Pharma Mar

June 2022

Corporate Presentation

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

Disclaimer

This presentation contains forward-looking statements that include information about possible or assumed future results of the business, financial condition, liquidity, results of operation, clinical program, plans and objectives of Pharma Mar, S.A. ("PharmaMar" or the "Company"). These forward-looking statements can be identified by the use of forward-looking terminology such as “may,” “will,” “should,” “expect,” “endeavor,” “anticipate,” “project,” “estimate,” “intend,” “continue” or “believe” or the negatives thereof or other variations thereon or comparable terminology. These forward-looking statements are based on the expectations of management under current assumptions at the time of this presentation, are not guarantees of future performance and are subject to risks and uncertainties that could cause actual results to materially differ from those contained in the forward-looking statements. All forward-looking statements in this presentation apply only as of the date made. Except as required by law, the Company is not obligated to, and does not intend to, update or revise any forward-looking statements, whether as a result of new information, future events or otherwise. To the extent that this presentation contains market data, industry statistics and other data that have been obtained from, or compiled from, information made available by third parties, the Company has not independently verified their data.

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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

Chief Operating Officer
PHM US

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

Aplidin plitidepsin

ZEPZELCA

Established European oncology sales force

Revenue Generating & Profitable

Revenues in 2021	**€230m**
EBITDA 2021	**€97.7m**
Cash 1Q22	**€250m**
Market cap	**€1.3bn**[1]

Discovery Platform Strengthening Oncology Pipeline

Diversified pipeline with late-stage asset and 2 early-stage assets about to enter the clinic

(1) As of 30th May 2022

The Plan for Growth

On Track to Deliver Value to Shareholders

Lurbinectedin development

- Phase 3 trial 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
- 2 new compounds to enter Phase 1

Corporate development

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

Pipeline – Expanding our Expertise in Oncology

			Phase 1	Phase 2	Phase 3	Market
Yondelis	Soft tissue sarcoma 2nd/3rd line	Monotherapy				
	Ovarian cancer 2nd/3rd line	+ Doxil (PLD)				
Aplidin plitidepsin	R/R Multiple Myeloma 3rd/4th line[1]	+ dexamethasone				
ZEPZELCA (lurbinectedin)	Small cell lung cancer 2nd line US	Monotherapy				
	Small cell lung cancer Maintenance	**+ Atezolizumab**				
	Small cell lung cancer 2nd line (LAGOON) (Registrational Europe and Confirmatory US)	**Lurbi vs. Lurbi+ Irinotecan vs. Topotecan or Irinotecan**				
(Lurbinectedin)	Mesothelioma ≥2nd line	+ IO				
	SCLC 2nd line IST Combos	+ Atezolizumab				
Ecubectedin (PM14)	Solid tumors	Monotherapy				
	Soft tissue sarcoma IST	Combination radiation				
	Solid tumors	Combination trials				

Roche

Jazz Pharmaceuticals

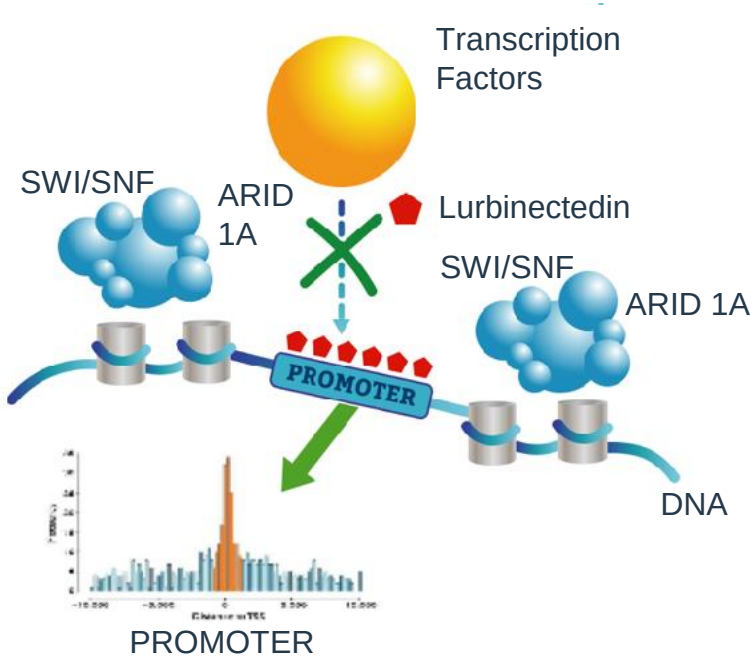
IST – Investigator Sponsored Trial

(1) Approved in Australia

Zepzelca – A Transcription Inhibitor Leading to Tumor Inhibition

Primary Effect

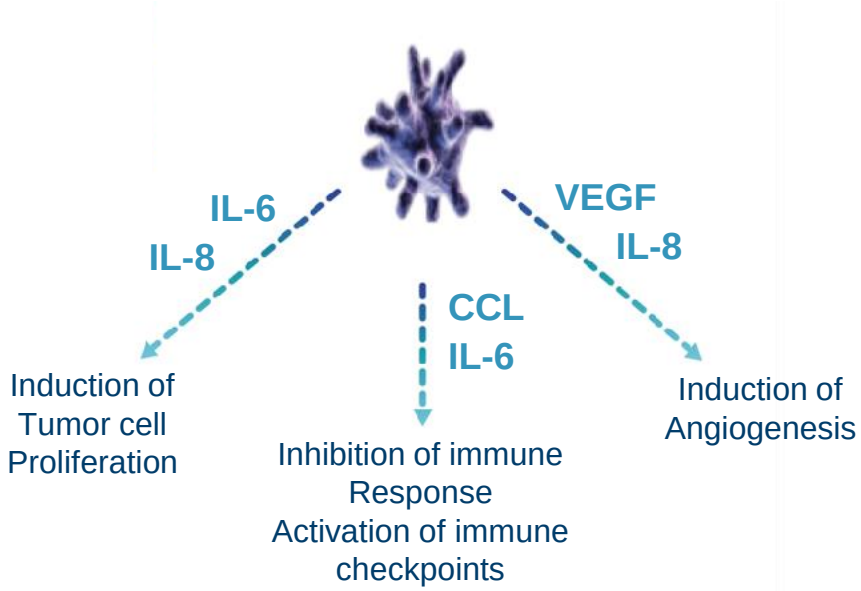
Cancer is frequently a transcriptional disease caused by deregulated oncogenic transcription factors



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

By inhibiting active transcription in Tumor Associated Macrophages (TAMs), lurbinectedin downregulates IL-6, IL-8, CCL2 and VEGF



Harlow et al, 2016; Cancer Res 72: 6657-68
Harlow et al, 2019; Clin Cancer Res doi: 10.1158/1078-0432.CCR-18-3511
Santamaría et al, 2016. Mol Cancer Ther 15:2399-412

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

Pharma Mar

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
- n=690 / Primary completion expected in **early 2025**

Small Cell Lung Cancer (SCLC)
An Underserved High Unmet Medical Need

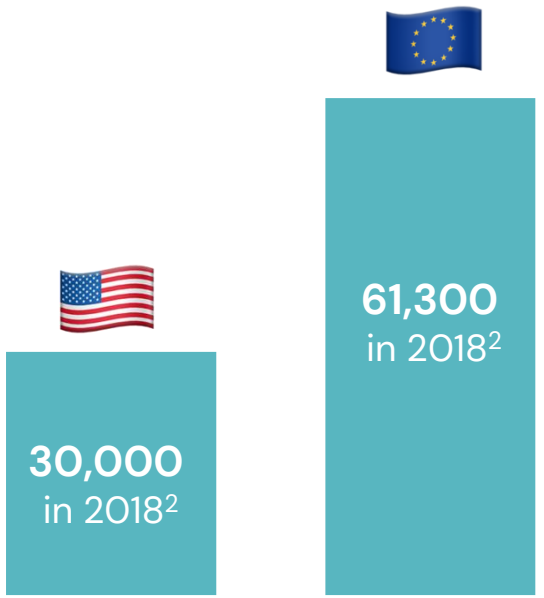
Among all Lung Cancers

SLCL
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) Market Spotlight, May 1 2018

Small Cell Lung Cancer (SCLC)
Development Lagging Behind NSCLC

SCLC

Zepzelca (Lurbinectedin) – The SCLC Treatment Paradigm

Strong Positioning Opportunity

SCLC

	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*	

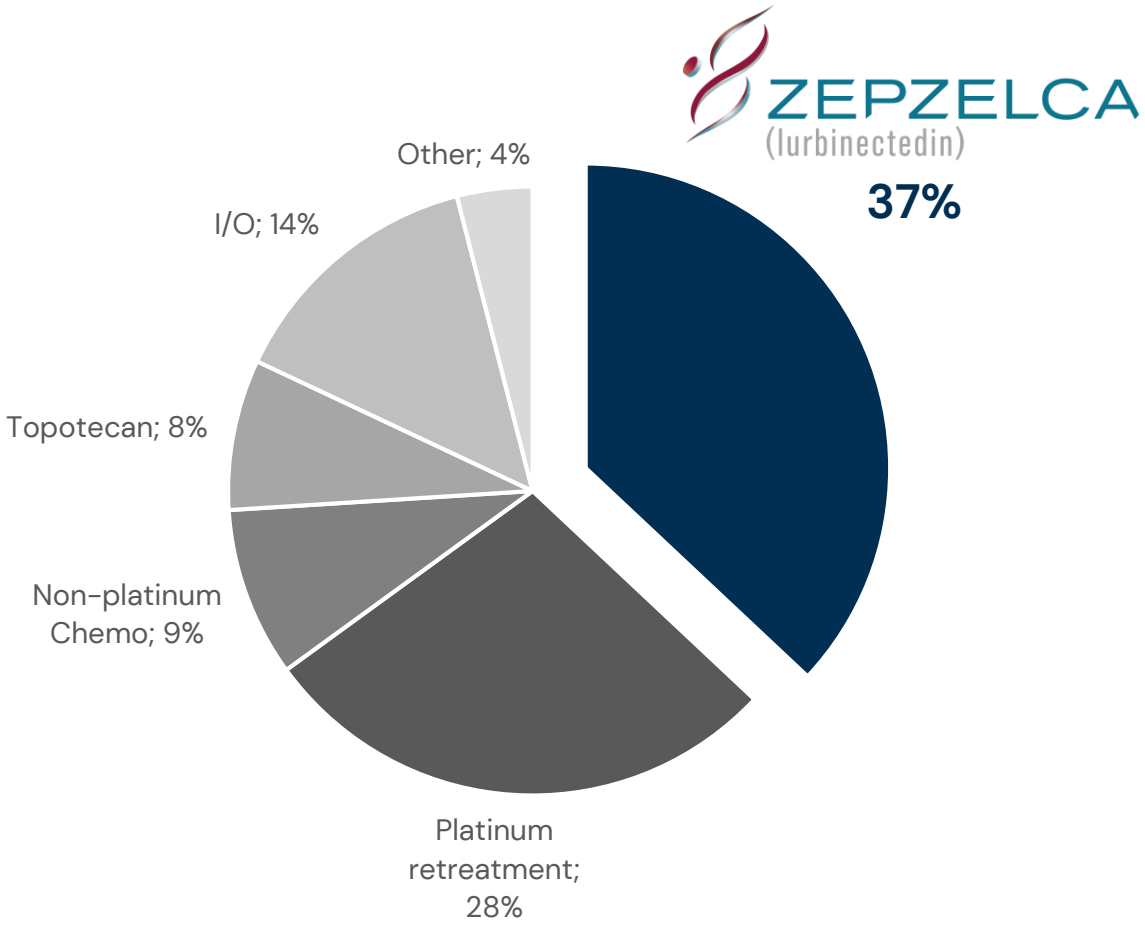
	1st Line	Maintenance	2nd Line	3rd Line
Phase 3 Trials		Zepzelca + atezolizumab	Onivyde[4]* (Data expected Sep 2022)	RRx-001*

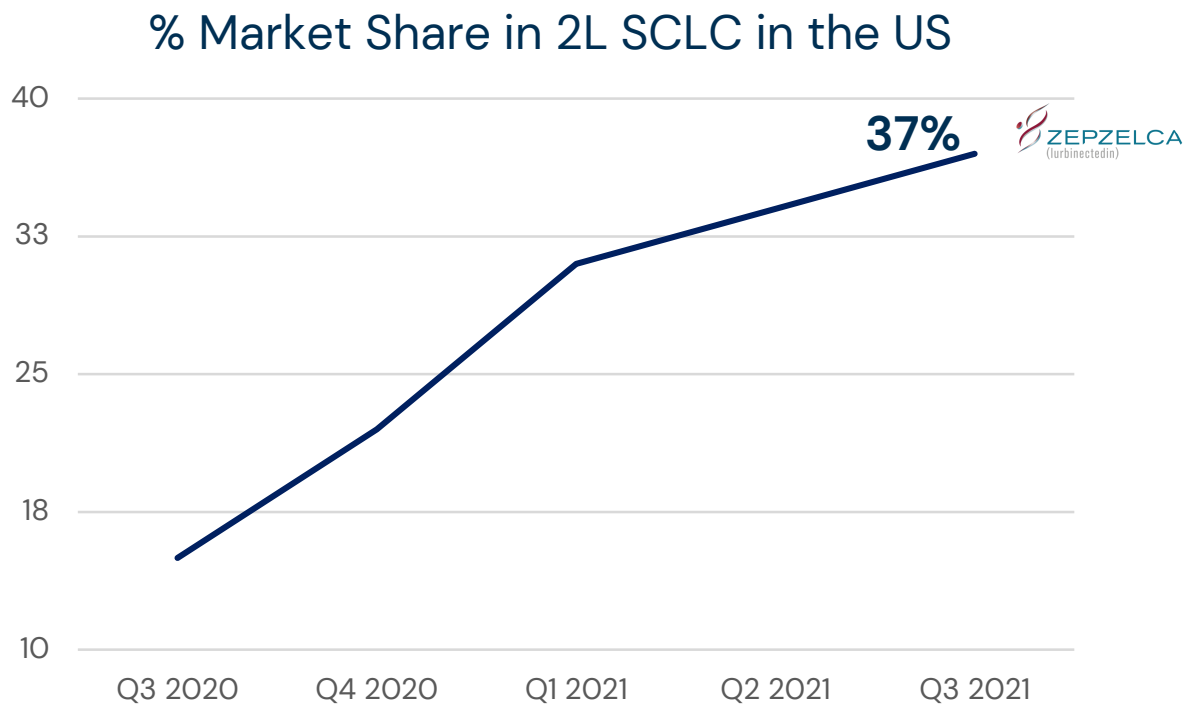
- Investigational drugs or not approved for this indication/line

1. NCCN guidelines v1.2022
2. ESMO guidelines Apr 13 2021
3. CAV: cyclophosphamide, adriamycin and vincristine
4. https://clinicaltrials.gov/ct2/show/NCT03088813?term=Onivyde&recrs=ab&draw=2&rank=2

Zepzelca Already Treatment of Choice in 2L SCLC
With Significant Room to Grow

SCLC





1. Adapted from Jazz Pharmaceuticals Q3 2021 presentation

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

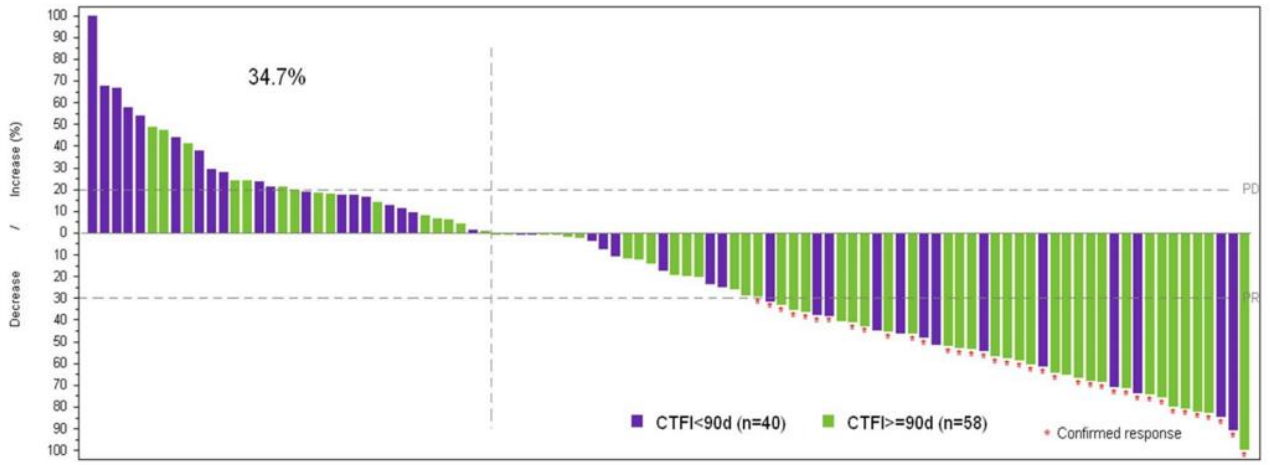
SCLC

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. 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. 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]

SCLC

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.

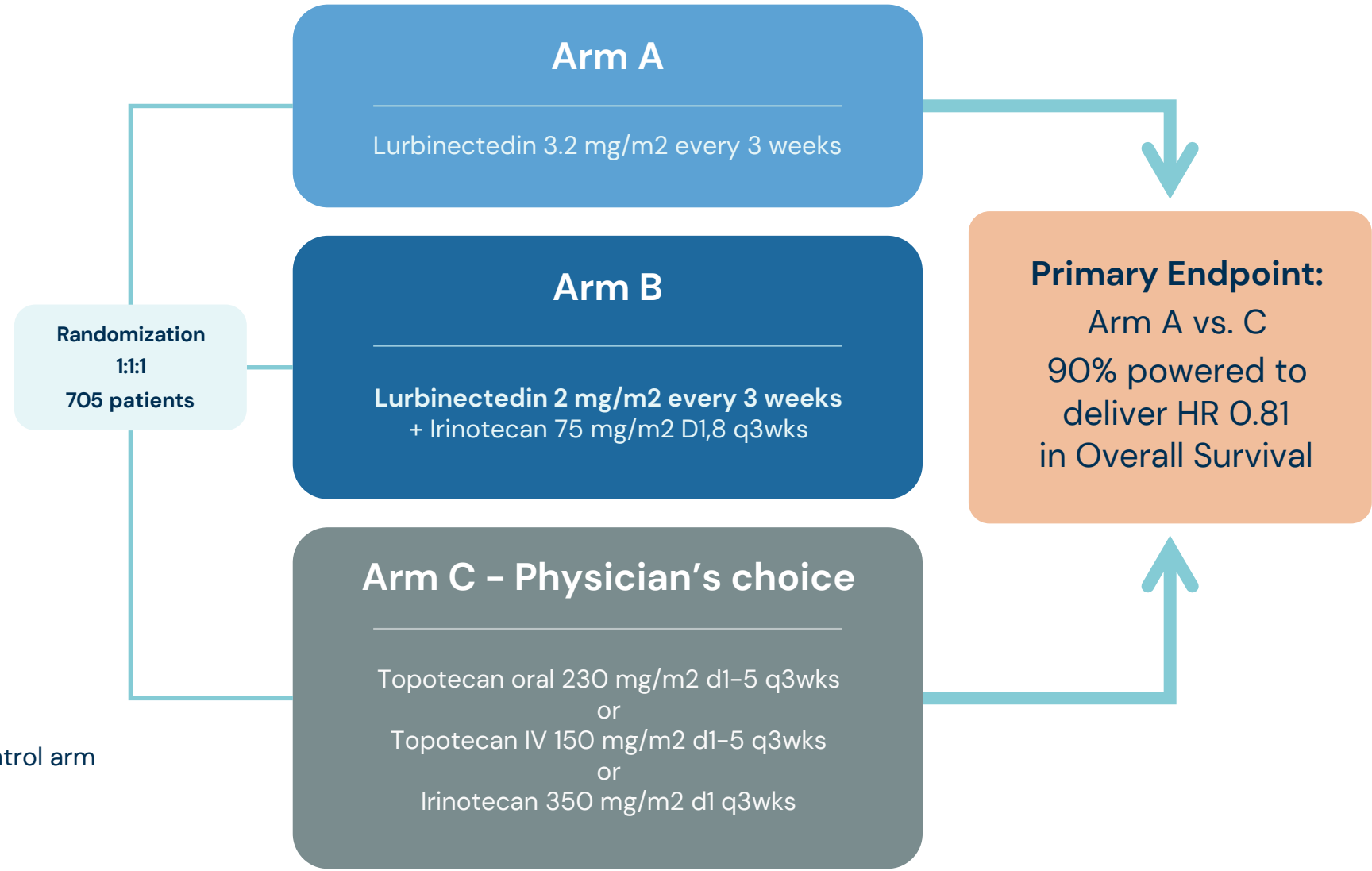
Zepzelca: Pathway to 2nd line in SCLC by EMA and Full Approval by FDA

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



ZEPZELCA
(lurbinectedin)

1st line-Maintenance Study in SCLC

SITC 2021: Lurbi-Atezo combo in relapsed SCLC (PoC trial)

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

Response	N=26
CR	8% (2)
PR	50% (13)
ORR	58% (15)
SD	27% (6)
DCR	85%
PD	12% (3)
mPFS (8 censored)	4.93m

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

Lurbinectedin: First line positioning

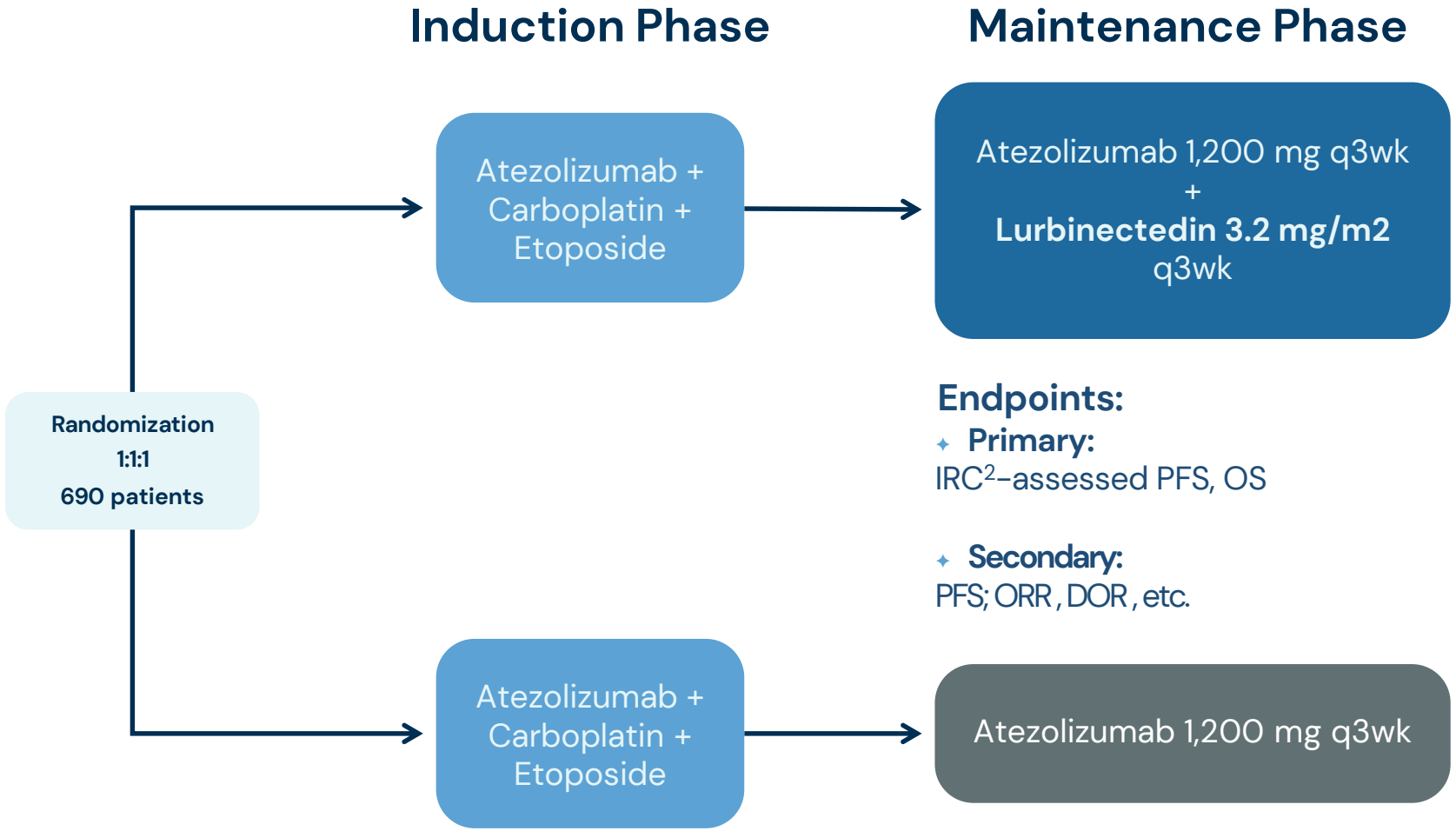
Phase 3 IMforte trial for First line–Maintenance SCLC

SCLC

Jazz Pharmaceuticals

Roche

- Extensive-stage SCLC (ES-SCLC)
- Ongoing response or stable disease per(RECIST)



Endpoints:

- **Primary:**
  IRC[2]–assessed PFS, OS
- **Secondary:**
  PFS; ORR , DOR , etc.

1. NCT05091567
2. Independent Review Committee

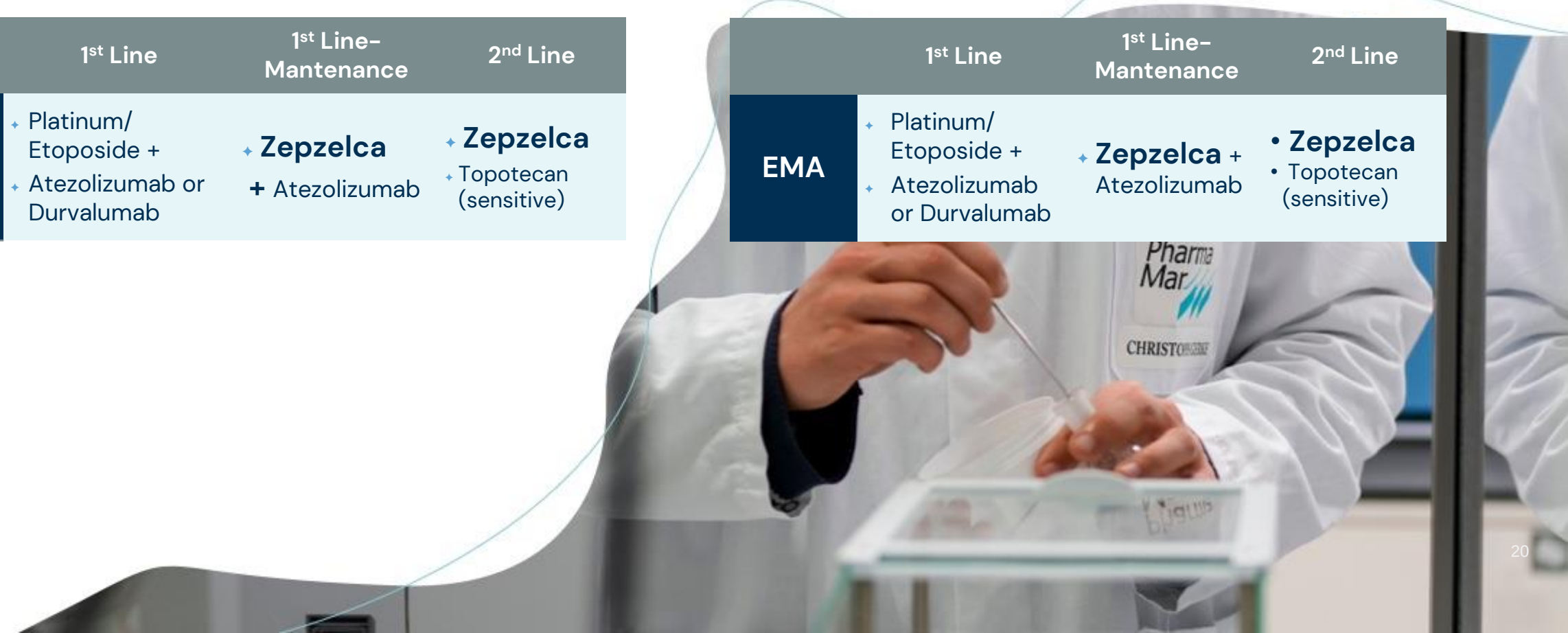
Strategic importance of Zepzelca Phase 3s in SCLC

Potential treatment landscape after Phase 3s

SCLC

	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)



Zepzelca (Lurbinectedin) in Maintenance

Could broaden to address more / healthier Patients and Extend Duration of Treatment

SCLC

%Treated

~90%	~80%	~70%
Maintenance	**2nd Line PD-L1**	**2nd Line Monotherapy**
Expected increased PFS	PFS 4.9 months[1]	PFS 3.5 months[2]

Expect longer duration of treatment if Zepzelca progresses upstream

European rights fully owned by PharmaMar

1. Based on Poster *2SMALL (NCT04253145) phase I part: Lurbinectidin (LUR) in combination with Atezolizumab (ATZ) for second line Extensive Stage Small Cell Lung Cancer (ES-SCLC) patients (pts)*
2. Zepzelca Full Prescribing Information

MPM

ZEPZELCA
(lurbinectedin)

Malignant Pleural Mesothelioma
Finalizing Trial Strategy

Pharma Mar

Zepzelca (Lurbinectedin) – Relapsed Malignant Pleural Mesothelioma
A Rare Disease with limited available Therapeutic Options

MPM

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

Incidence ~3,000[1] patients diagnosed in the US per year

	1st Line	2nd Line
FDA Approved	• Nivolumad + Ipilimumab • Pemetrexed + Platinum • Gemcitabine + Cisplatin	• Pembrolizumab[3] (TMB high)
NCCN[4] Guidelines	• Pemetrexed + platinum + Bevacizumab[4]	• Pemetrexed[3] (only in naïve patients) • Vinorelbine • Gemcitabine + Cisplatin • Pembrolizumab

Incidence and ~11,000 in Europe[2]

	1st Line	2nd Line
EMA Approved	• Pemetrexed + Platinum • Nivolumab + Ipilimumab	
ESMO[6] Guidelines	• Pembro, Nivo or Nivo+Ipilumab[7] • Pemetrexed +/- Platinum • Gemcitabine +/-ramucirumab • Vinorelbine	

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

1. www.cancer.org/content/dam/CRC/PDF/Public/8733.00.pdf
2. Daniel H Sterman, MDLeslie A Litzky, MDLarry R Kaiser, MD, "Epidemiology of malignant pleural mesothelioma" Epidemiology of malignant pleural mesothelioma – UpToDate
3. NCCN Category 1
4. NCCN Guidelines v1.2022; All recommendations category 2A except where stated
5. Not approved in this indication
6. ESMO guidelines Nov 2021
7. Only in IO naive patients

Zepzelca (Lurbinectedin) – PFS Benefit in Malignant Pleural Mesothelioma

Phase 2 Study[1]

MPM

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

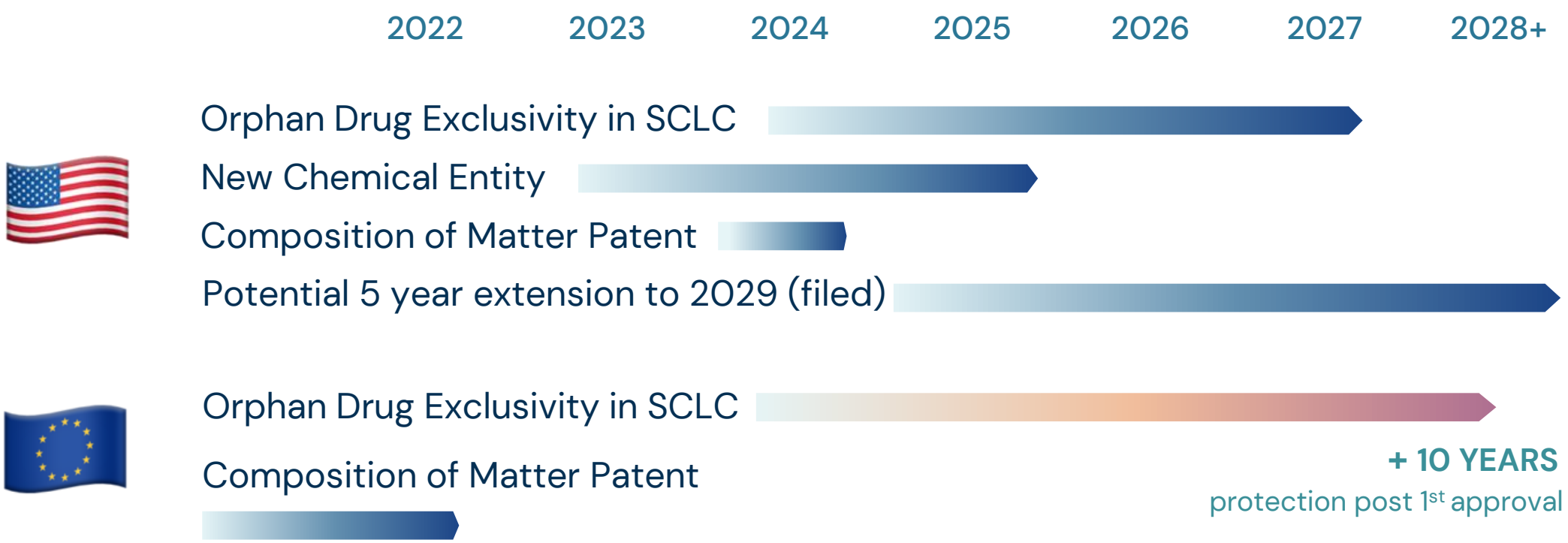
- Primary endpoint PFS at 12 weeks:
  - Primary endpoint met (p=0.015)
- mPFS 4.1 months
- mOS 11.1 months
- Grade 3-4 AEs (>10%):
- Neutropenia 24%
- Fatigue 17%
- Febrile neutropenia 12%

Planning Phase 3 combo with IO

1. https://pubmed.ncbi.nlm.nih.gov/32085891/

Zepzelca (Lurbinectedin) – Intellectual property

Life cycle management plans under way



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

19 Regional Partners for Local Distribution

~100 Sales force infrastructure

PharmaMar

Development and regulatory expertise

FDA U.S. FOOD & DRUG ADMINISTRATION

EUROPEAN MEDICINES AGENCY

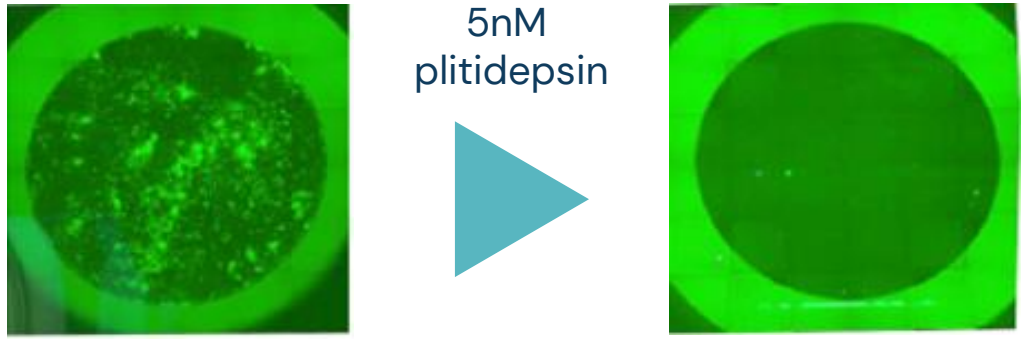
MHRA Regulating Medicines and Medical Devices

swissmedic

Other opportunities

Plitidepsin in COVID-19 Patients Following Positive Multi-Center Clinical Trial

- SARS-COV2 cells co-opt EF1A from host to replicate
- Positive multi-center clinical trial
  - Safety primary endpoint met for 3 doses
  - Viral load and CRP reduced
- Pivotal Phase 3 ongoing (Neptuno / NCT04784559)



HCoV-229E infected cells

Science
AAAS

Cite as: K. M. White *et al.*, *Science* 10.1126/science.abf4058 (2021).

Plitidepsin has potent preclinical efficacy against SARS-CoV-2 by targeting the host protein eEF1A

Kris M. White[1,2*†], Romel Rosales[1,2*], Soner Yildiz[1,2], Thomas Kehrer[1,2], Lisa Miorin[1,2], Elena Moreno[1,2], Sonia Jangra[1,2], Melissa B. Uccellini[1,2], Raveen Rathnasinghe[1,2], Lynda Coughlan[3], Carles Martinez-Romero[1,2], Jyoti Batra[4,5,6,7], Ajda Rojc[4,5,6,7], Mehdi Bouhaddou[4,5,6,7], Jacqueline M. Fabius[4,6], Kirsten Obernier[4,5,6,7], Marion Dejosez[8], María José Guillén[9], Alejandro Losada[9], Pablo Avilés[9], Michael Schotsaert[1,2], Thomas Zwaka[8], Marco Vignuzzi[10], Kevan M. Shokat[4,6,7,11], Nevan J. Krogan[1,4,5,6,7†], Adolfo García-Sastre[1,2,12,13†]

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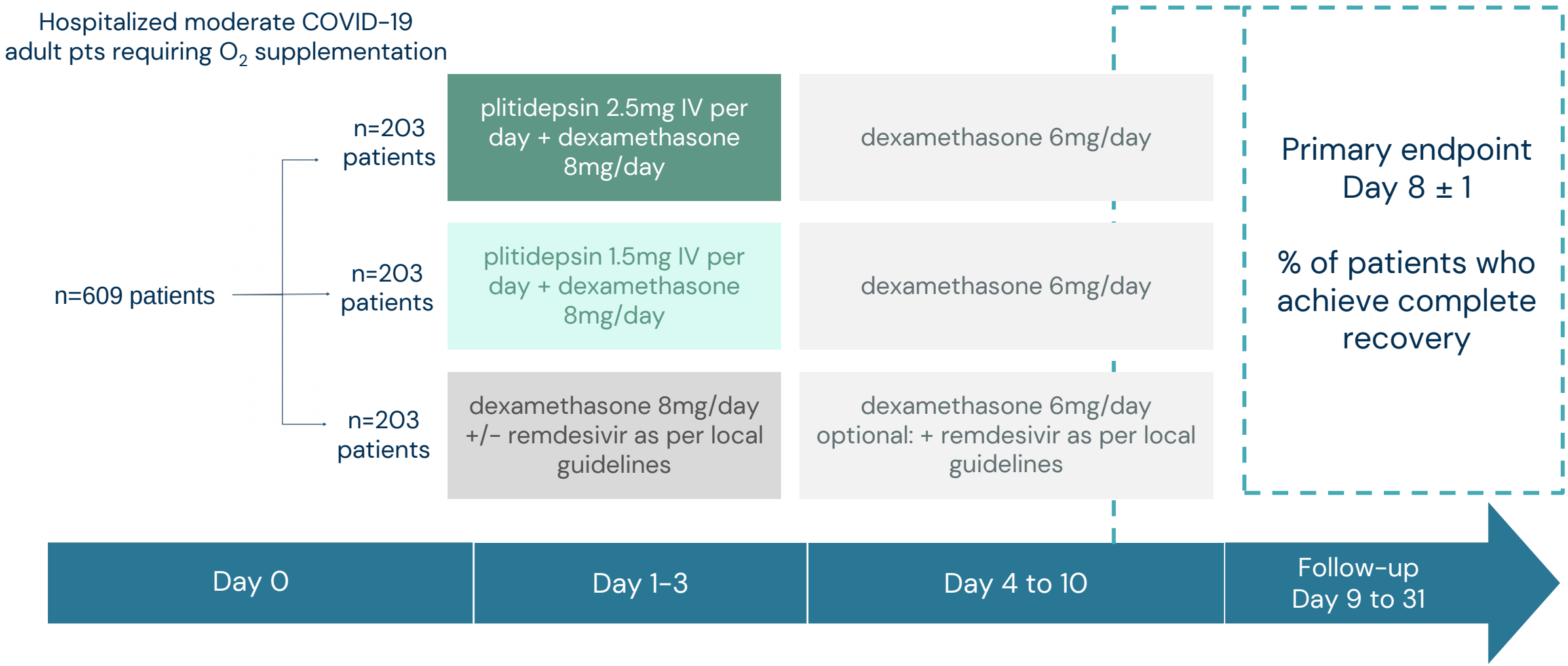
SARS-CoV-2 viral proteins interact with the eukaryotic translation machinery and inhibitors of translation have potent antiviral effects. Here we report that the drug plitidepsin (aplidin), which has limited clinical approval, possesses antiviral activity (IC_{90} = 0.88 nM) 27.5-fold more potent than remdesivir against SARS-CoV-2 in vitro, with limited toxicity in cell culture. Through the use of a drug resistant mutant, we show that the antiviral activity of plitidepsin against SARS-CoV-2 is mediated through inhibition of the known target eEF1A. We demonstrate the in vivo efficacy of plitidepsin treatment in two mouse models of SARS-CoV-2 infection with a reduction of viral replication in the lungs by two orders of magnitude using prophylactic treatment. Our results indicate that plitidepsin is a promising therapeutic candidate for COVID-19.

1. Sources: Zhou et al; The Nucleocapsid Protein of Severe Acute Respiratory Syndrome Coronavirus Inhibits Cell Cytokinesis and Proliferation by Interacting with Translation Elongation Factor 1α; Journal if Virology, July 2008, p. 6962–6971, and Losada et al; Translation Elongation Factor eEF1A2 is a Novel Anticancer Target for the Marine Natural Product Plitidepsin; Scientific Reports 6:35100 10/7/16

Plitidepsin COVID-19 Phase 3[1] Study Design in COVID-19
Adult Patients with Moderate Disease



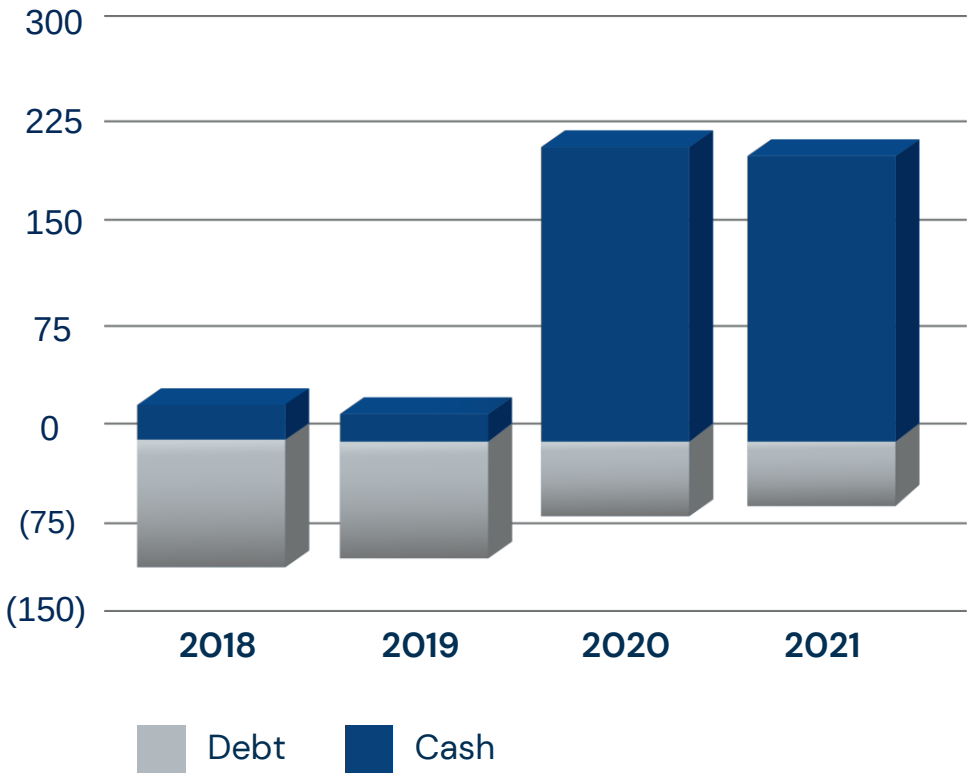
1. NCT04784559

Financials

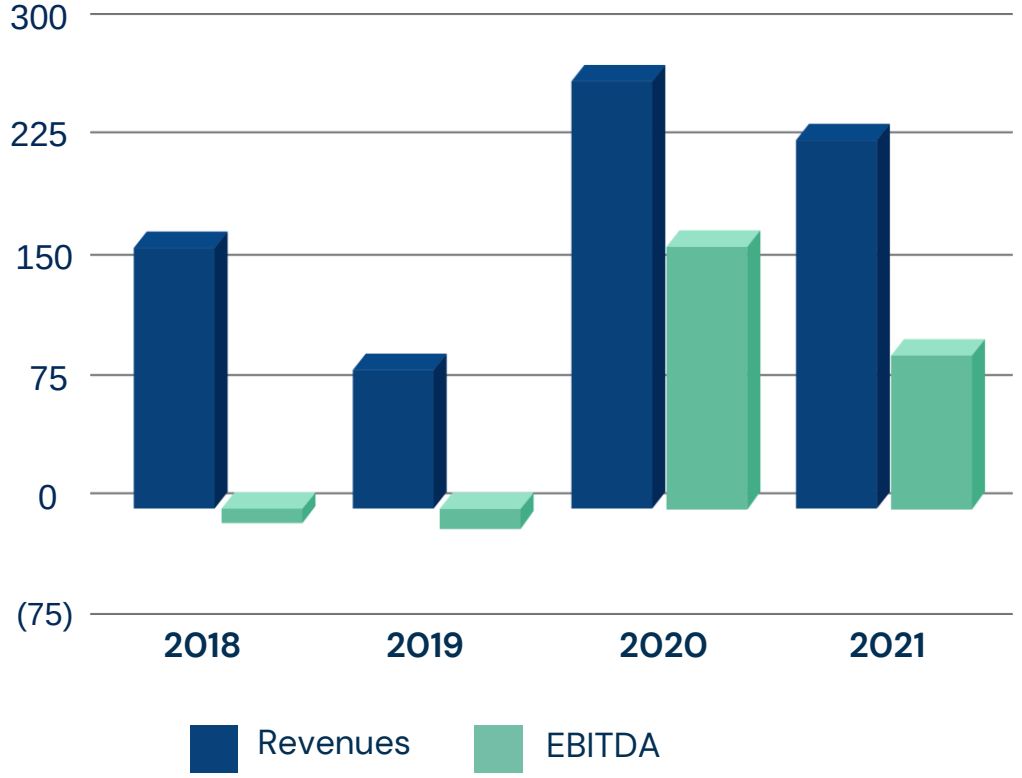
Financials

Well financed to support next stages of development

Robust Cash Position (€m)



Profitable (€m)



Key Events
Catalyst Calendar

Lurbi Combo Atezo data presented at SITC	✓
Zepzelca approved in additional countries UAE, Singapore, Australia, Canada	✓
2nd line Phase 3 SCLC trial initiation	✓
Ecubectedin "First Patient In" Phase 2	✓
Potential first Zepzelca sales milestone	✓
Potential lurbinectedin approvals in other countries	✓
Lurbi+Irinotecan Phase 2 update	2022 and beyond
Phase I new products in pipeline	2022
Potential in-licensing	2022
Further trials in Covid with plitidepsin	NA NA

Investment Case – Building the Next Phase of Growth

2021-2026

Profitable Biotech company with **3 commercialized assets** in oncology and cash to support growth

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

Strong Zepzelca **Intellectual Property**

Leveraging proven oncology drugs in **new indications** and expanding into new territories

Solid financial capabilities to **broaden and accelerate R&D** engine

Fuel leading European distribution platform with new products through **additional licensing and partnerships**

2021 – 2026 Objectives

- 3 approved drugs
- Lurbinectedin in 3 Phase 3 trials; potentially all three filed for approval
- 2 in-licensed assets adding to revenue in Europe
- Ecubectedin in Phase 2/3 trials
- 2 new assets in the clinic

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