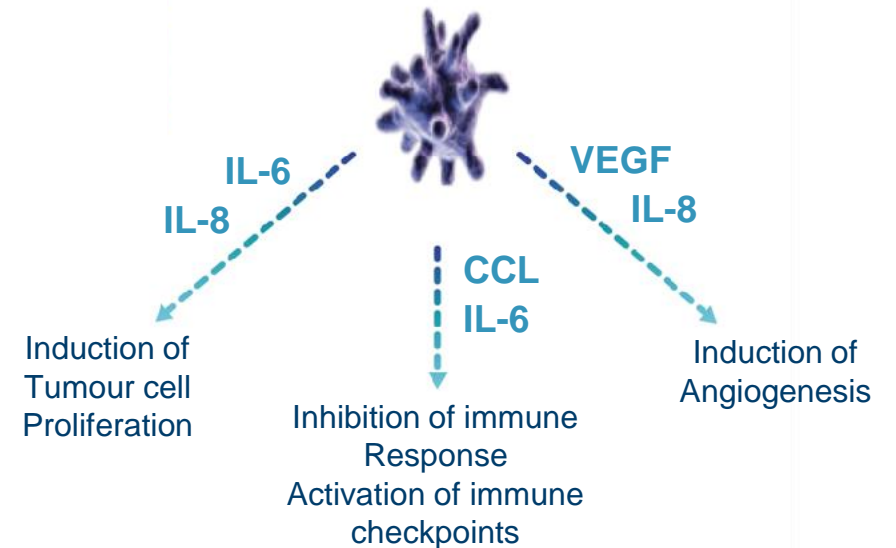
Cancer is frequently a transcriptional disease caused by deregulated oncogenic transcription factors



## Secondary Effect

Marked effect on the tumour microenvironment by inhibiting the transcription and secretion of tumour-growth promoting cytokines by Tumour Associated Macrophages (TAMs)<sup>1</sup>

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







**ZEPZELCA**  
(lurbinectedin)

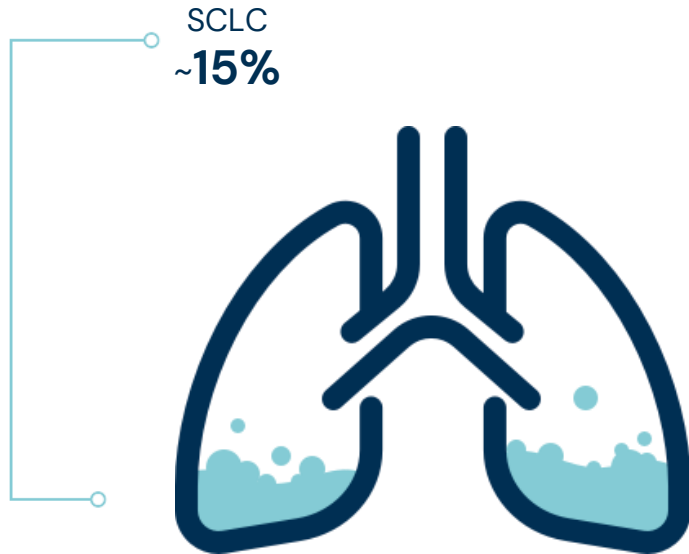
1<sup>st</sup> FDA approved drug in over **24 years**  
for Relapsed Small Cell Lung Cancer  
(SCLC)

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

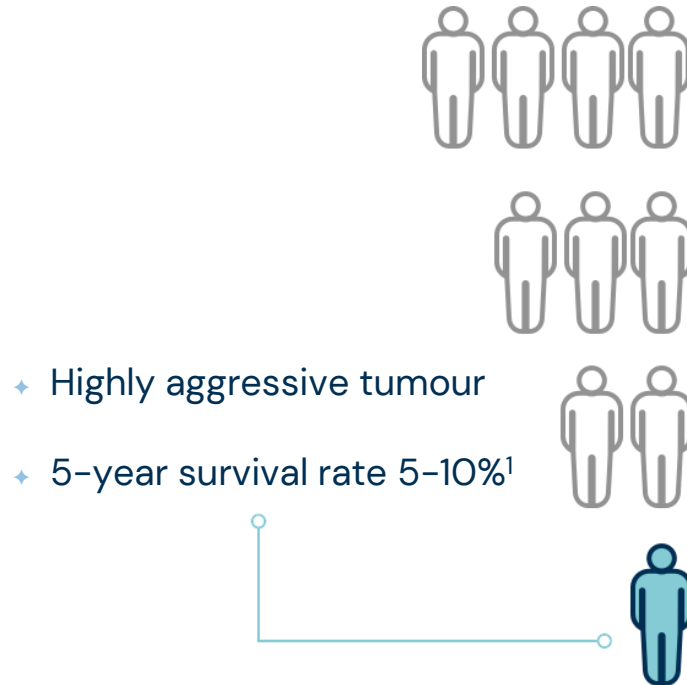
# Small Cell Lung Cancer (SCLC)

A high unmet medical need

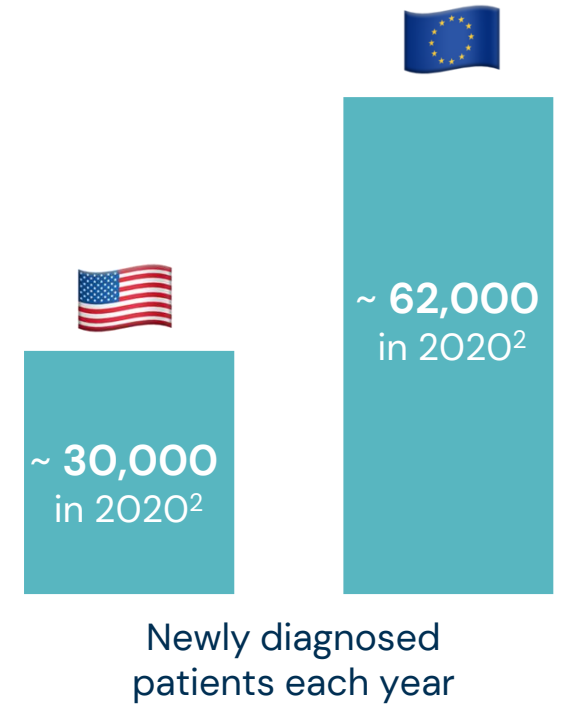
## Among all Lung Cancers



## Low survival rate at 5 years

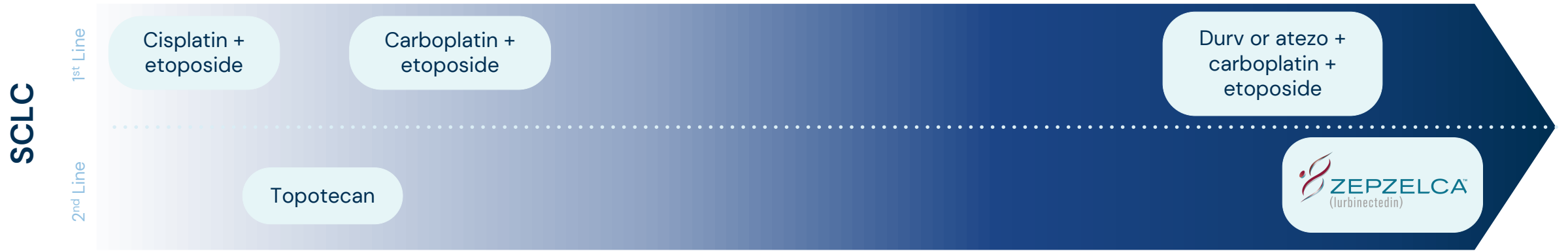


## Limited treatment options in both the US and Europe



# Small Cell Lung Cancer (SCLC)

Development lagging behind NSCLC; FDA approvals



Pre - 1993    1996    ← **24 years** →    2020



# Zepzelca (Lurbinectedin) – The SCLC Treatment Paradigm

Strong positioning opportunity



	1 <sup>st</sup> Line	Maintenance	2 <sup>nd</sup> Line	3 <sup>rd</sup> Line		1 <sup>st</sup> Line	2 <sup>nd</sup> Line	3 <sup>rd</sup> Line
FDA Approved	<ul style="list-style-type: none"> <li>Platinum/ Etoposide +</li> <li>Atezolizumab or Durvalumab</li> </ul>		<ul style="list-style-type: none"> <li><b>Zepzelca</b></li> <li>Topotecan (sensitive)</li> </ul>		EMA Approved	<ul style="list-style-type: none"> <li>Platinum/ Etoposide +</li> <li>Atezolizumab or Durvalumab</li> </ul>	<ul style="list-style-type: none"> <li>Topotecan</li> </ul>	
		Subsequent Therapy					Subsequent Therapy	
NCCN Guidelines <sup>1</sup>			CTFI >6m <ul style="list-style-type: none"> <li>Rechallenge</li> <li>Irinotecan</li> </ul>	CTFI <6m <ul style="list-style-type: none"> <li>Irinotecan</li> <li>Rechallenge</li> <li>Nivo/pembro</li> <li>Taxane</li> <li>Temozolomide</li> <li>CAV<sup>3</sup></li> <li>Gemcitabine</li> </ul>	ESMO Guidelines <sup>2</sup>		<ul style="list-style-type: none"> <li><b>Lurbinectedin</b></li> <li>CAV<sup>3</sup></li> <li>Re-challenge</li> </ul>	

1. NCCN guidelines v2.2024  
 2. ESMO guidelines Apr 13 2021  
 3. CAV: cyclophosphamide, adriamycin and vincristine



# 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<sup>1</sup>

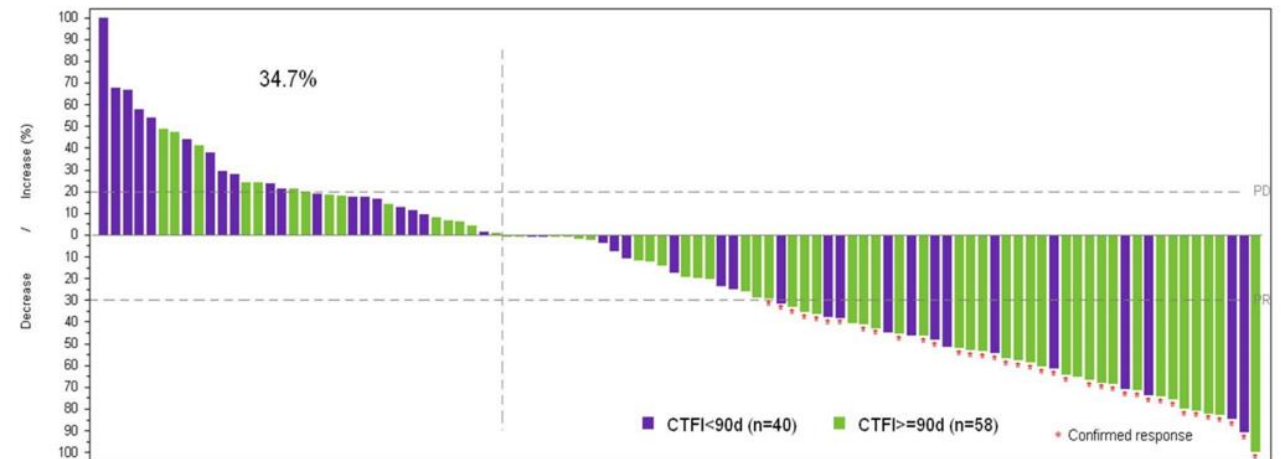
	Overall (n=105)	Resistant CTFI < 90 days (n=45)	Sensitive CTFI ≥ 90 days (n=60)
ORR (confirmed responses), median (95% c.i.)*	35.2% (26.2–45.2)	22.2% (11.2–37.1)	45.0% (32.1–58.4)
Duration of response (months), median (95% c.i.)	5.3 (4.1–6.4)	4.7 (2.6–5.6)	6.2 (3.5–7.3)
Disease Control Rate %**, (95%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

CTFI – Cancer Therapy-Free Interval

Decrease in tumour size in **65%** patients<sup>2</sup>



# Zepzelca Already Treatment of Choice in 2L SCLC

Low rate of AEs and manageable hematological safety profile despite low use of G-CSF <sup>1,2</sup>

## 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

# Zepzelca: Pathway to 2<sup>nd</sup> line in SCLC by EMA and Full Approval by FDA

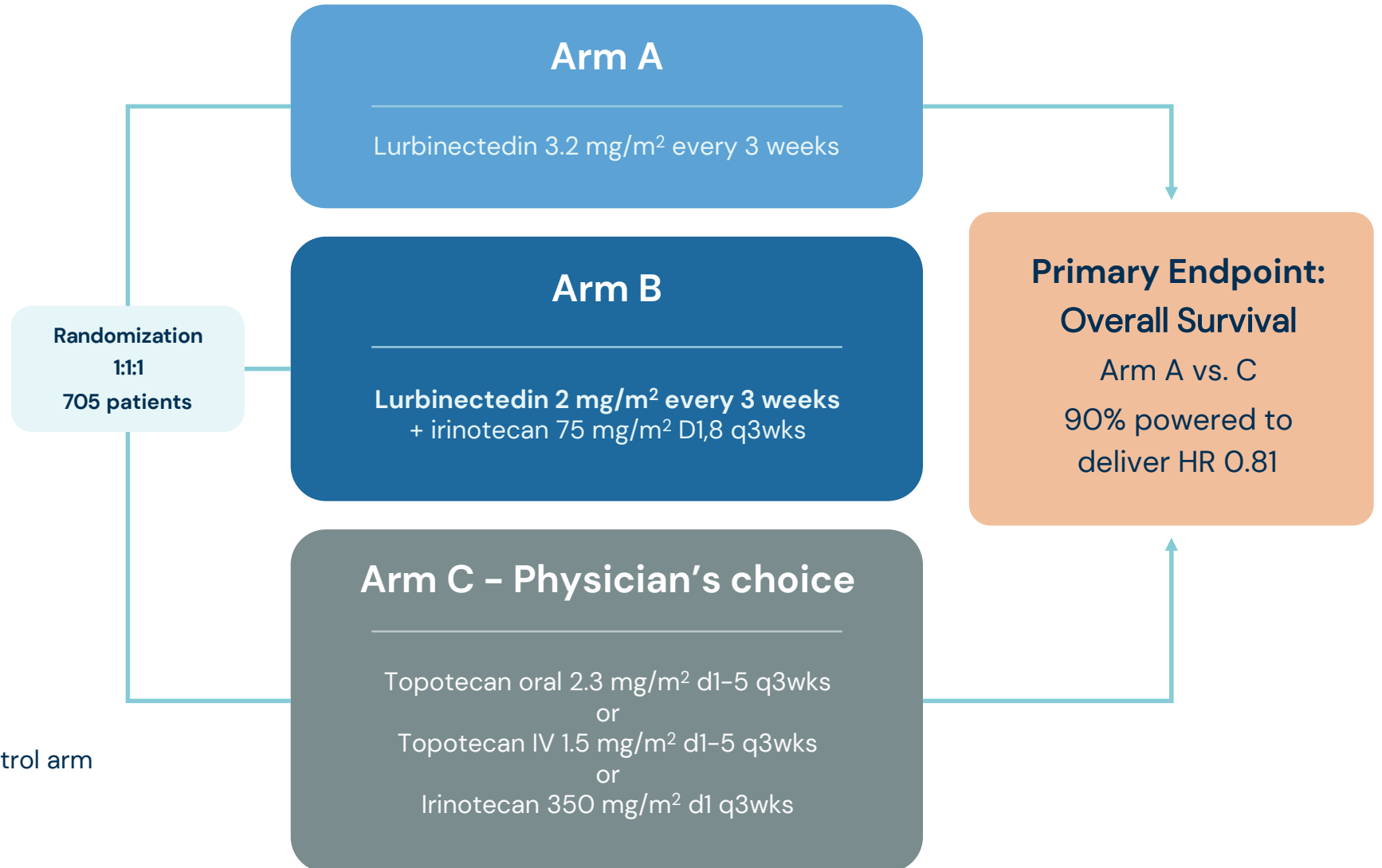
## Phase 3 (LAGOON) randomized trial



- ◆ Relapsed SCLC
- ◆ One prior platinum containing regimen
- ◆ CTFI  $\geq$ 30 days
- ◆ ECOG 0-2

### Stratification Factors

- CTFI ( $\geq$  90 days,  $<$ 90 days)
- Prior PD-L1/PD-1 (Y/N)
- LDH ( $>$  ULN or  $\leq$  ULN)
- CNS involvement (Y/N)
- Investigator's preference of the control arm



1. NCT05153239





## 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 data from different trials.
- In a prior trial, **we allowed stable brain mets**. Partly due to protocol violations this proved the worst subgroup, HR 1.2911. 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.





**ZEPZELCA**  
(lurbinectedin)

1st line–Maintenance Study in SCLC

# SITC 2021

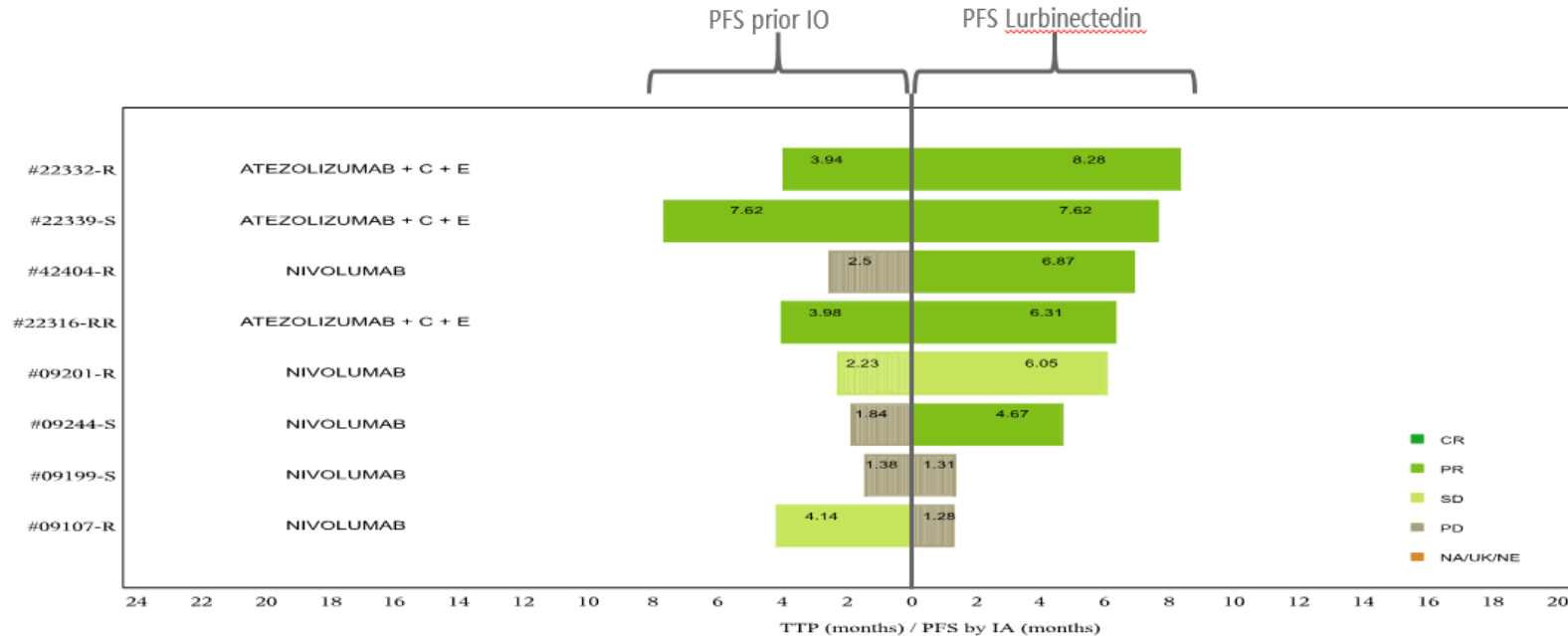
Combo with IO delivers efficacy not seen for either drug as single agent

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<sup>2</sup> (n=5) followed by lurbi 3.2mg/m<sup>2</sup> (n=21, full dose)

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

## LURBI AFTER IO: BASKET TRIAL SUBSET PFS TO PRIOR IO AND PFS AFTER LURBINECTEDIN<sup>1</sup>

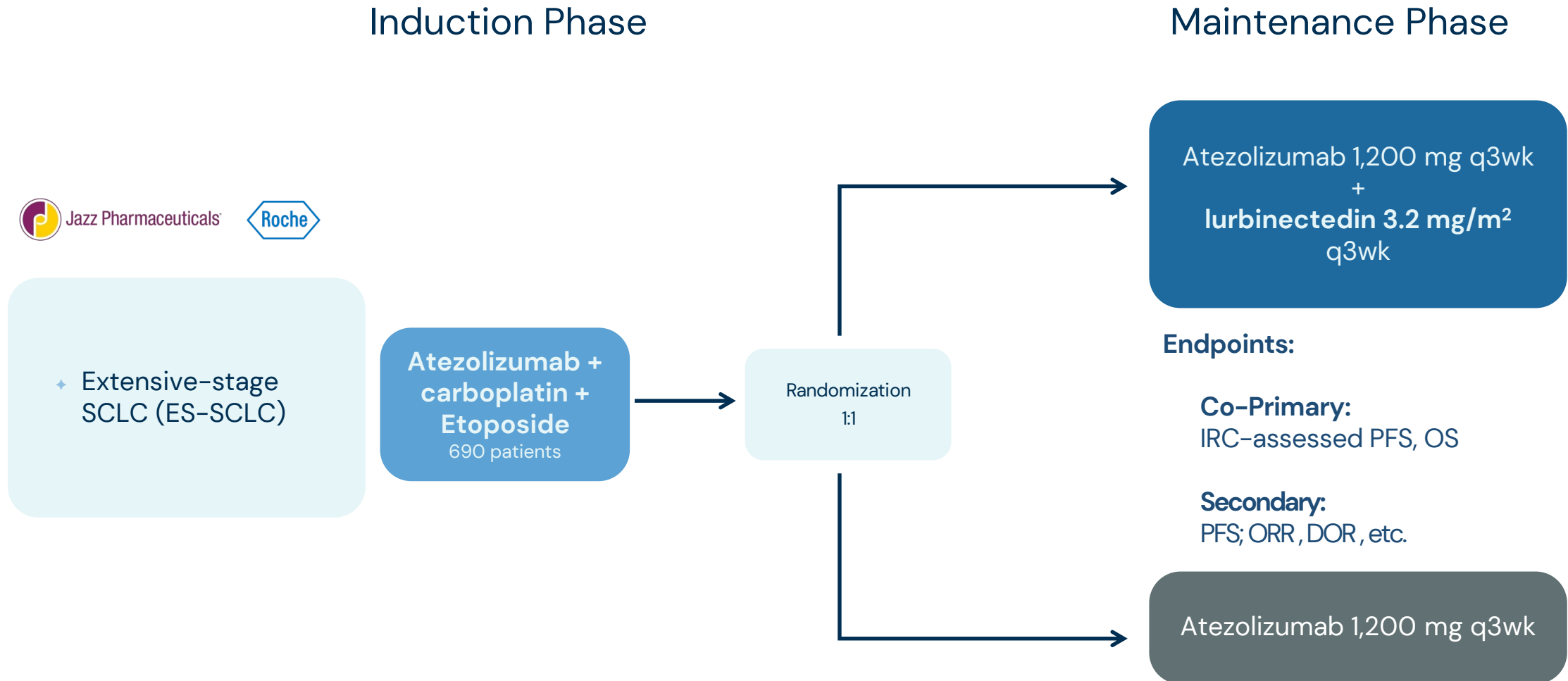


Basket trial: 6 of 8 had lurbi PFS  $\geq$  PFS with prior IO including 5 CRs, 2 of which happened in 2L post PD

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

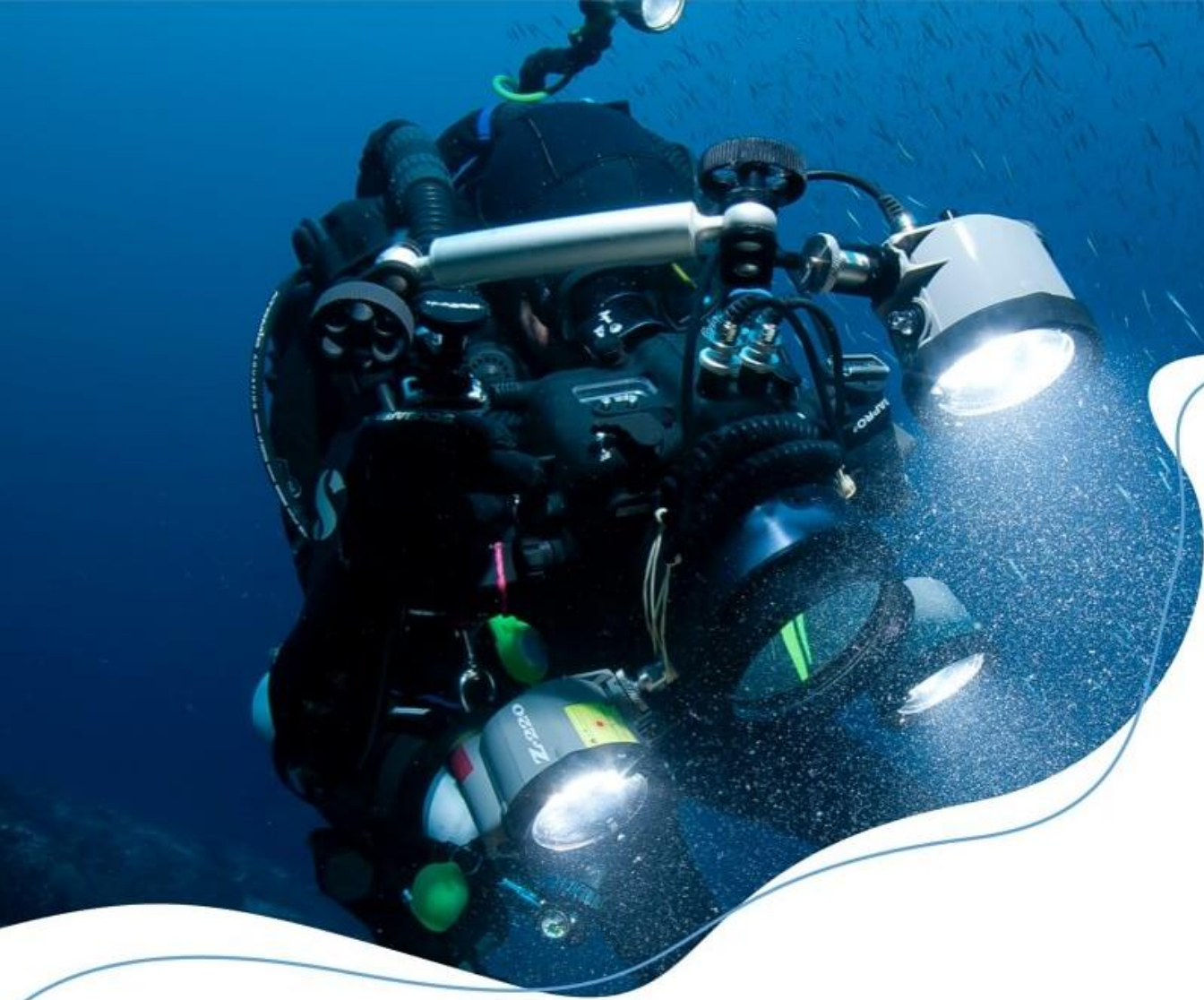
# Lurbinectedin: First-line maintenance positioning

## Phase 3 trial for first line-maintenance SCLC



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<sup>(1)</sup> in USA

	1 <sup>st</sup> Line	2 <sup>nd</sup> Line
<b>FDA Approved</b>	<ul style="list-style-type: none"> <li>✦ Doxorubicin</li> <li>✦ Ifosfamide</li> </ul>	<ul style="list-style-type: none"> <li>✦ Trabectedin</li> <li>✦ Pazopanib</li> </ul>
<b>NCCN Guidelines</b>		<ul style="list-style-type: none"> <li>✦ Dacarbazine</li> <li>✦ Ifosfamide</li> <li>✦ Gemcitabine based regimen</li> </ul>



Incidence

and ~4,500<sup>(2)</sup> in Europe

	1 <sup>st</sup> Line	2 <sup>nd</sup> Line
<b>EMA Approved</b>	<ul style="list-style-type: none"> <li>✦ Doxorubicin</li> <li>✦ Ifosfamide</li> </ul>	<ul style="list-style-type: none"> <li>✦ Trabectedin</li> <li>✦ Pazopanib</li> </ul>
<b>ESMO Guidelines</b>		<ul style="list-style-type: none"> <li>✦ Gemcitabine+ docetaxel</li> <li>✦ Dacarbazine-gemcitabine</li> </ul>

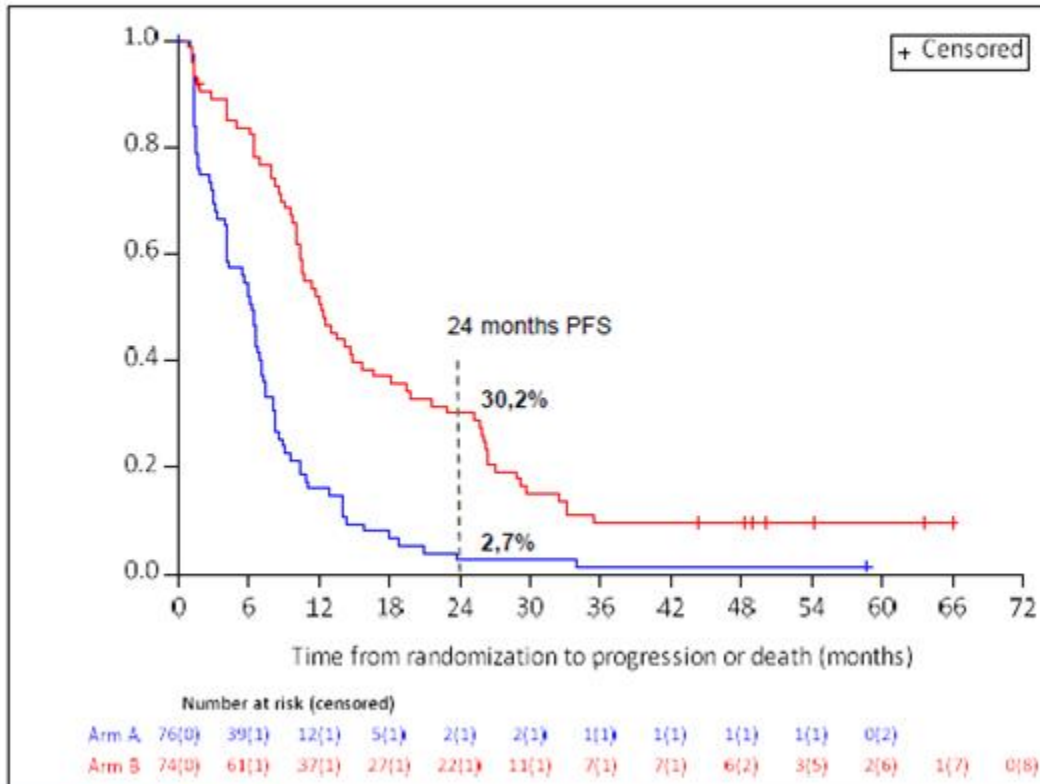
1. The American Cancer Society
2. ESMO Sarcoma guidelines 2021

# 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



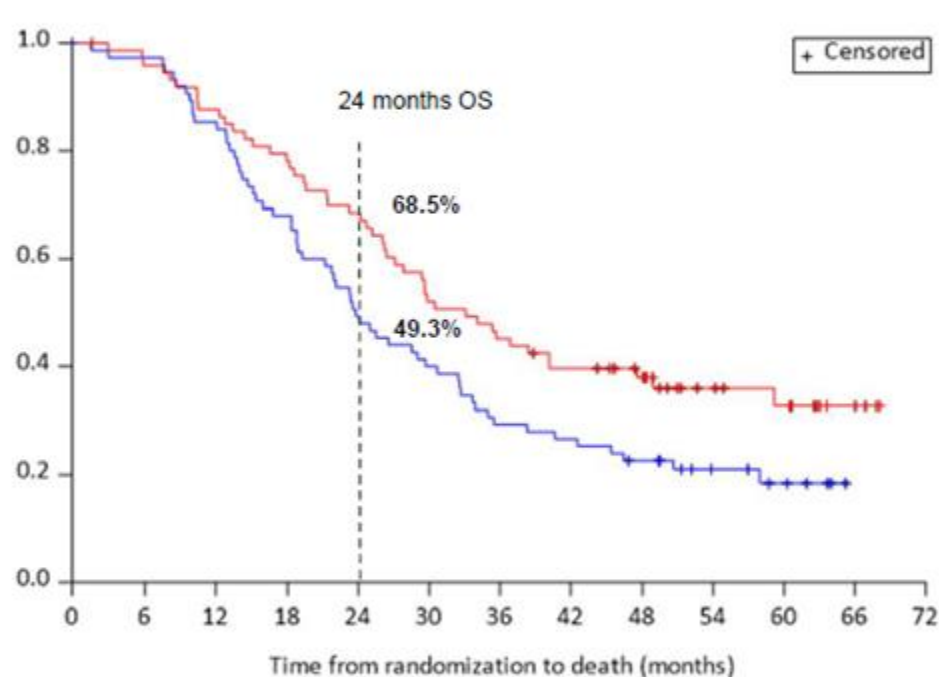
# Leiomyosarcoma

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

## Overall Survival

LMS-04 study

Median Follow-up : 55 months



	0	6	12	18	24	30	36	42	48	54	60	66	72
Number at risk (censored)	76(0)	73(1)	64(1)	51(1)	37(1)	30(1)	22(1)	20(1)	16(2)	10(7)	5(11)	0(16)	
Arm A	74(0)	70(1)	64(1)	57(1)	50(1)	38(1)	33(1)	28(2)	23(6)	13(15)	10(17)	4(23)	0(27)

	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



# Zepzelca (lurbinectedin)-Leiomyosarcoma

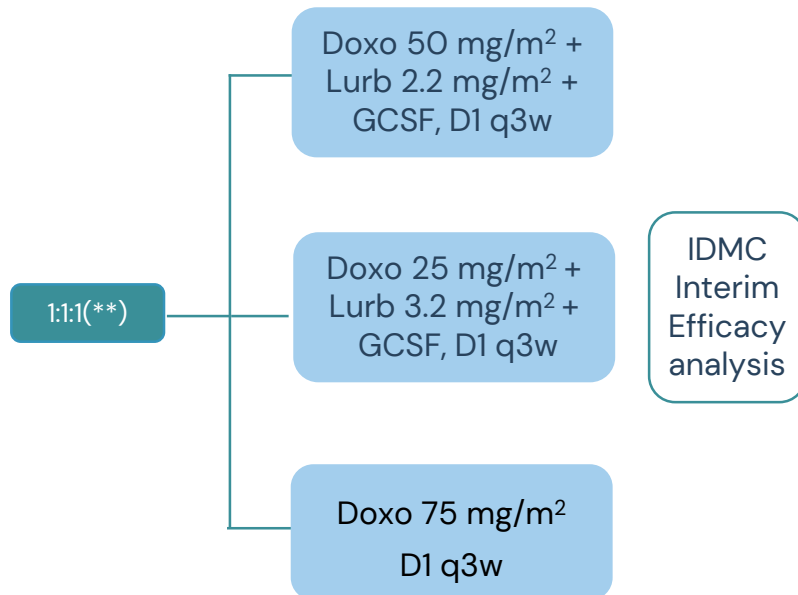
## Phase IIb/III adaptive trial

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

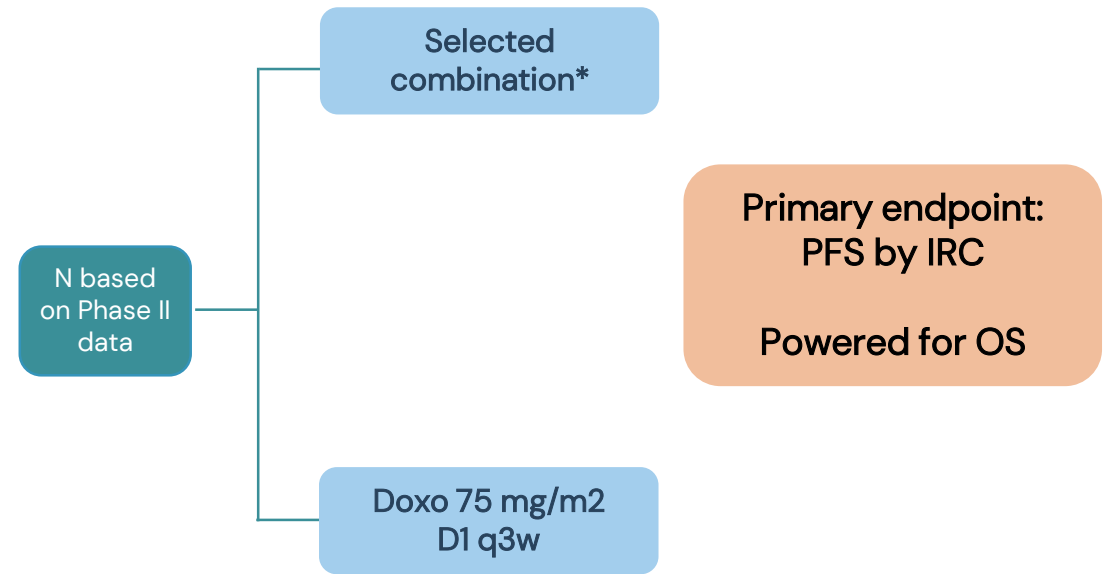
### Stratification:

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

### Phase IIb



### Phase III



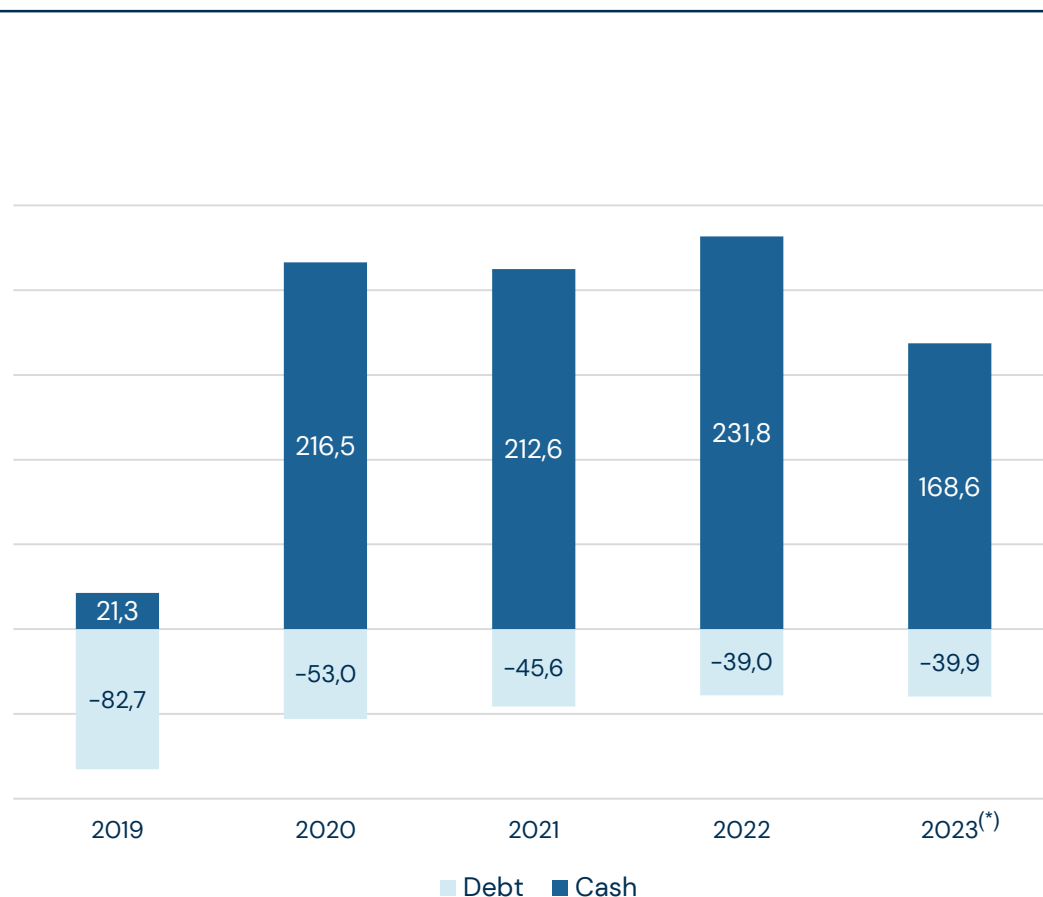
(\*) Treatment may continue until PD, tox or up to a maximum cumulative dose of doxo of 450mg/m<sup>2</sup> (continuing lurbi 3.2mg/m<sup>2</sup> D1 q3w in experimental arms)

(\*\*) Cohort sizes to be finalized by IDMC as trial evolves

# Financials

## Profitable and solid and stable financial position

### Robust cash position (€ mn)



### Historical revenues evolution (€ mn)

	2021	2022	2023 <sup>(*)</sup>
<b>Recurring revenues</b>	<b>164.8</b>	<b>155.9</b>	<b>123.7</b>
Oncology sales	118.9	100.7	70.7
Other sales	4.9	4.9	1.2
Royalties	41.0	50.3	52.3
<b>Non-recurring revenues</b>	<b>65.0</b>	<b>40.4</b>	<b>34.1</b>
License agreements	64.8	40.2	33.6
Other	0.2	0.2	0.5
<b>Total revenues</b>	<b>229.8</b>	<b>196.3</b>	<b>158.2</b>

(\*) First full year of generics of trabectedin in the European market.

# Key Events Catalyst Calendar



Zepzelca approved in Switzerland for SCLC



Lurbi + Irinotecan Phase 2 topline data

ASCO 2024

Potential lurbinectedin approval in China

2024

Potential lurbinectedin approvals and launches in other countries

Ongoing

End of recruitment LAGOON

2024

Potential in-licensing

Ongoing

IMforte PFS top line data

~YE24/1Q25

# Building the Next Phase of Growth

2021-2026

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

Strong Zepzelca I.P. exclusivity period

Financial strength allows broadening and accelerating R&D engine

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

Leveraging proven oncology platform in **new indications**

Fuel leading EU sales

## 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





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