



March 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

Revenue Generating &
Profitable

Revenues in 2022 €196.3m

EBITDA 2022 €51.4m

Cash 2022 €231.8m

Market cap €1.0Bn¹



3 Approved Oncology
Products

Yondelis
(trabectedin)

Aplidin[®]
plitidepsin

ZEPZELCA
(lurbinectedin)

Established European oncology
sales force

Discovery Platform
Strengthening Oncology
Pipeline

Diversified pipeline with late
and early stage assets

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



\$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
- ◆ **Initiated Phase 3** in 1L maintenance ES-SCLC in combination with Tecentriq® in collaboration with Roche

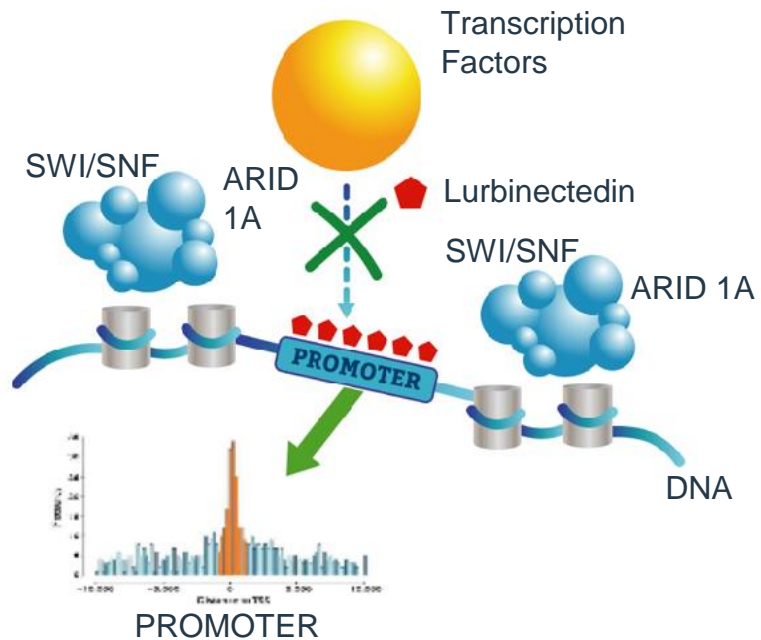
Pipeline – Expanding our Expertise in Oncology

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

Zepzelca – A Transcription Inhibitor Leading to Tumor Inhibition

Primary Effect

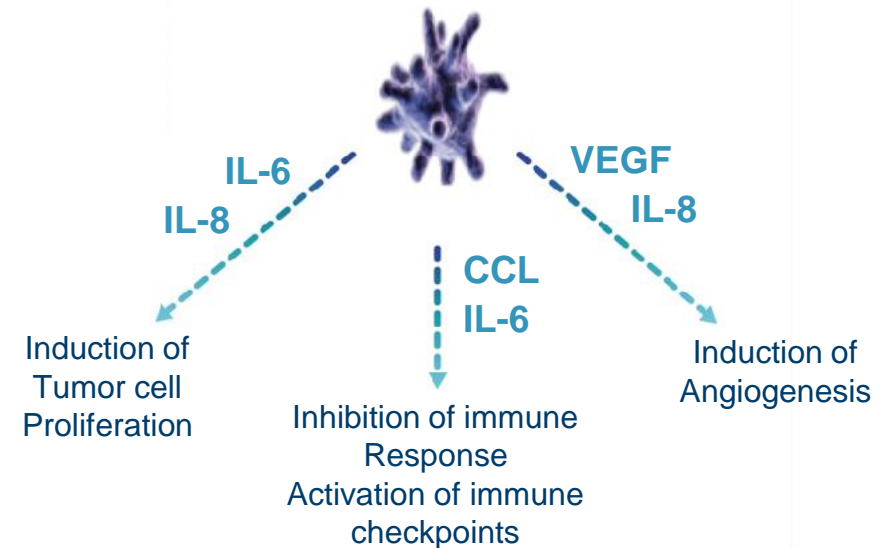
Cancer is frequently a transcriptional disease caused by deregulated oncogenic transcription factors



Secondary Effect

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

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



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

SCLC



ZEPZELCA
(lurbinectedin)

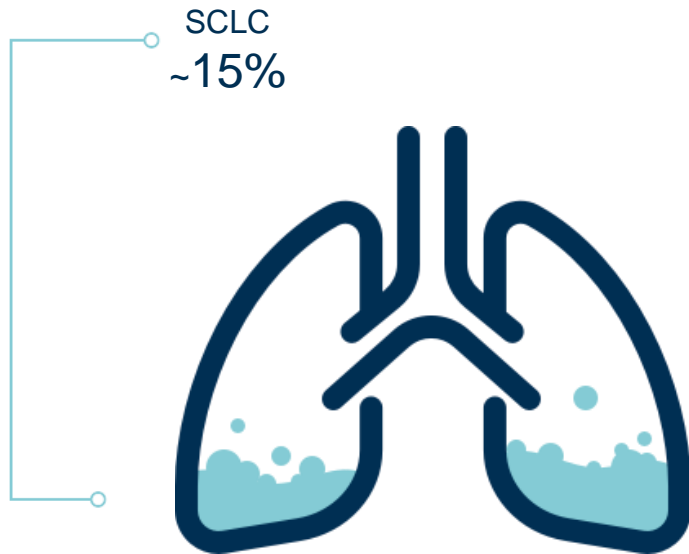
1st FDA approved drug in over 24 years for Relapsed Small Cell Lung Cancer (SCLC)

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

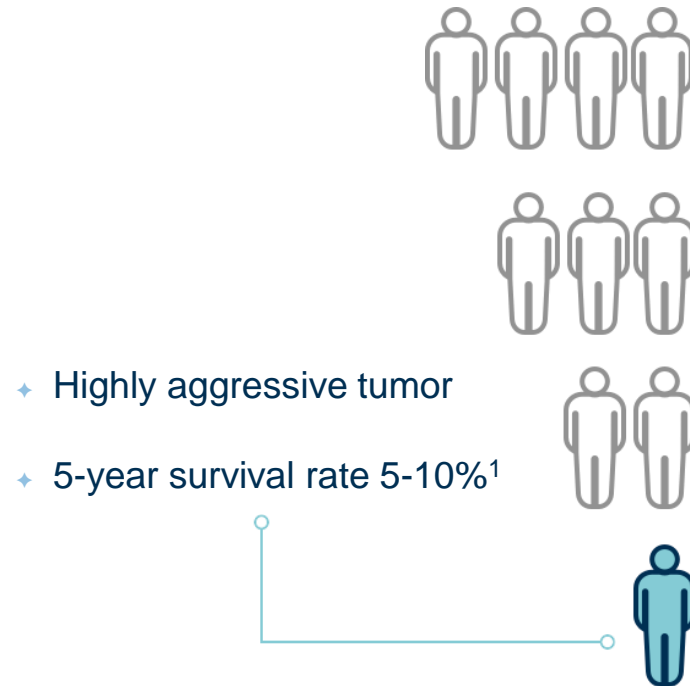
Small Cell Lung Cancer (SCLC)

An high unmet medical need

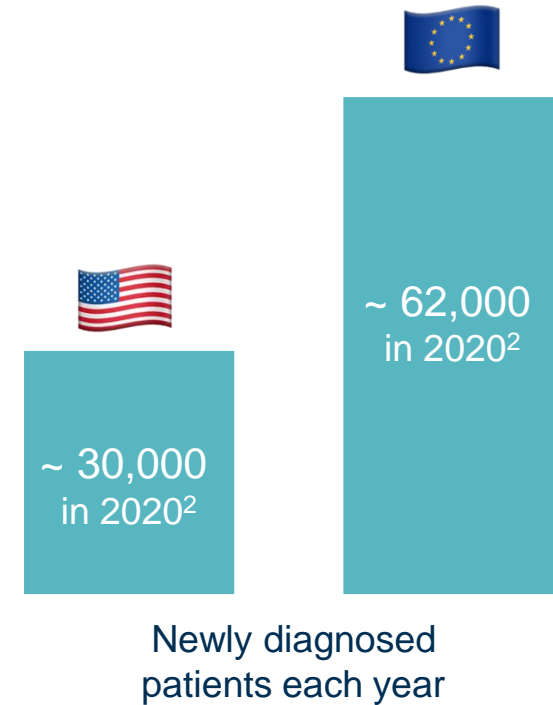
Among all Lung Cancers



Low survival rate at 5 years

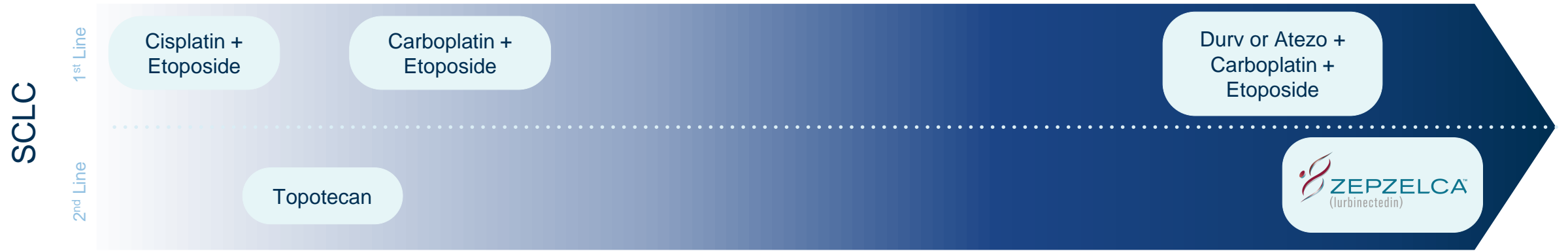


Limited treatment options in both the US and Europe



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 st Line	2 nd Line	3 rd Line		1 st Line	2 nd Line	3 rd Line
FDA Approved	<ul style="list-style-type: none"> Platinum/ Etoposide + Atezolizumab or Durvalumab 	<ul style="list-style-type: none"> Zepzelca Topotecan (sensitive) 		EMA Approved	<ul style="list-style-type: none"> Platinum/ Etoposide + Atezolizumab or Durvalumab 	<ul style="list-style-type: none"> Topotecan 	
		Subsequent Therapy				Subsequent Therapy	
NCCN Guidelines* ¹		<ul style="list-style-type: none"> Bendamustine CAV³ Docetaxel Gemcitabine Irinotecan Nivo 	<ul style="list-style-type: none"> Oral etoposide Paclitaxel Pembro Rechallenge Temozolomide Vinorelbine 	ESMO Guidelines* ²		<ul style="list-style-type: none"> Lurbinectedin CAV³ Re-challenge 	
	1 st Line		Maintenance		2 nd Line		3 rd 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

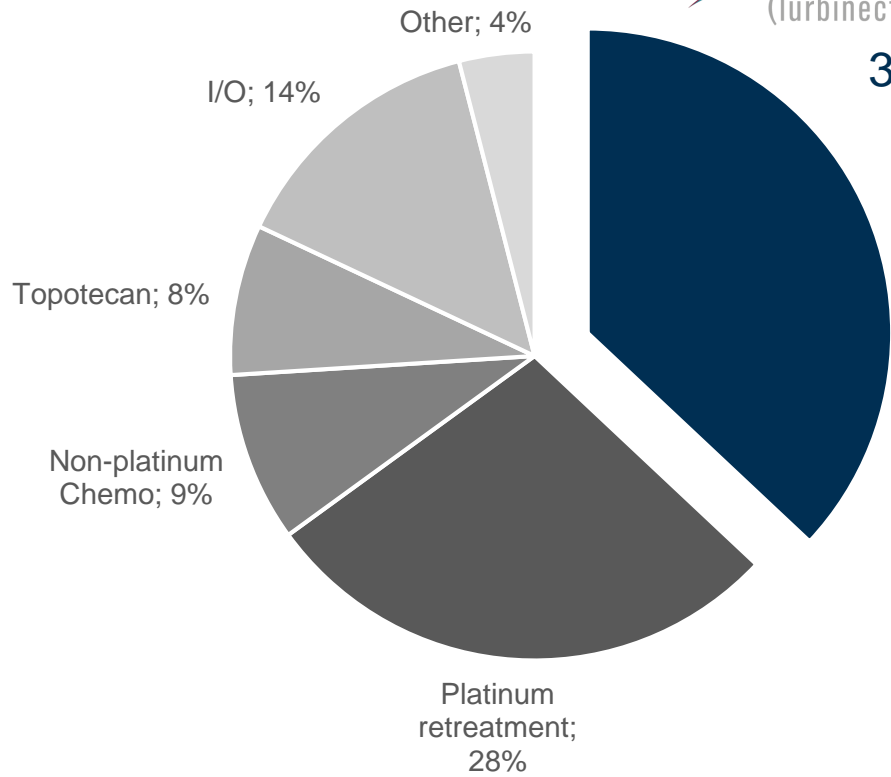
3. CAV: cyclophosphamide, adriamycin and vincristine

4. <https://clinicaltrials.gov/ct2/show/NCT05091567>

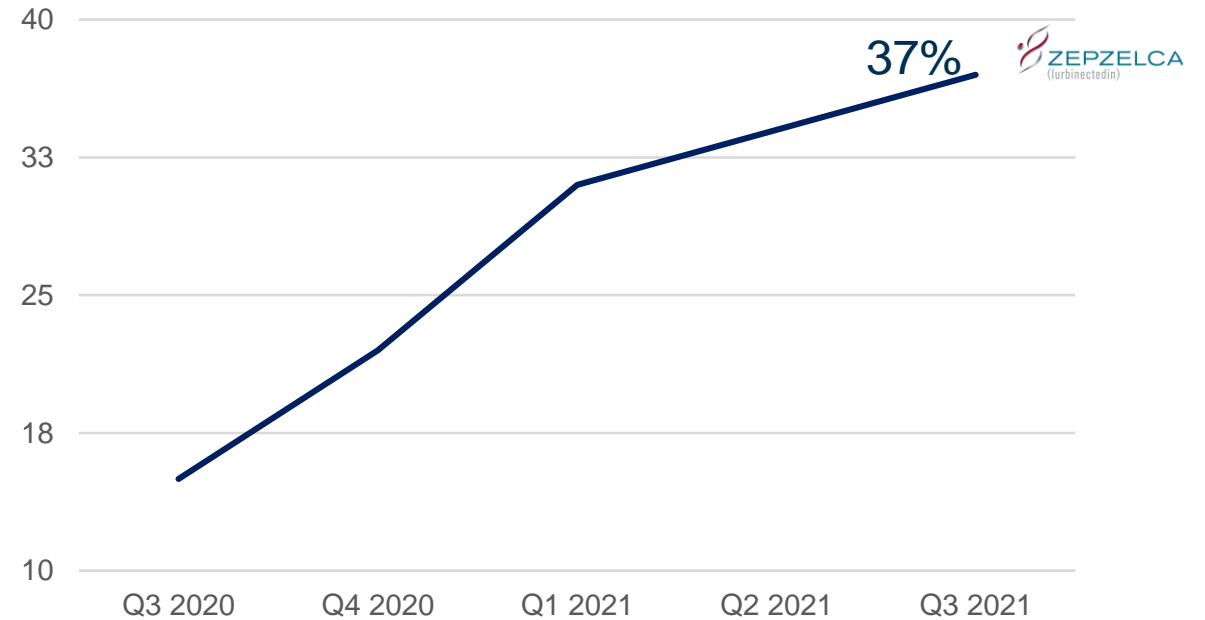
5. <https://clinicaltrials.gov/ct2/show/NCT05153239>

Zepzelca Already Treatment of Choice in 2L SCLC

Opportunities for future growth



% Market Share in 2L SCLC in the US



Zepzelca Already Treatment of Choice in 2L SCLC

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

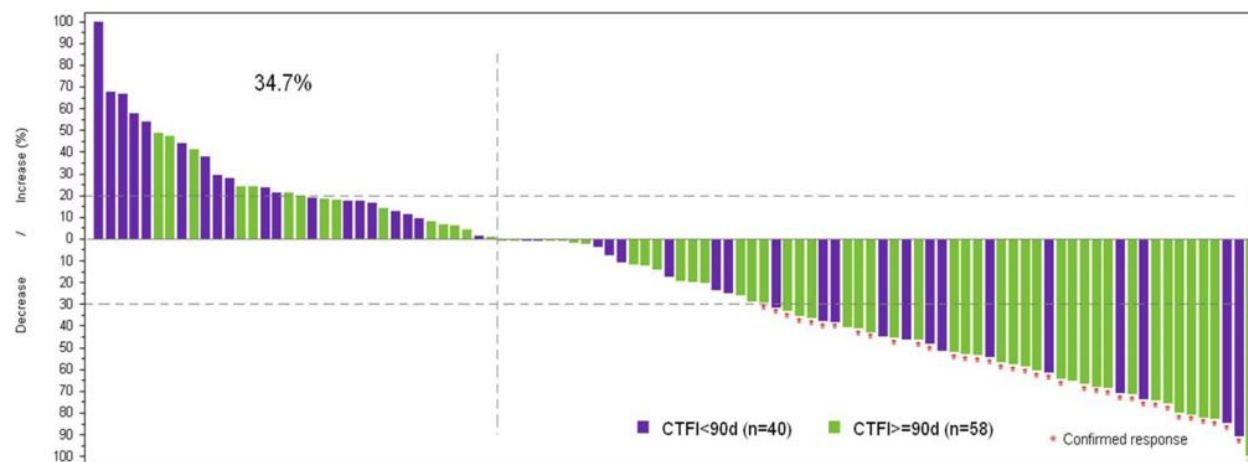


In relapsed SCLC as monotherapy under accelerated approval based on Phase 2 monotherapy data¹

	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% patients²



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

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

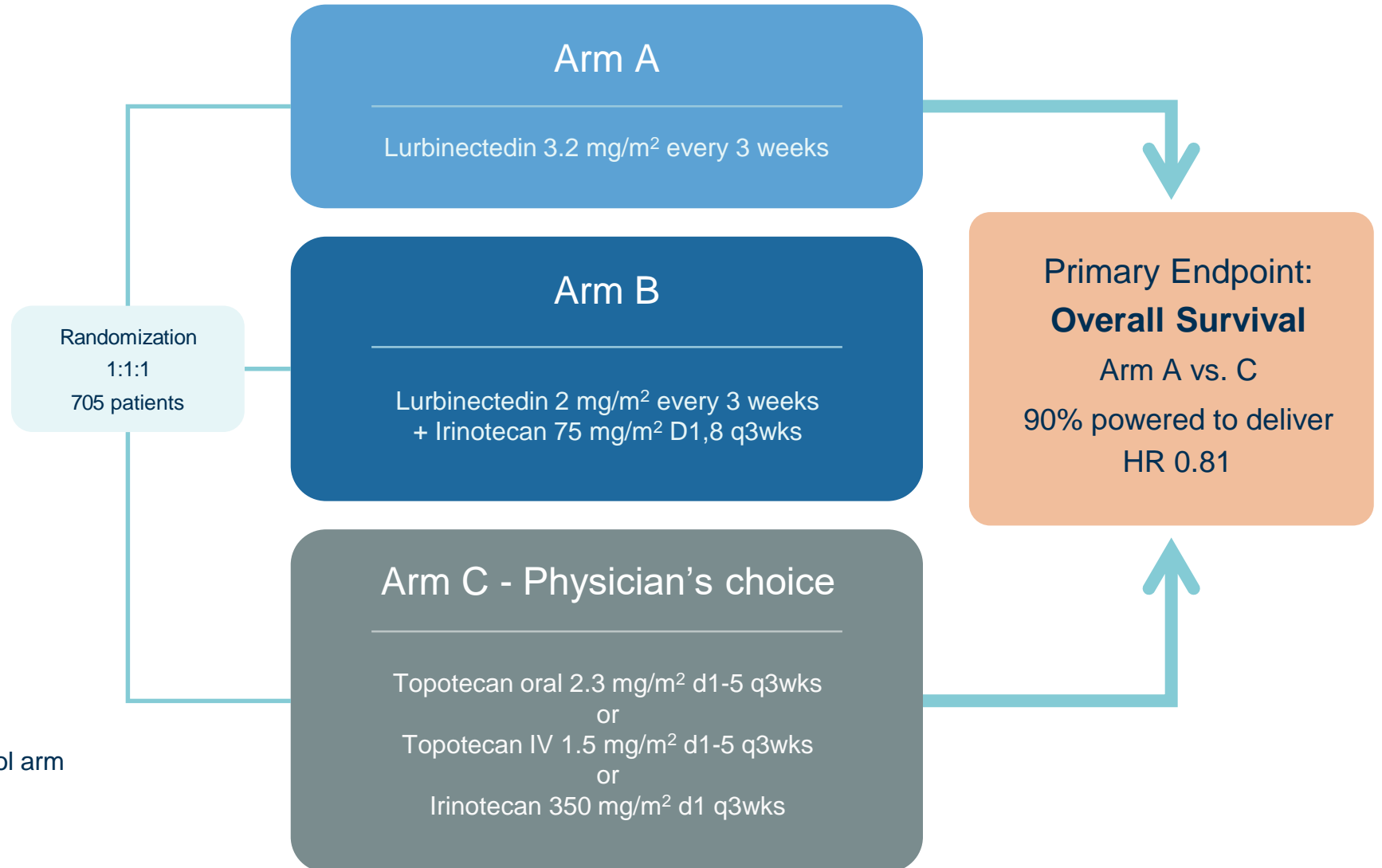
Phase 3 (LAGOON) randomized trial



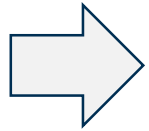
- ✦ Relapsed SCLC
- ✦ One prior platinum containing regimen
- ✦ CTFI ≥ 30 days
- ✦ ECOG 0-2

Stratification Factors

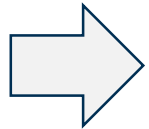
- CTFI (≥ 90 days, <90 days)
- Prior PD-L1/PD-1 (Y/N)
- LDH ($> ULN$ or $\leq ULN$)
- CNS involvement (Y/N)
- Investigator's preference of the control arm



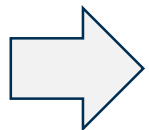
Positioning LAGOON for success



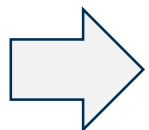
70% of patients to have had prior IO. There is no evidence of additive or synergistic benefit for control arm. For lurbinectedin, there are three pieces of data.



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 1.291¹. 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.

SCLC



 **ZEPZELCA**
(lurbinectedin)

1st line-Maintenance Study in SCLC

SITC 2021

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

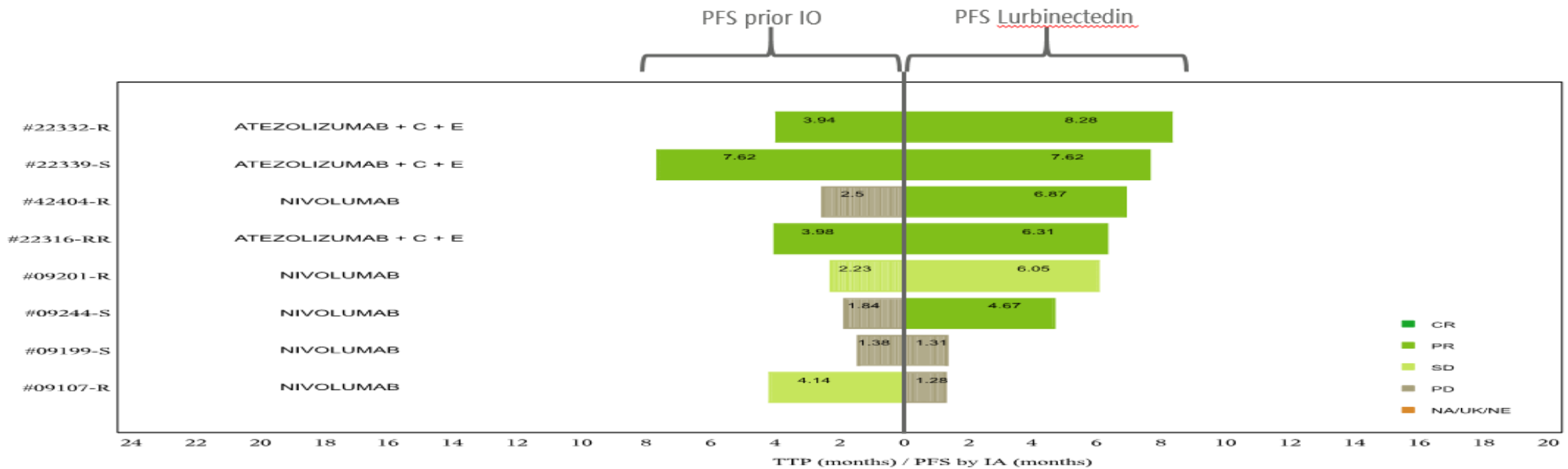
- Phase I open label dose ranging trial in pts who had progressed on platinum. ECOG 0-1
- Full dose Atezo (1200 mg) + L2.5mg/m² (n=5) followed by L3.2mg/m² (n=21, full dose)

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)

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

Basket trial: 6 of 8 had lurbi PFS \geq 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 LURBINECTEDIN¹



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/m² q3wk

Endpoints:

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

Atezolizumab 1,200 mg q3wk

Strategic importance of Zepzelca Phase 3s in SCLC

Potential treatment landscape after Phase 3s



	1 st Line	1 st Line- Maintenance	2 nd Line
FDA	<ul style="list-style-type: none"> Platinum/ Etoposide + Atezolizumab or Durvalumab 	<ul style="list-style-type: none"> Zepzelca + Atezolizumab 	<ul style="list-style-type: none"> Zepzelca Topotecan (sensitive)



	1 st Line	1 st Line- Maintenance	2 nd Line
EMA	<ul style="list-style-type: none"> Platinum/ Etoposide + Atezolizumab or Durvalumab 	<ul style="list-style-type: none"> Zepzelca + Atezolizumab 	<ul style="list-style-type: none"> Zepzelca Topotecan (sensitive)



Malignant Pleural Mesothelioma Trial start 2023

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

~3,500¹ patients diagnosed in the US per year

	1 st Line	2 nd Line
FDA Approved	<ul style="list-style-type: none"> † Nivo + Ipi † Pemetrexed + Plat † Gemcitabine + Cis 	
NCCN³ Guidelines	<ul style="list-style-type: none"> † Pemetrexed + plati+bev⁴ 	<ul style="list-style-type: none"> † Pemetrexed⁴ (IO naïve) † Ramucirumab⁴ † Vinorelbine † Gemz + Cis



Incidence

and ~13,700¹ in Europe²

	1 st Line	2 nd Line
EMA Approved	<ul style="list-style-type: none"> † Pemetrexed + Plat † Nivol + Ipi 	
ESMO⁵ Guidelines		<ul style="list-style-type: none"> † Pembro, Nivo +/-Ipi⁶ † Pemetrexed +/- Plat † Gemz +/-ramu † Vinorelbine

Phase 3 Trials

Atezolizumab⁵

Durvalumab⁵

Pembrolizumab⁵

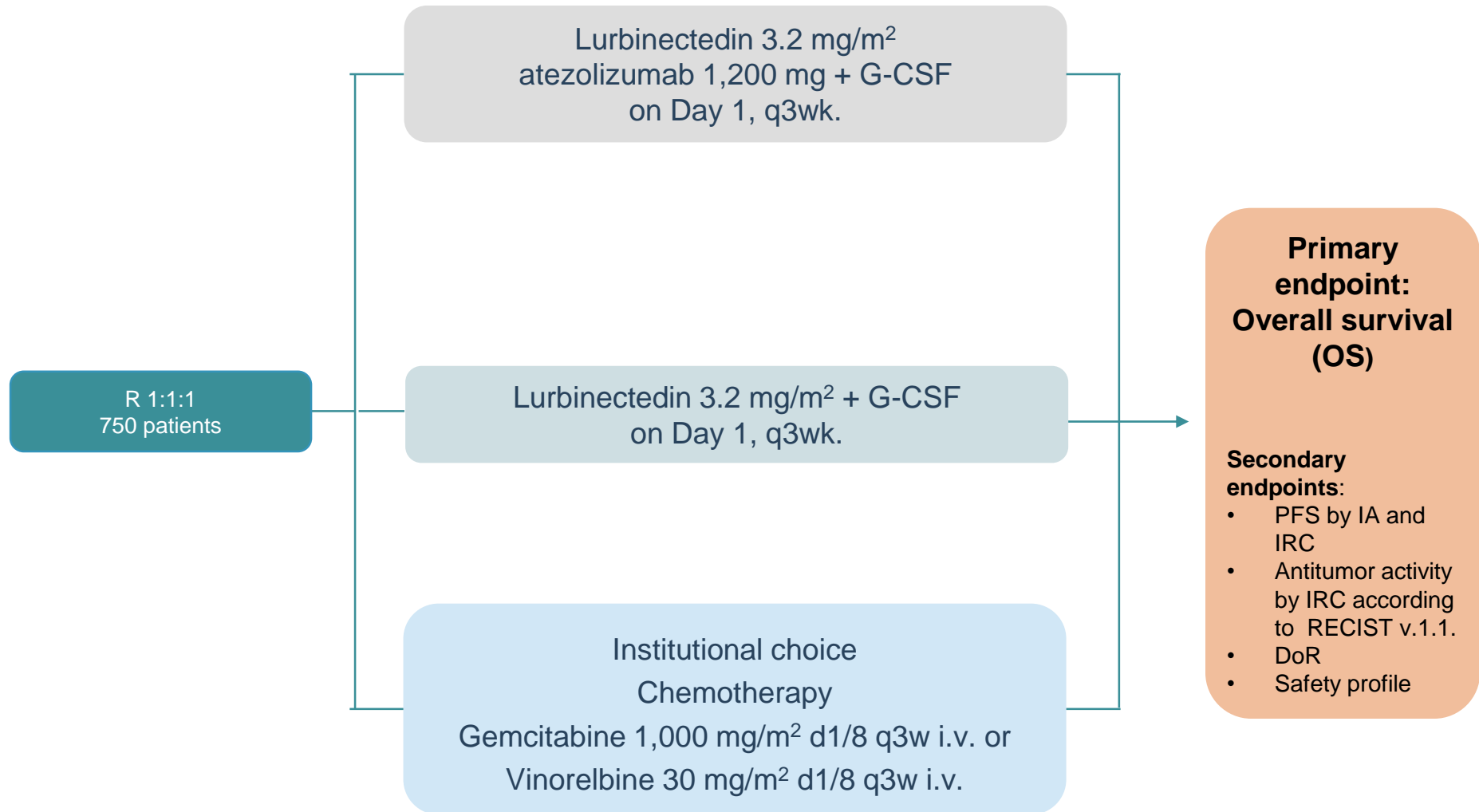
1. Data Monitor: Globocan 2020. All ages, both genders
2. [Contributors – UpToDate](#)
3. NCCN Guidelines v1.2022; All recommendations category 2A except where stated

4. Not approved in this indication
5. ESMO guidelines Nov 2021
6. Only in IO naïve patients

Zepzelca (Lurbinectedin) – SEALIGHT

Phase III trial starting 2023

- Malignant pleural mesothelioma
- Progression after no more than 2 prior treatment lines
- ECOG 0-1
- Adequate hematological, renal and liver functions



STS



ZEPZELCA
(lurbinectedin)

Leiomyosarcoma
Trial start 2023

Leiomyosarcoma

Incidence and treatment paradigm

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



Incidence

~2,100 in USA

	1 st Line	2nd Line
FDA Approved	<ul style="list-style-type: none"> ◆ Doxorubicine ◆ Ifosfamide 	<ul style="list-style-type: none"> ◆ Trabectedin ◆ Pazopanib
NCCN Guidelines		<ul style="list-style-type: none"> ◆ Dacarbazine ◆ Ifosfamide ◆ Gemcitabine based regimen



Incidence

and ~4,500 in Europe

	1 st Line	2nd Line
EMA Approved	<ul style="list-style-type: none"> ◆ Doxorubicine ◆ Ifosfamide 	<ul style="list-style-type: none"> ◆ Trabectedin ◆ Pazopanib
ESMO Guidelines		<ul style="list-style-type: none"> ◆ Gemcitabine+ docetaxel ◆ Dacarbazine-gemcitabine

Zepzelca (Lurbinectedin)-Leiomyosarcoma Phase IIb/III trial

Co PIs:

- Mass Gen, USA
- Gustave Roussy, France

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

Stratification:

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

Phase IIb

R
n ~ 120
1:1:1

Doxo 50 mg/m² +
Lurb 2.2 mg/m² +
GCSF
D1 q3w

Doxo 25 mg/m² +
Lurb 3.2 mg/m² +
GCSF
D1 q3w

Doxo 75 mg/m²
D1 q3w

Interim
Efficacy
analysis
by
IDMC

Phase III

R
n ~ 120
1:1

Phase IIb Selected
combination

Doxo 75 mg/m²
D1 q3w

Primary endpoint:
PFS by IRC

FPI



Mid '23

Aprox 80 sites in 9 European countries +USA

DATA



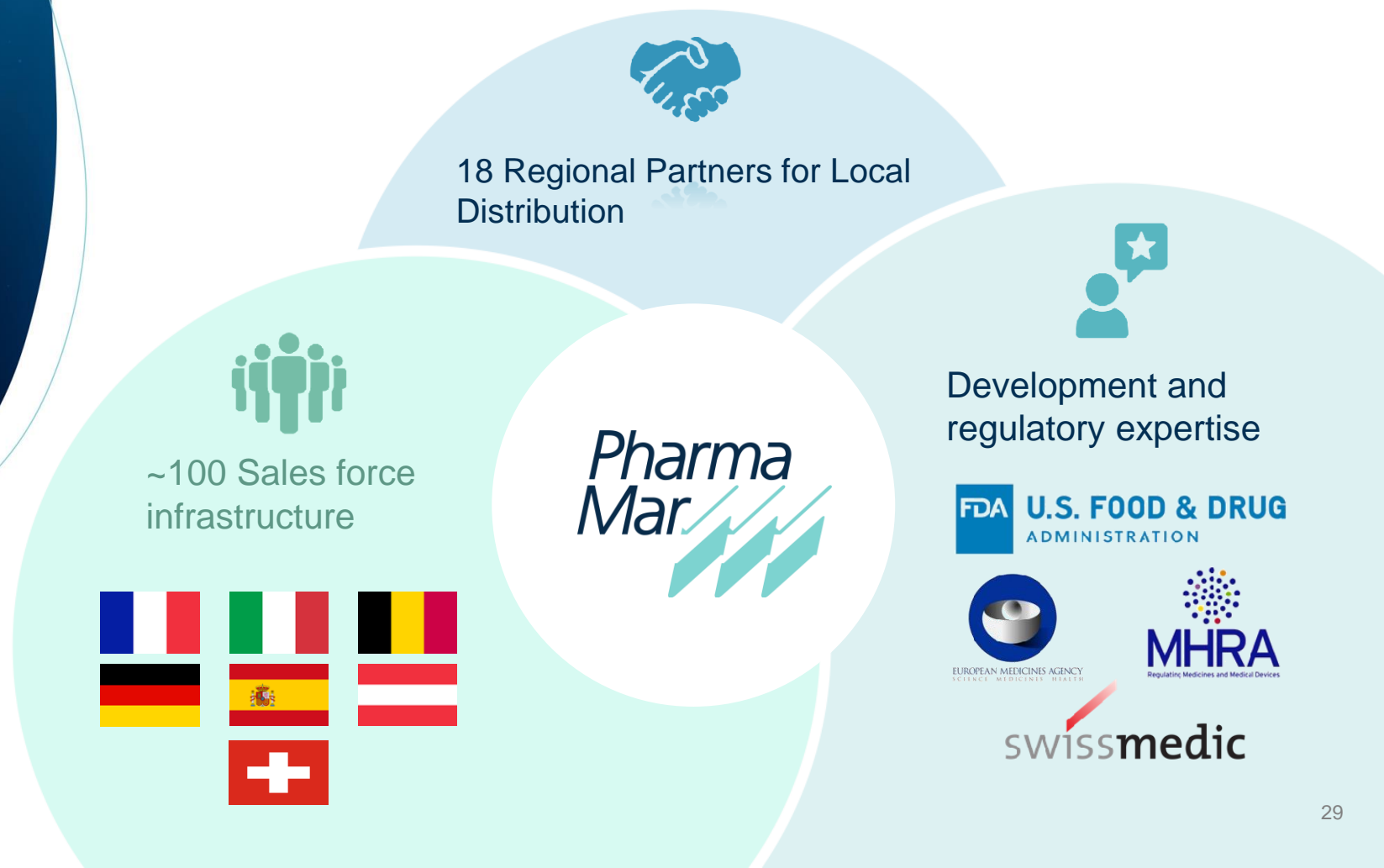
End '26

28

European experience:

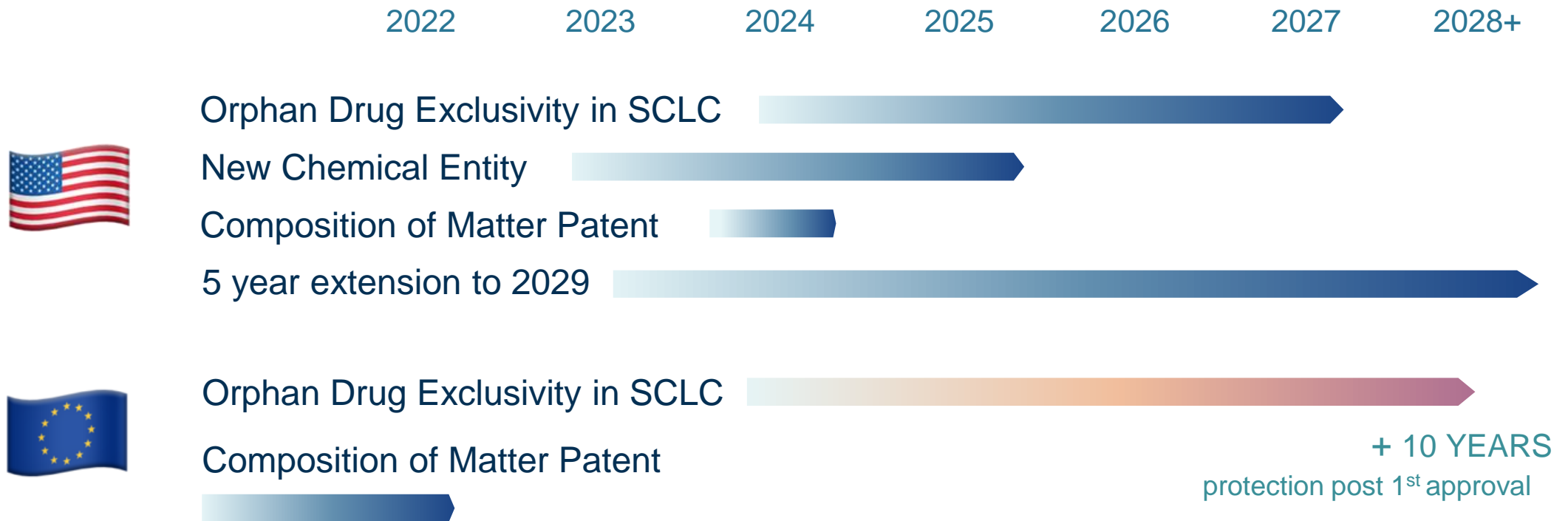
- ◆ Strong KOL connections in solid tumors
- ◆ Navigation of EU, UK and CH regulators
- ◆ Logistics in place for distribution
- ◆ Expertise in multi-language labelling
- ◆ Broad knowledge in reimbursement procedures, market access and negotiations in key European countries
- ◆ Engaged in multiple negotiations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

Leveraging Commercial Infrastructure in Europe PharmaMar positioned as a partner of choice in Europe



Zepzelca (Lurbinectedin) – Intellectual property

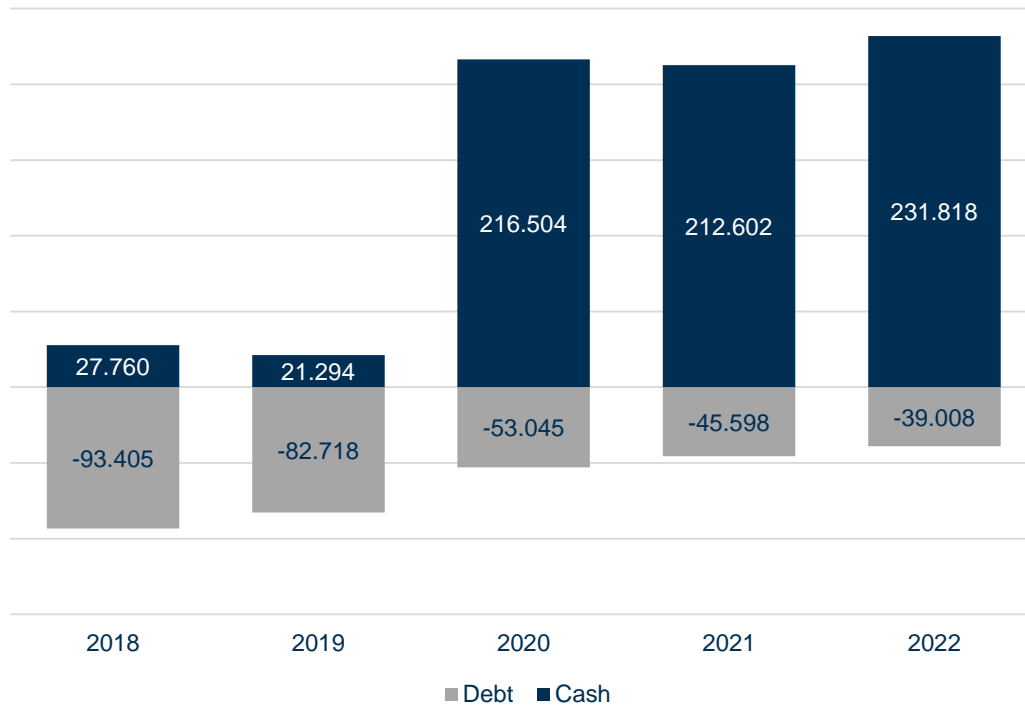
Life cycle management plans under way



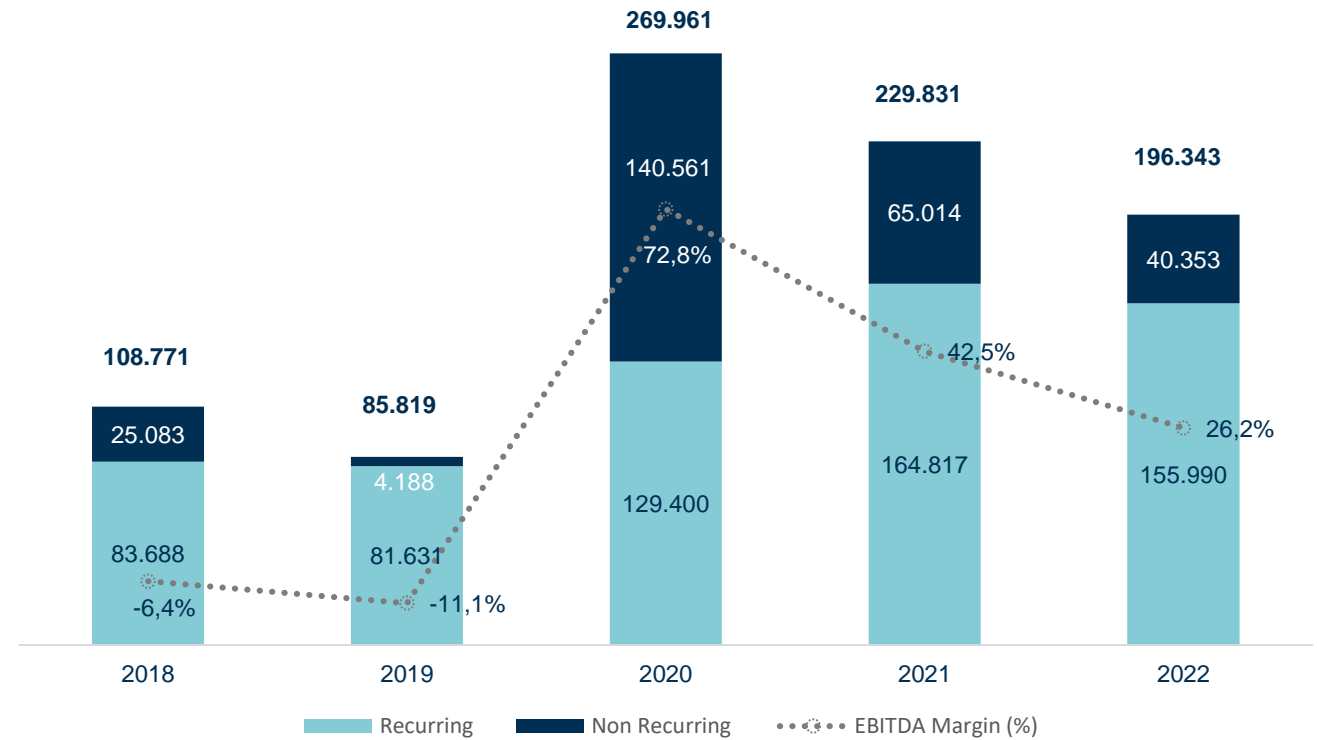
Financials

Well financed to support next stages of development

Robust Cash Position (€m)



Profitable (€m)



Key Events Catalyst Calendar



Zepzelca approved in Switzerland for SCLC



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

Building the Next Phase of Growth

2021-2026

Strong Zepzelca I.P

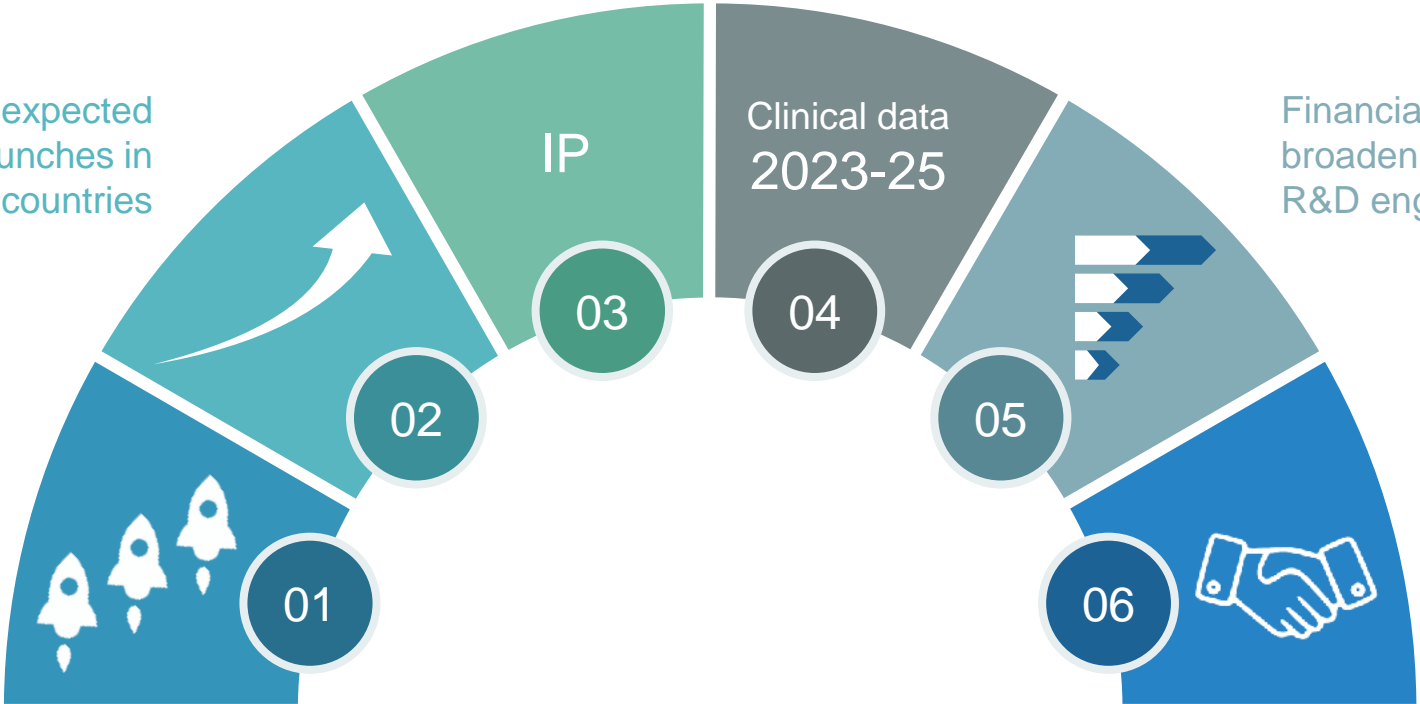
Leveraging proven oncology platform in new indications

Zepzelca expected approvals/launches in non-EMA countries

Clinical data 2023-25

Financial strength allows broadening and accelerating R&D engine

Profitable Biotech with 3 commercial assets and cash to support growth



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



Pharma
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