



July 2022

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
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

Revenue Generating &
Profitable

Revenues in 2021	€230m
EBITDA 2021	€97.7m
Cash 1Q22	€250m
Market cap	€1.2bn ¹



3 Approved Oncology
Products



Established European oncology
sales force

Discovery Platform
Strengthening Oncology
Pipeline

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

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

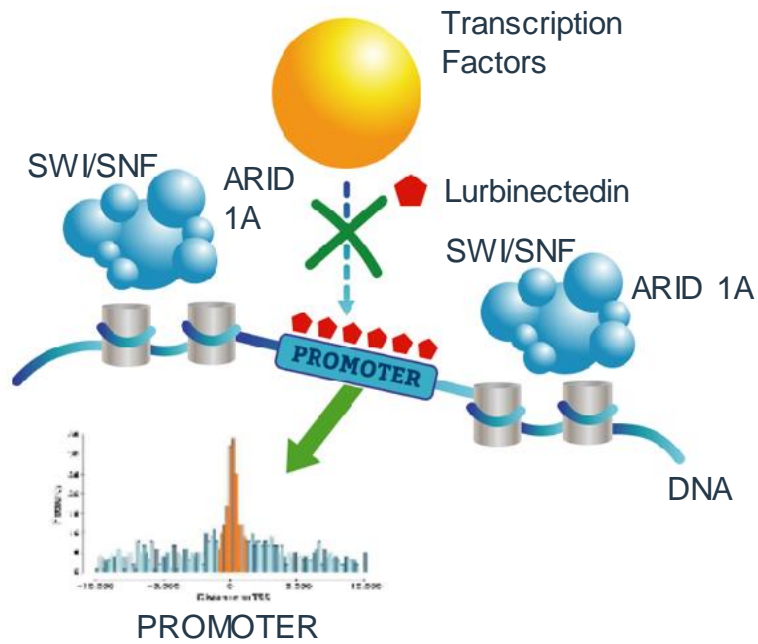
Pipeline – Expanding our Expertise in Oncology

				Phase 1	Phase 2	Phase 3	Market
	Soft tissue sarcoma	2 nd /3 rd line	Monotherapy	▶			
	Ovarian cancer	2 nd /3 rd line	+ Doxil (PLD)	▶			
	R/R Multiple Myeloma ¹	3 rd /4 th line	+ dexamethasone	▶			
	Small cell lung cancer	2 nd line US	Monotherapy	▶			
	Small cell lung cancer Maintenance		+ Atezolizumab	▶ IMforte		▶	 
	Small cell lung cancer 2 nd line (Registrational Europe and Confirmatory US)		Lurbi vs. Lurbi+ Irinotecan vs. Topotecan or Irinotecan	▶ LAGOON			
	(Lurbinectedin)	Mesothelioma	≥2 nd line	+ IO	▶		
	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	▶			

Zepzelca – A Transcription Inhibitor Leading to Tumor Inhibition

Primary Effect

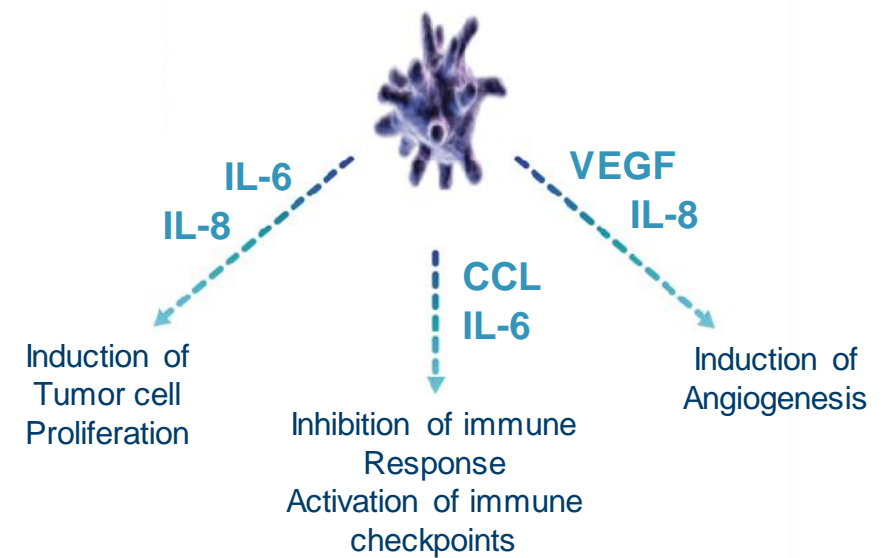
Cancer is frequently a transcriptional disease caused by deregulated oncogenic transcription factors



Secondary Effect

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

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



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

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

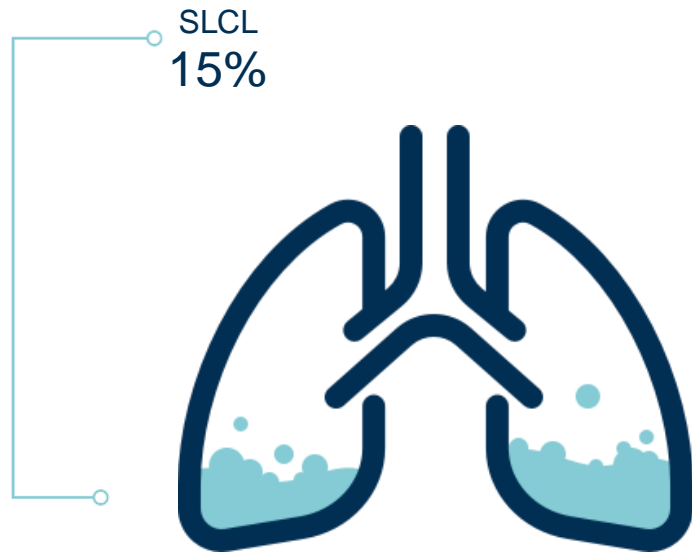


- ◆ 2021 sales = \$46m royalties for PharmaMar
- ◆ High teens to 30% Royalties on US/Canada sales
- ◆ Initiated Phase 3 in 1L maintenance ES-SCLC in combination with Tecentriq® in collaboration with Roche

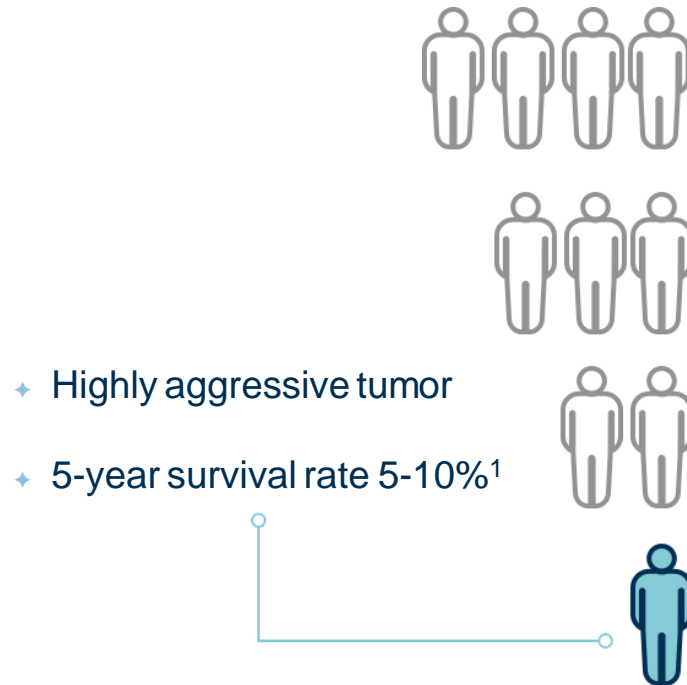
Small Cell Lung Cancer (SCLC)

An Underserved High Unmet Medical Need

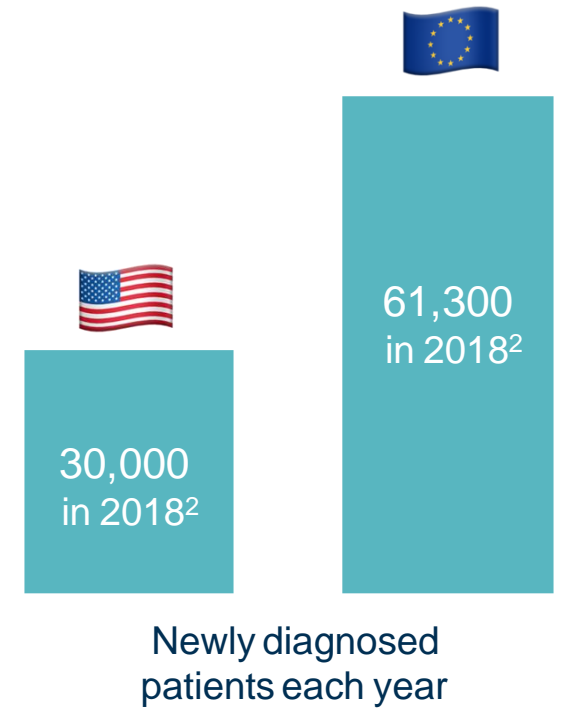
Among all Lung Cancers



Low survival rate at 5 years

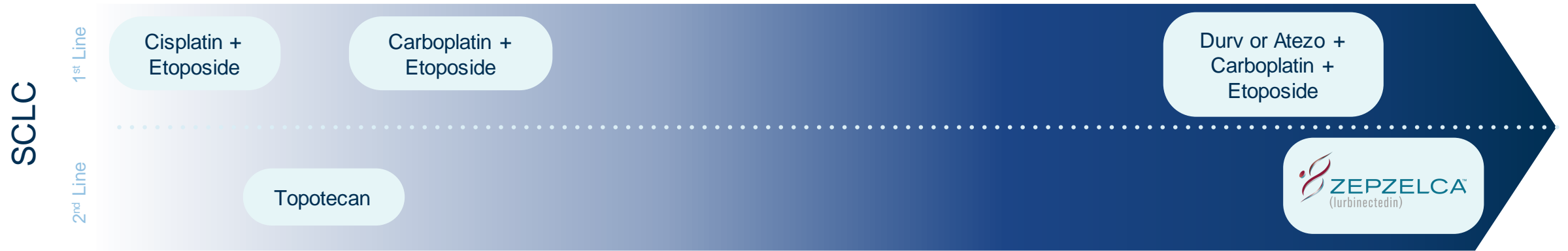


Limited treatment options in both the US and Europe



Small Cell Lung Cancer (SCLC) Development Lagging Behind NSCLC

SCLC



Pre - 1993 1996 ← 24 years → 2020



Zepzelca (Lurbinectedin) – The SCLC Treatment Paradigm

Strong Positioning Opportunity

SCLC

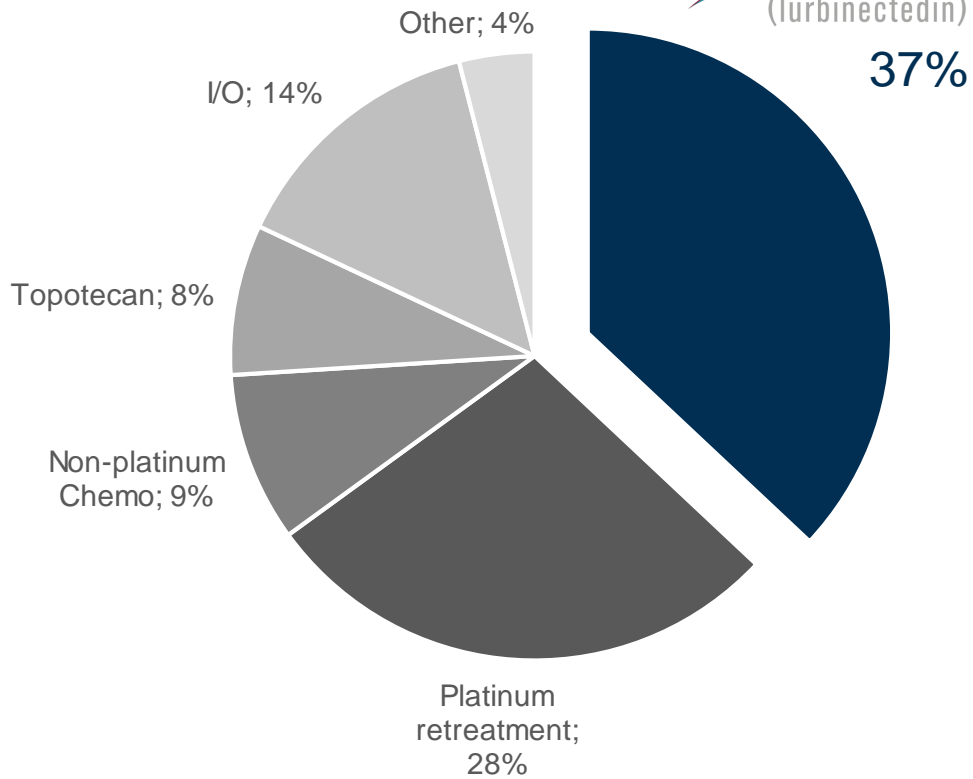


	1 st Line	2 nd Line	3 rd Line		1 st Line	2 nd Line	3 rd Line
FDA Approved	<ul style="list-style-type: none"> Platinum/ Etoposide + Atezolizumab or Durvalumab 	<ul style="list-style-type: none"> Zepzelca Topotecan (sensitive) 		EMA Approved	<ul style="list-style-type: none"> Platinum/ Etoposide + Atezolizumab 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		Onivyde ⁴ (Data expected Sep 2022)	RRx-001	

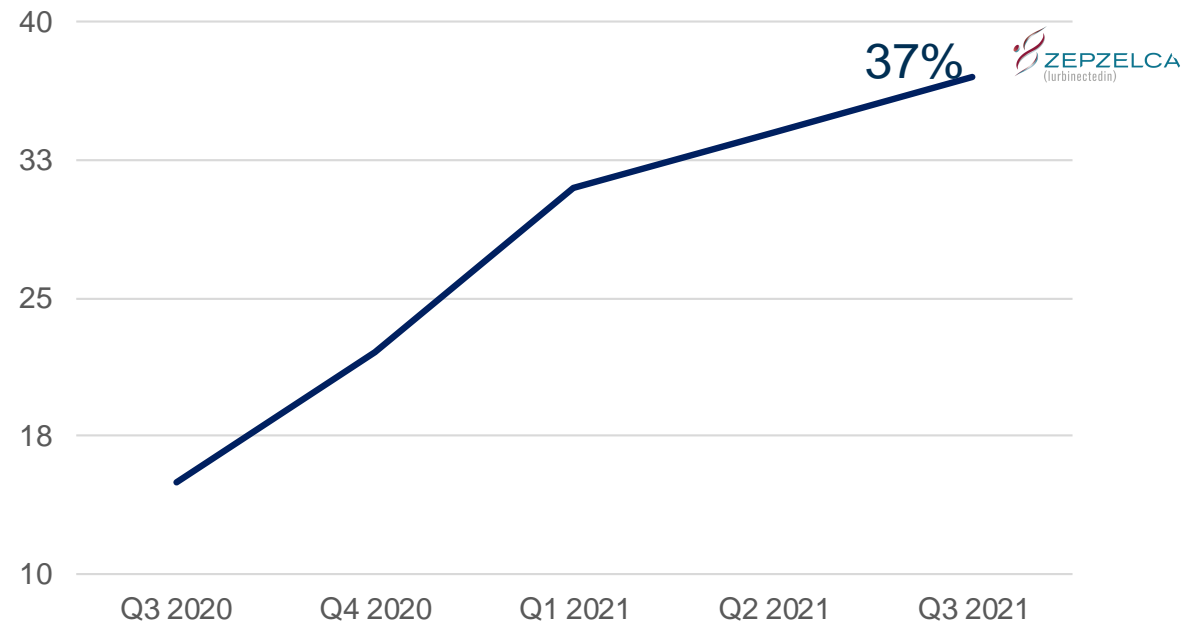
- Investigational drugs or not approved for this indication/line
- 1. NCCN guidelines v1.2022
- 2. ESMO guidelines Apr 13 2021
- 3. CAV: cyclophosphamide, adriamycin and vincristine
- 4. <https://clinicaltrials.gov/ct2/show/NCT03088813?term=Onivyde&recrs=ab&draw=2&rank=2>

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

SCLC



% Market Share in 2L SCLC in the US



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

SCLC

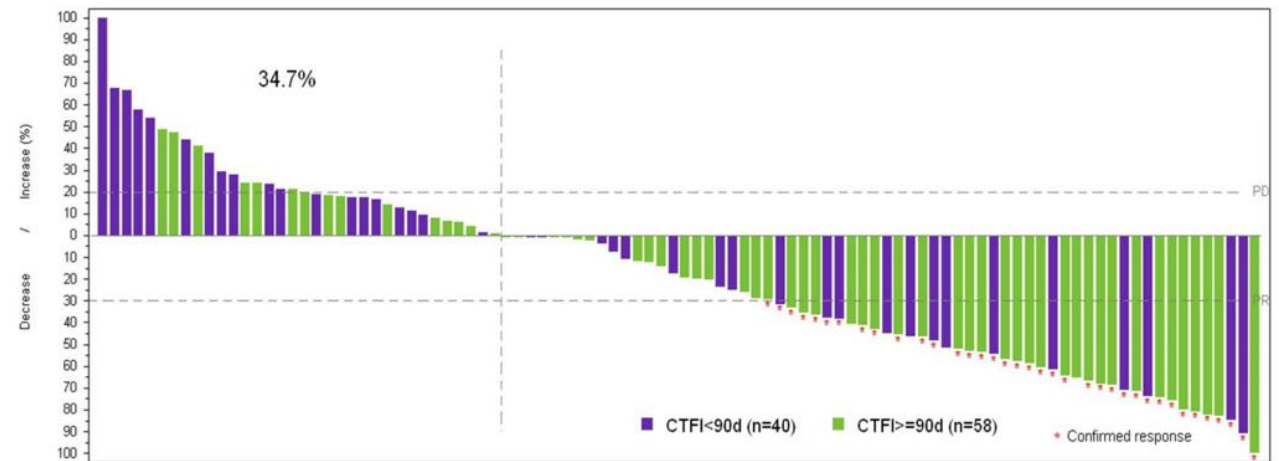


In relapsed SCLC as monotherapy under accelerated approval based on Phase 2 monotherapy data¹

	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
 CTFI – Cancer Therapy-Free Interval

Decrease in tumor size in 65% patients²



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

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

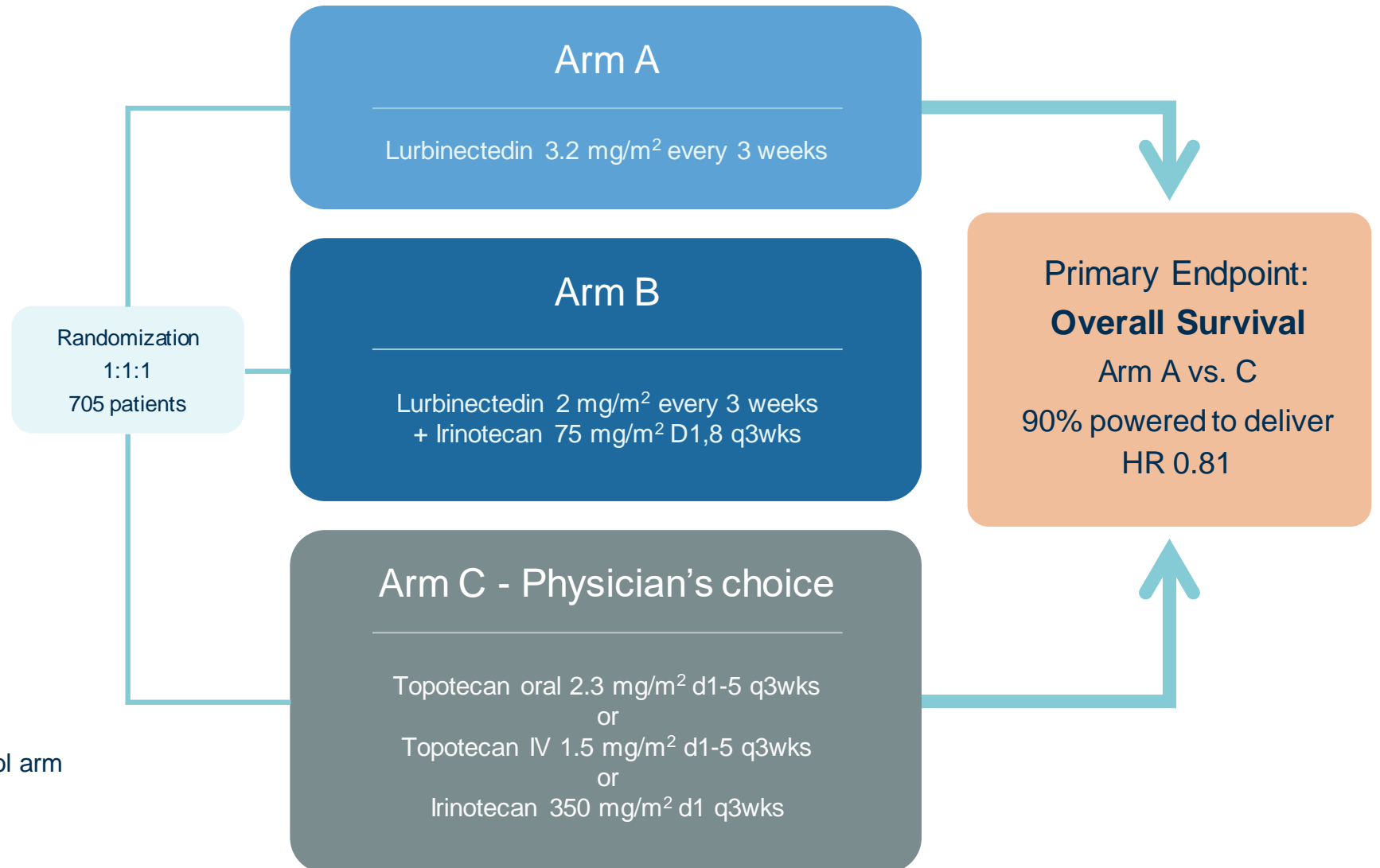
Phase 3 (LAGOON) randomized trial



- ✦ 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 ($> \text{ULN}$ or $\leq \text{ULN}$)
- CNS involvement (Y/N)
- Investigator's preference of the control arm



SCLC



1st line-Maintenance Study in SCLC

Lurbinectedin-Atezolizumab 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

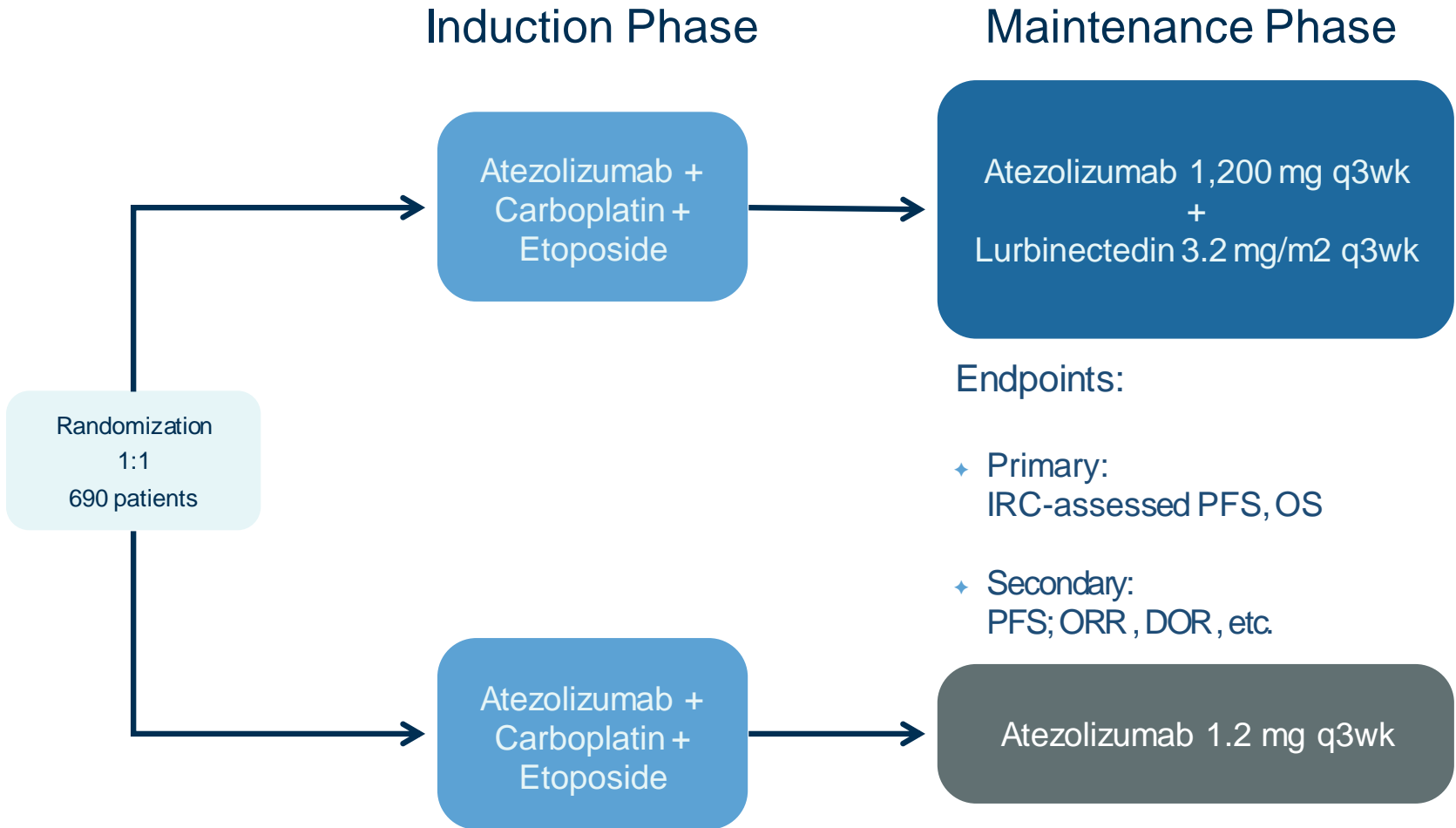
Lurbinectedin: First line positioning

Phase 3 IMforte trial for First line-Maintenance SCLC

SCLC



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



Strategic importance of Zepzelca Phase 3s in SCLC

Potential treatment landscape after Phase 3s

SCLC



	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)

Zepzelca (Lurbinectedin) in Maintenance

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

SCLC



Expect longer duration of treatment if Zepzelca progresses upstream

European rights fully owned by PharmaMar

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



Malignant Pleural Mesothelioma Finalizing Trial Strategy

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

~3,000¹ patients diagnosed in the US per year



Incidence

and ~11,000 in Europe²

	1 st Line	2 nd Line
FDA Approved	<ul style="list-style-type: none"> † Nivolumab + Ipilimumab † Pemetrexed + Platinum † Gemcitabine + Cisplatin 	<ul style="list-style-type: none"> † Pembrolizumab³ (TMB high)
NCCN ⁴ Guidelines	<ul style="list-style-type: none"> † Pemetrexed + platinum + Bevacizumab⁴ 	<ul style="list-style-type: none"> † Pemetrexed³ (only in naïve patients) † Vinorelbine † Gemcitabine + Cisplatin † Pembrolizumab

	1 st Line	2 nd Line
EMA Approved	<ul style="list-style-type: none"> † Pemetrexed + Platinum † Nivolumab + Ipilimumab 	
ESMO ⁶ Guidelines	<ul style="list-style-type: none"> † Pembro, Nivo or Nivo+Ipilumab⁷ † Pemetrexed +/- Platinum † Gemcitabine +/-ramucirumab † Vinorelbine 	

Phase 3 Trials

Atezolizumab⁵

Durvalumab⁵

Pembrolizumab⁵



1. www.cancer.org/content/dam/CRC/PDF/Public/8733.00.pdf

2. Daniel H Stermn, MD, Leslie A Litzky, MD, Larry 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 naïve patients

Zepzelca (Lurbinectedin) – PFS Benefit in Malignant Pleural Mesothelioma Phase 2 Study¹

MPM

- ✦ 42 patients progression on 1 prior platinum based therapy
- ✦ Lurbinectedin at 3.2 mg/m² 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%

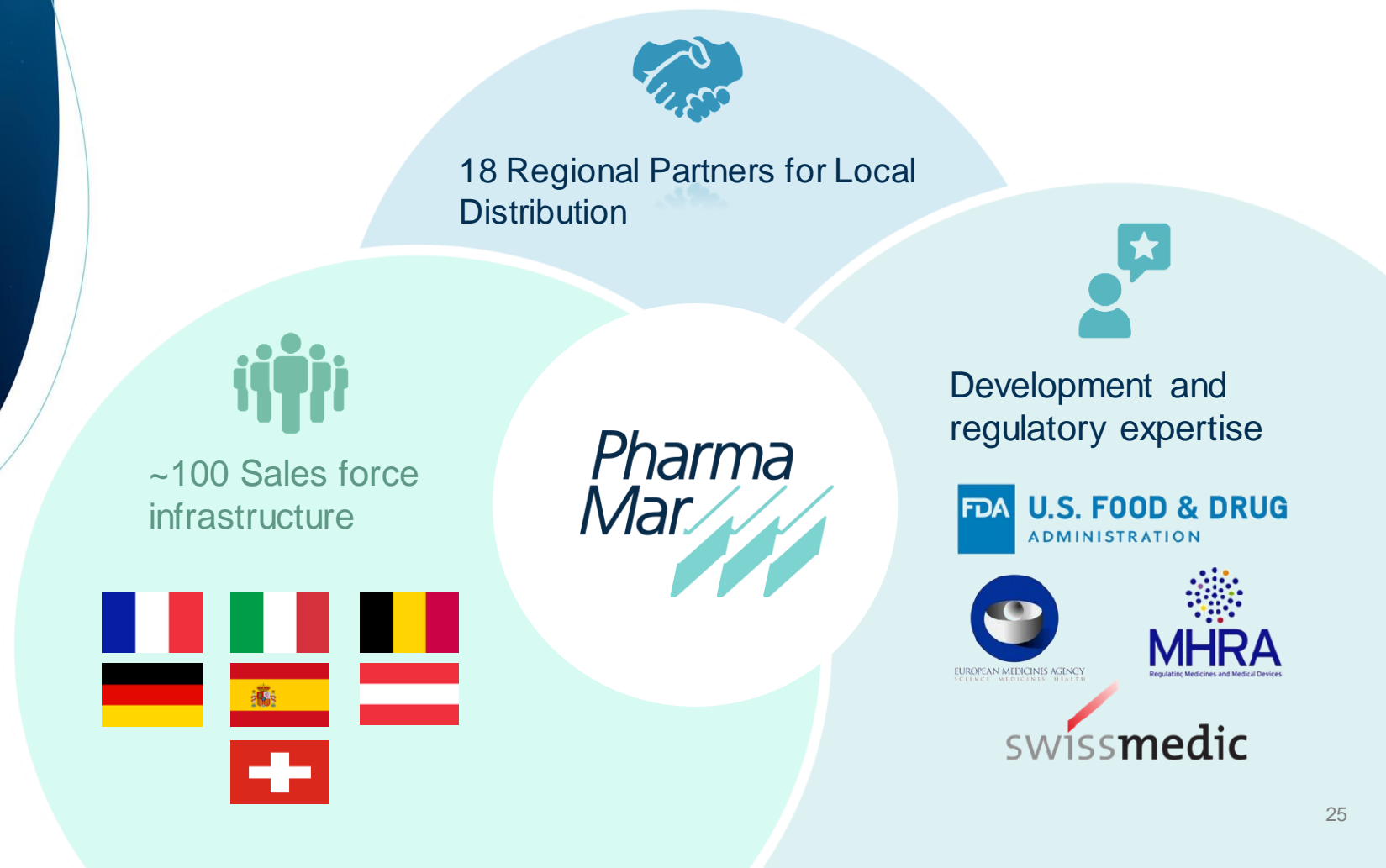
Planning Phase 3
combo with IO

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

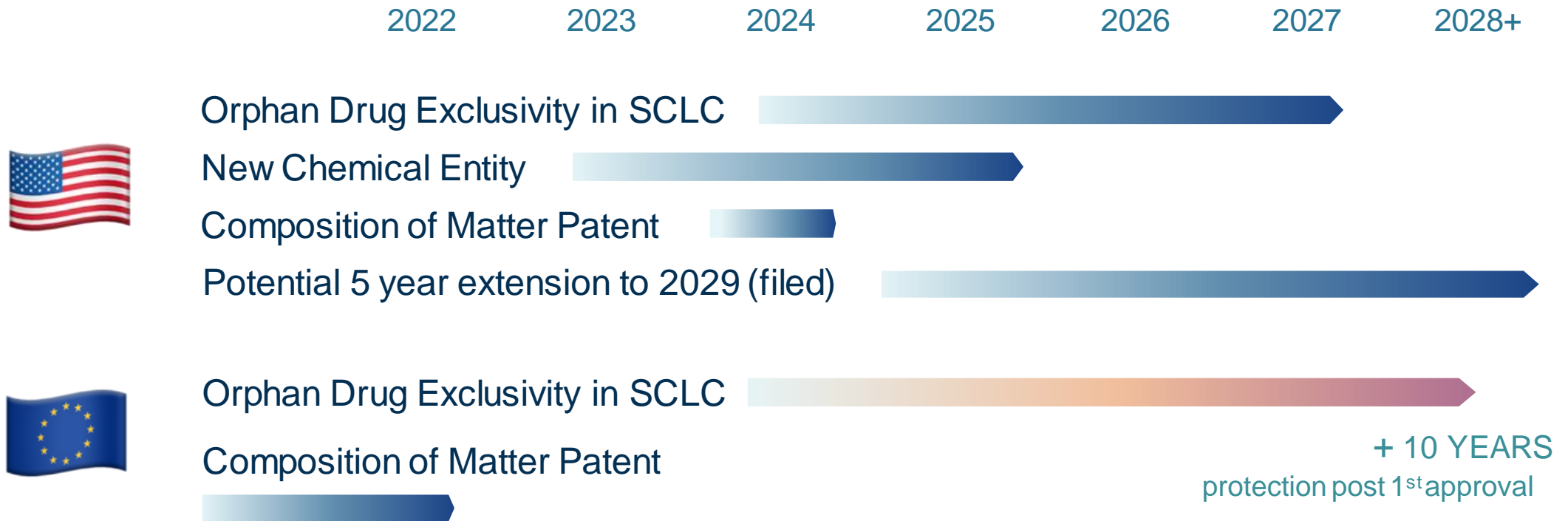
Leveraging Commercial Infrastructure in Europe

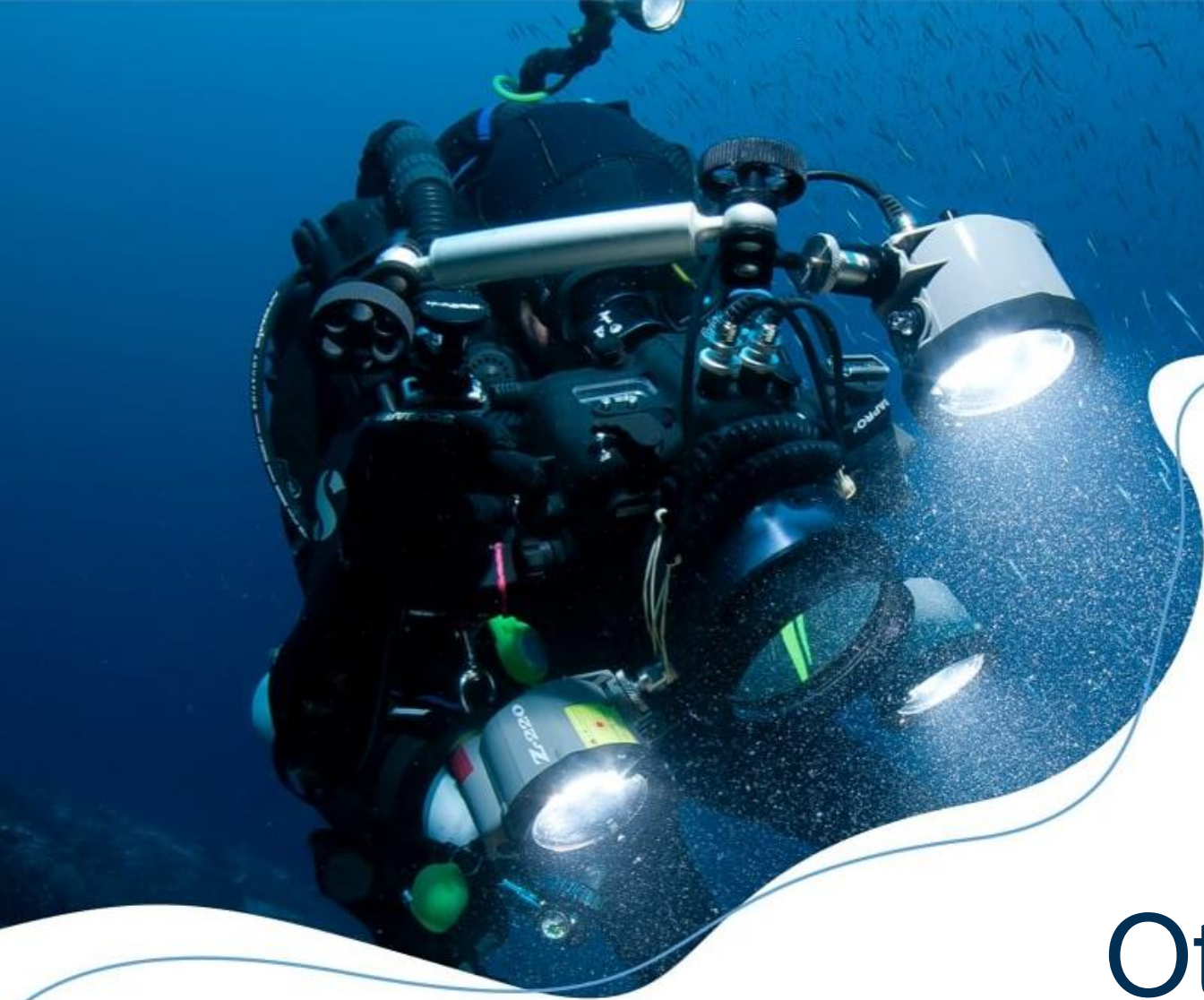
PharmaMar positioned as a partner of choice in Europe



Zepzelca (Lurbinectedin) – Intellectual property

Life cycle management plans under way

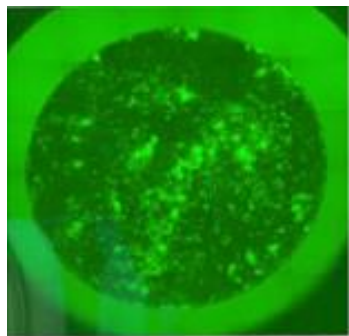




Other opportunities

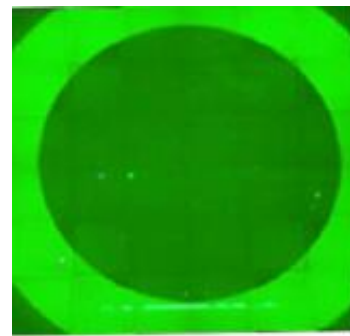
Plitidepsin in SARS-CoV-2 Patients

- ✦ SARS-CoV-2 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

5nM
plitidepsin



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 Coughlan³, Carles Martinez-Romero^{1,2}, Jyoti Batra^{4,5,6,7}, Ajda Rojce^{4,5,6,7}, Mehdi Bouhaddou^{4,5,6,7}, Jacqueline M. Fabius^{4,6}, Kirsten Obernier^{4,5,6,7}, Marion Dejosez⁸, María José Guillén⁹, Alejandro Losada⁹, Pablo Avilés⁹, Michael Schotsaert^{1,2}, Thomas Zwaka⁸, Marco Vignuzzi¹⁰, 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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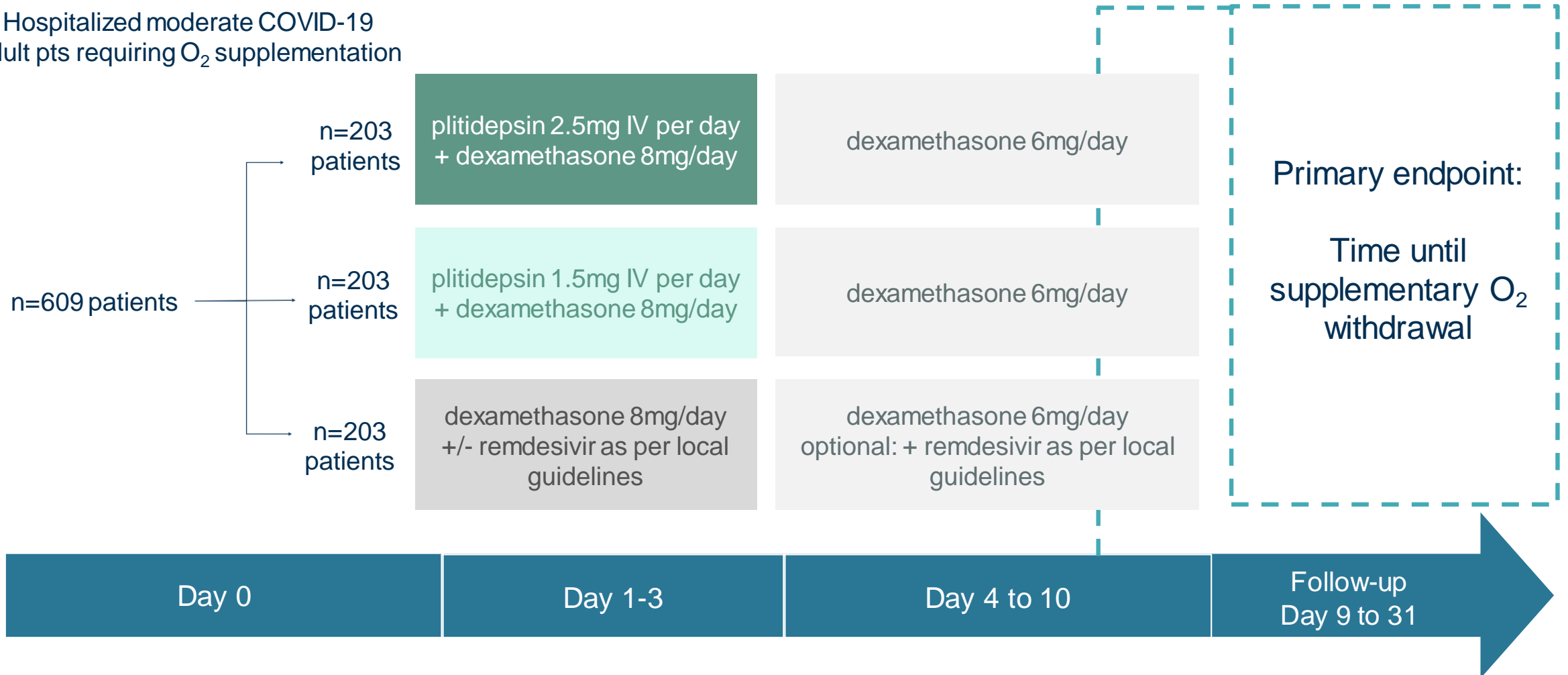
SARS-CoV-2 viral proteins interact with the eukaryotic translation machinery and inhibitors of translation have potent antiviral effects. Here we report that the drug plitidepsin (aplidin), which has limited clinical approval, possesses antiviral activity (IC₉₀ = 0.88 nM) 27.5-fold more potent than remdesivir 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 1 α ; Journal of 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 in SARS-CoV-2 Patients: Phase 3 Study NEPTUNO¹

Adult Patients with Moderate Disease

Hospitalized moderate COVID-19
adult pts requiring O₂ supplementation



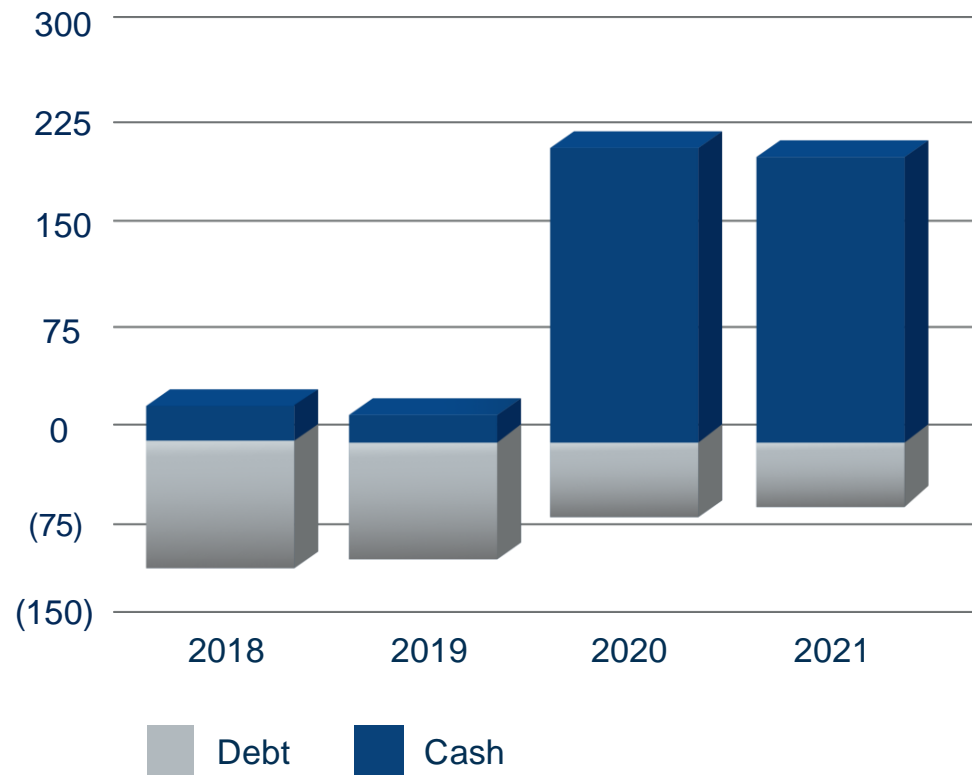
Financials



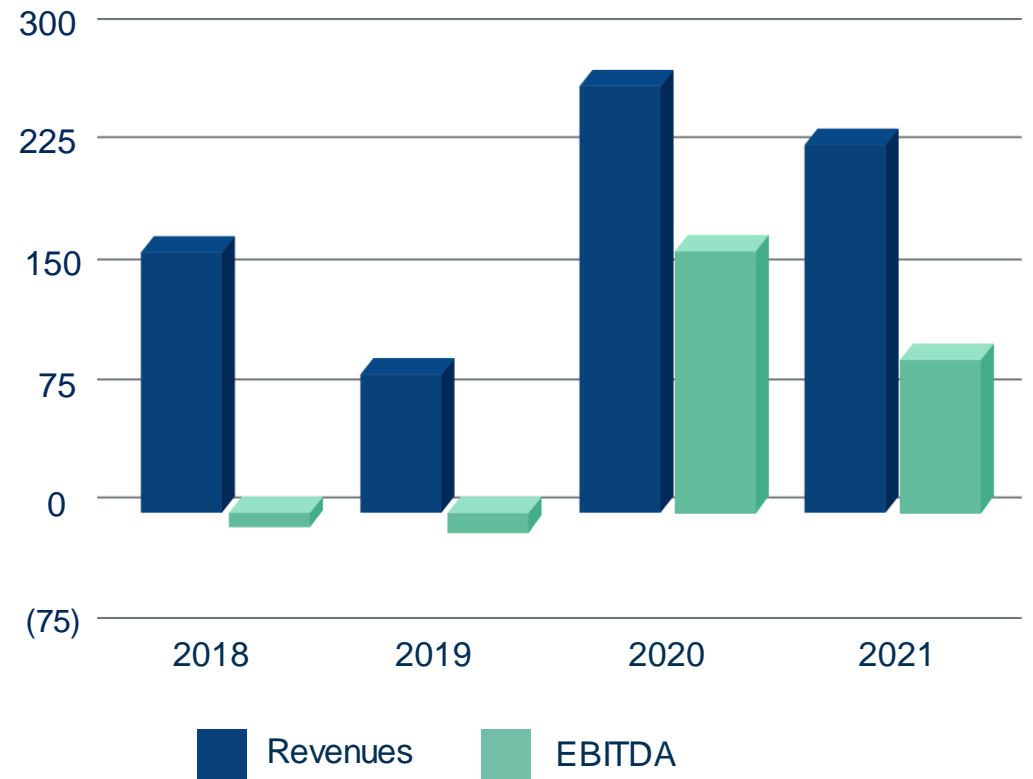
Financials

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

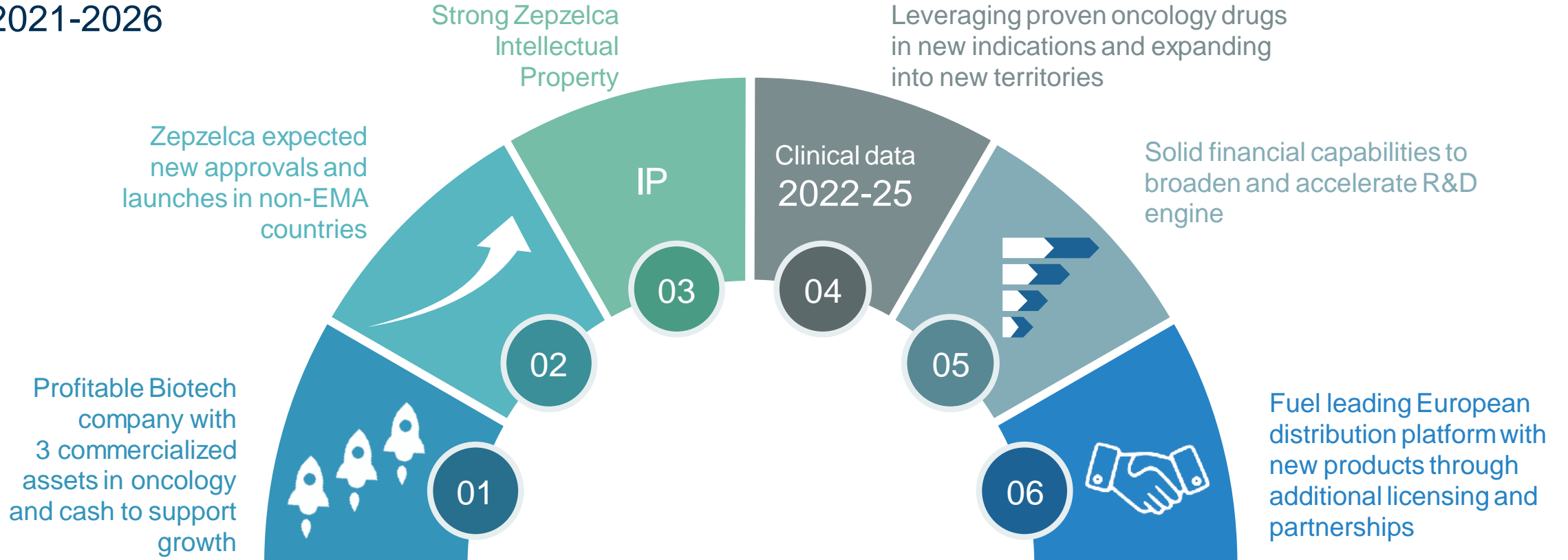
Further trials in Covid with plitidepsin

NA

NA

Building the Next Phase of Growth

2021-2026



2021 – 2026 Objectives

- ✦ Lurbinectedin in 3 Phase 3 trials; potentially all three 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



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