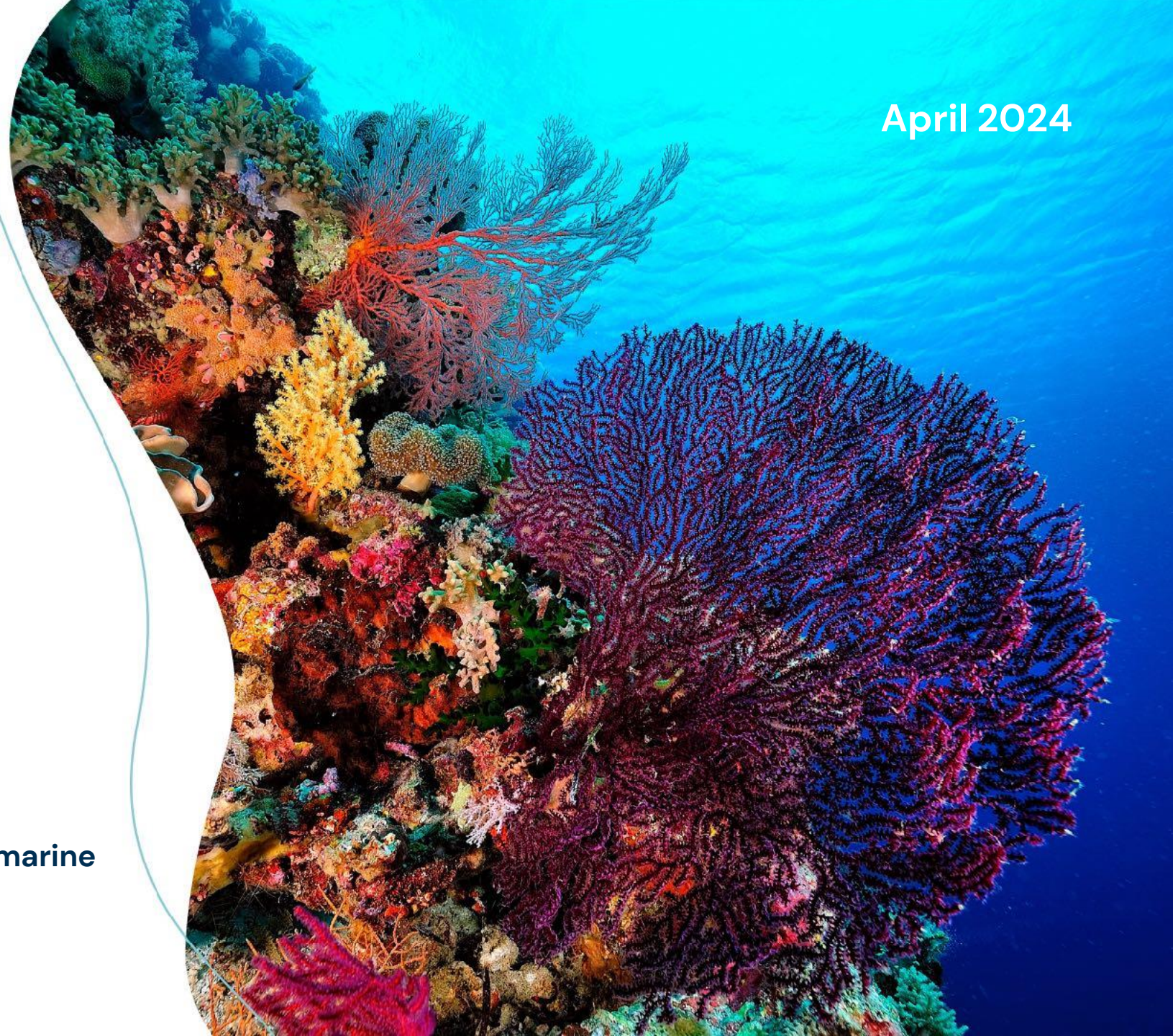
April 2024

# 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.

This presentation is made pursuant to Section 5(d) of the U.S. Securities Act of 1933, as amended, and is intended solely for investors that are either qualified institutional buyers or institutions that are accredited investors (as such terms are defined under U.S. Securities and Exchange Commission ("SEC") rules) solely for the purpose of determining whether such investors might have an interest in a securities offering contemplated by the Company. Any such offering of securities will only be made by means of a registration statement (including a prospectus) to be filed with the SEC, after such registration statement has become effective. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy these securities, nor shall there be any sale of these securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.

# 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


## 3 Approved Oncology Products

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

Established European oncology sales force

## Revenue Generating & Profitable

| | |
|---|---|
| Revenues in 2023 | **€158.2m** |
| EBITDA 2023 | **€2.1m** |
| Cash 2023 | **€168.6m** |
| Market cap | **~ €511mn[1]** |

## Discovery Platform Strengthening Oncology Pipeline

Diversified pipeline with late and early stage assets

(1) As of 2nd April 2024

# 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 2/3 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.**

# Pipeline – Expanding our Expertise in Oncology

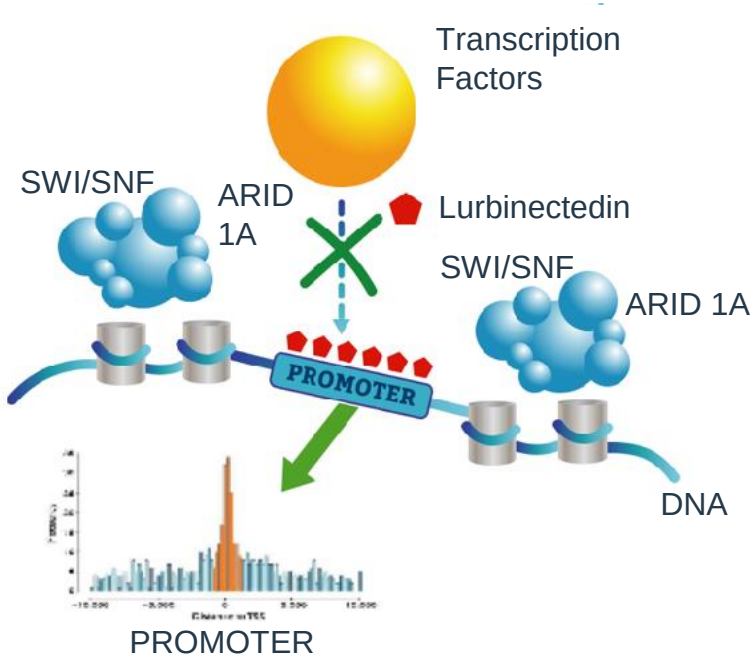
| | | | Phase 1 | Phase 2 | Phase 3 | Market |
|---|---|---|---|---|---|---|
| Yondelis (trabectedin) | Soft tissue Sarcoma | Monotherapy | 2nd/3rd line | | | |
| | Ovarian cancer | + PLD (pegylated liposomal doxorubicin) | 2nd/3rd line | | | |
| Aplidin (plitidepsin) | R/R Multiple Myeloma[1] | + dexamethasone | 3rd/4th line | | | |
| ZEPZELCA (lurbinectedin) | Small cell lung cancer | Monotherapy | 2nd line US / other countries | | | |
| | Small cell lung cancer maintenance | + atezolizumab | 1st line maintenance | | | Roche / Jazz Pharmaceuticals |
| | Small cell lung cancer | Lurbi vs. lurbi+ irinotecan vs. topotecan or irinotecan | 2nd line | | LAGOON | |
| | Leiomyosarcoma | + doxorubicin | 1st line | Phase IIb/III | | |
| | Small cell lung cancer | + irinotecan | 2nd line | | | |
| | Small cell lung cancer combo[2] | + atezolizumab | 2nd line | | | |
| Ecubectedin (PM14) | Solid tumours (basket trial) | Monotherapy | | | | |
| | Soft tissue sarcoma[2] | Combination radiation | | | | |
| | Prostate cancer | Monotherapy | | | | |
| | Solid tumours | Combination trials | | | | |
| PM534 | Solid tumours | Monotherapy | | | | |
| PM54 | Solid tumours | Monotherapy | | | | |

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

# Zepzelca – A Transcription Inhibitor Leading to Tumour Inhibition

## Primary Effect

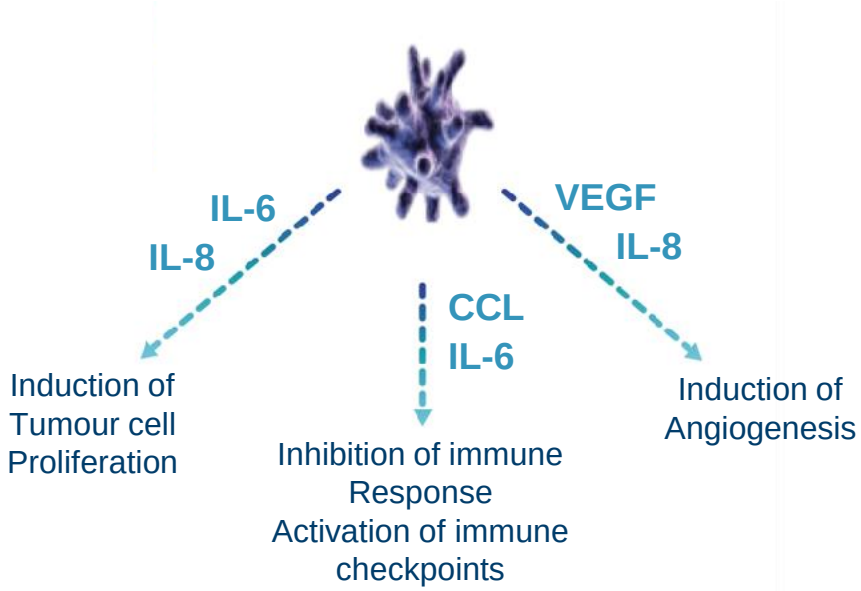
Cancer is frequently a transcriptional disease caused by deregulated oncogenic transcription factors




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

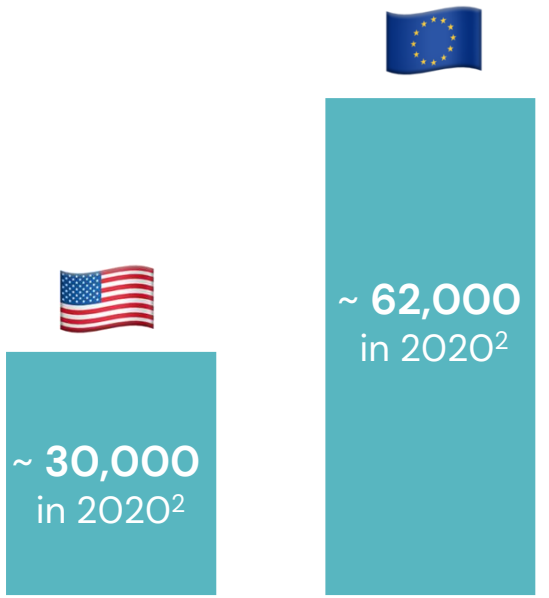
### Among all Lung Cancers

SCLC
**~15%**

### Low survival rate at 5 years

- Highly aggressive tumour
- 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 +<br>• Atezolizumab or Durvalumab ----▶ | ----▶ | • **Zepzelca**<br>• Topotecan (sensitive) | |
| | | | Subsequent Therapy | |
| NCCN Guidelines[1] | | | CTFI>6m<br>• Rechallenge<br>• Irinotecan | CTFI <6m<br>• Irinotecan<br>• Rechallenge<br>• Nivo/pembro<br>• Taxane<br>• Temozolomide<br>• CAV[3]<br>• Gemcitabine |

| | 1st Line | 2nd Line | 3rd Line |
|---|---|---|---|
| EMA Approved | • Platinum/ Etoposide +<br>• Atezolizumab or Durvalumab | • Topotecan | |
| | | Subsequent Therapy | |
| ESMO Guidelines[2] | | • **Lurbinectedin**<br>• CAV[3]<br>• Re-challenge | |

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

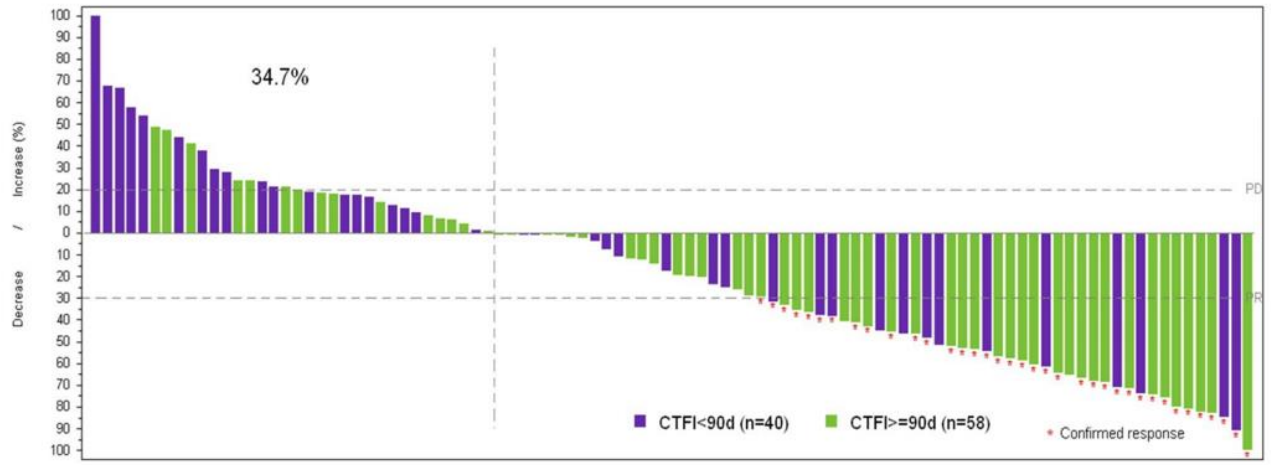
## Zepzelca Demonstrated Efficacy in Sensitive and Resistant Small Cell Lung Cancer patients

In relapsed SCLC as monotherapy under accelerated approval based on Phase 2 monotherapy data[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 tumour size in **65%** patients[2]




1. Trigo J. *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 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

**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

### 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

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

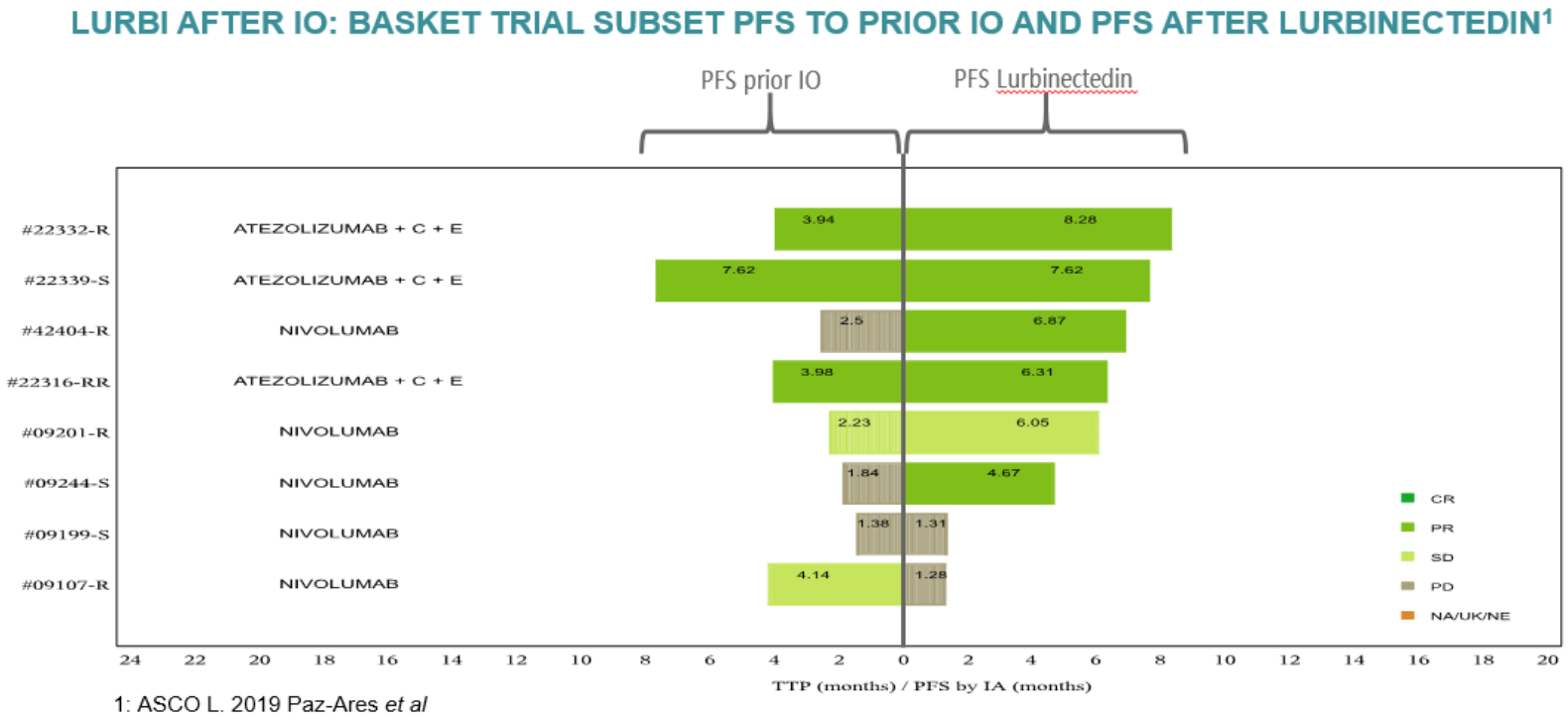
## Combo with IO delivers efficacy not seen for either drug as single agent

| 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$^2$ (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



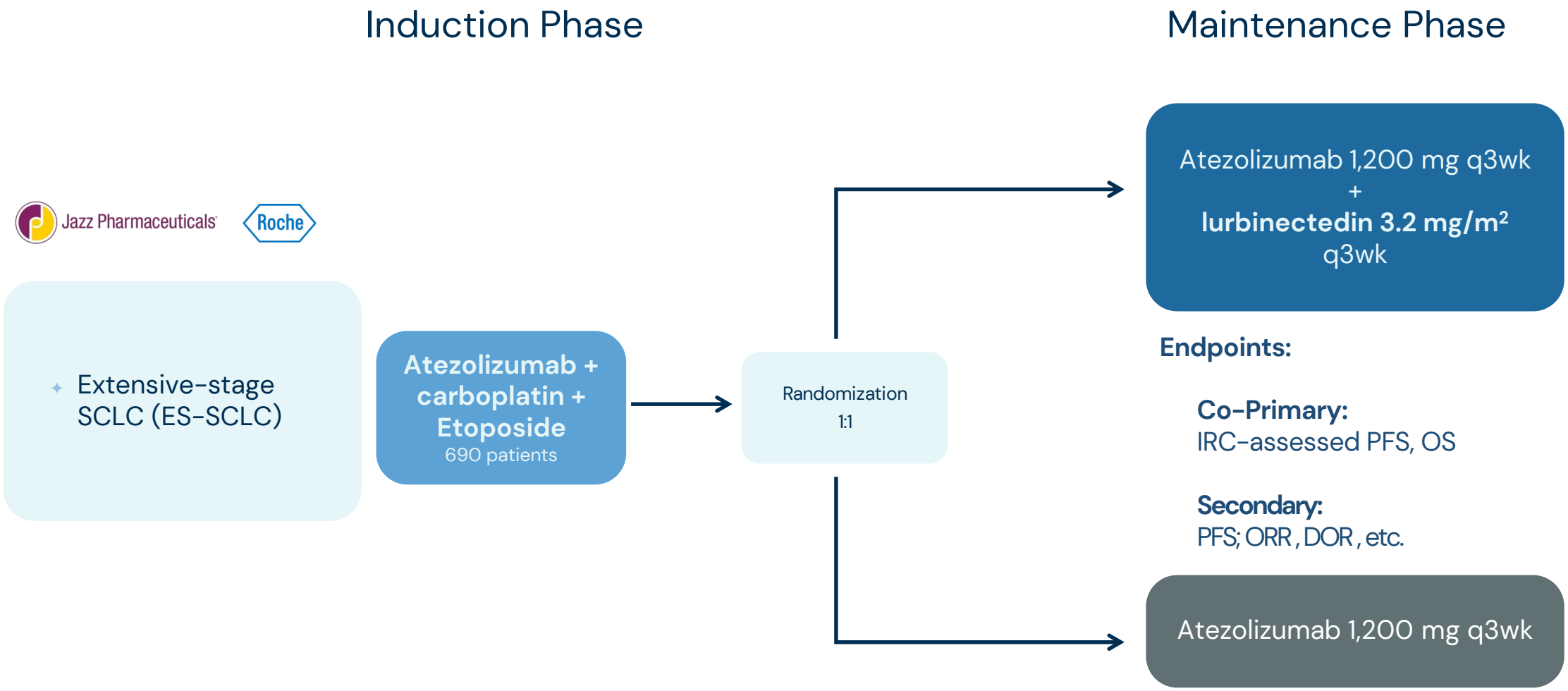

1: ASCO L. 2019 Paz-Ares *et al*

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




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<br>• Ifosfamide | • Trabectedin<br>• Pazopanib |
| **NCCN Guidelines** | | • Dacarbazine<br>• Ifosfamide<br>• Gemcitabine based regimen |

**Incidence** and ~4,500[2] in Europe

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

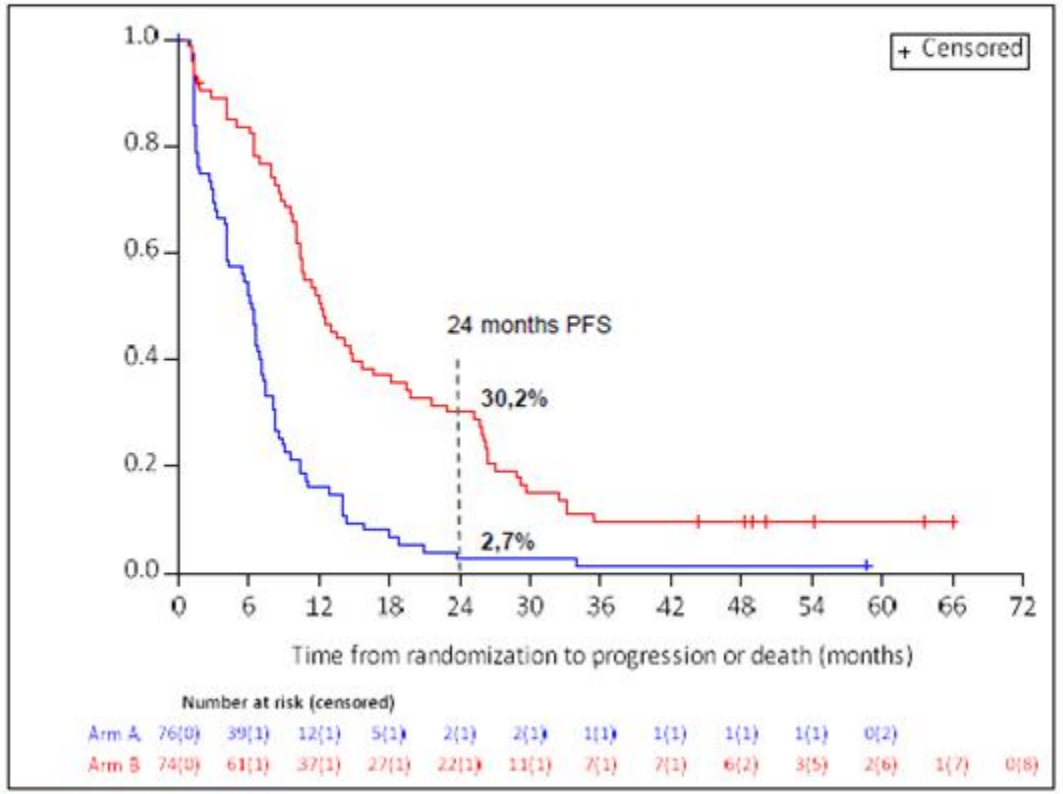
1. The American Cancer Society
2. ESMO Sarcoma guidelines 2021

# 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**

MADRID 2023 ESMO congress

Patricia Pautier

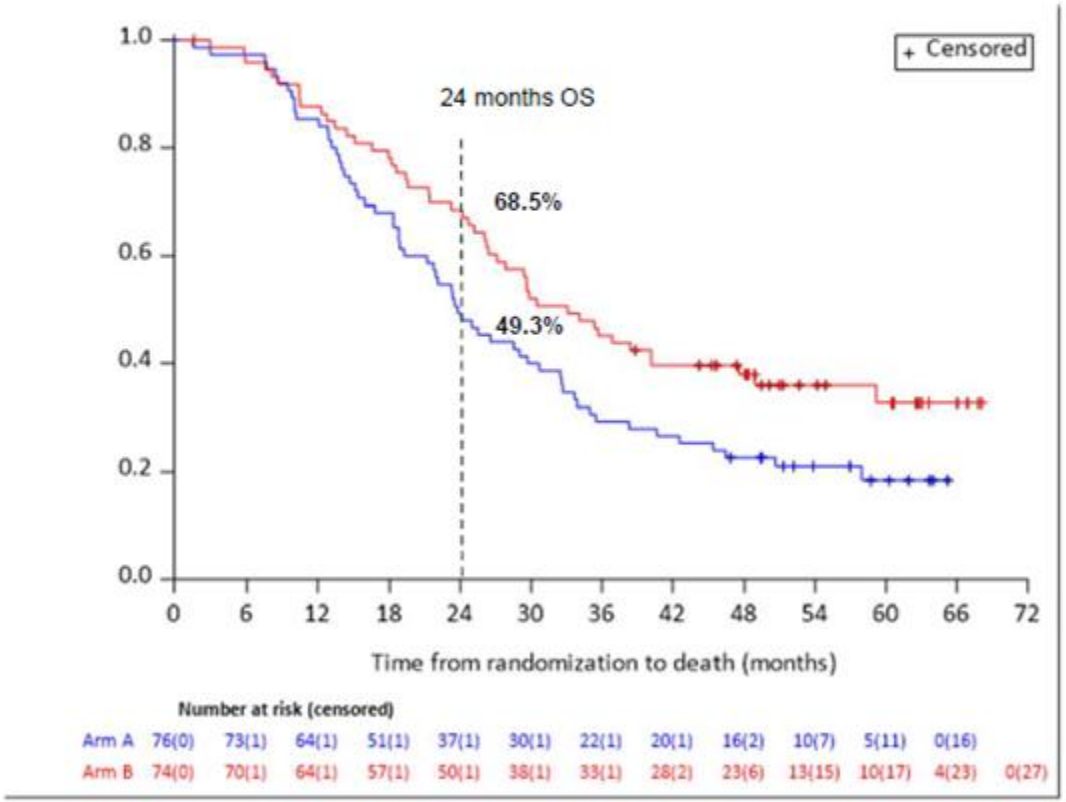
# Leiomyosarcoma

## 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**

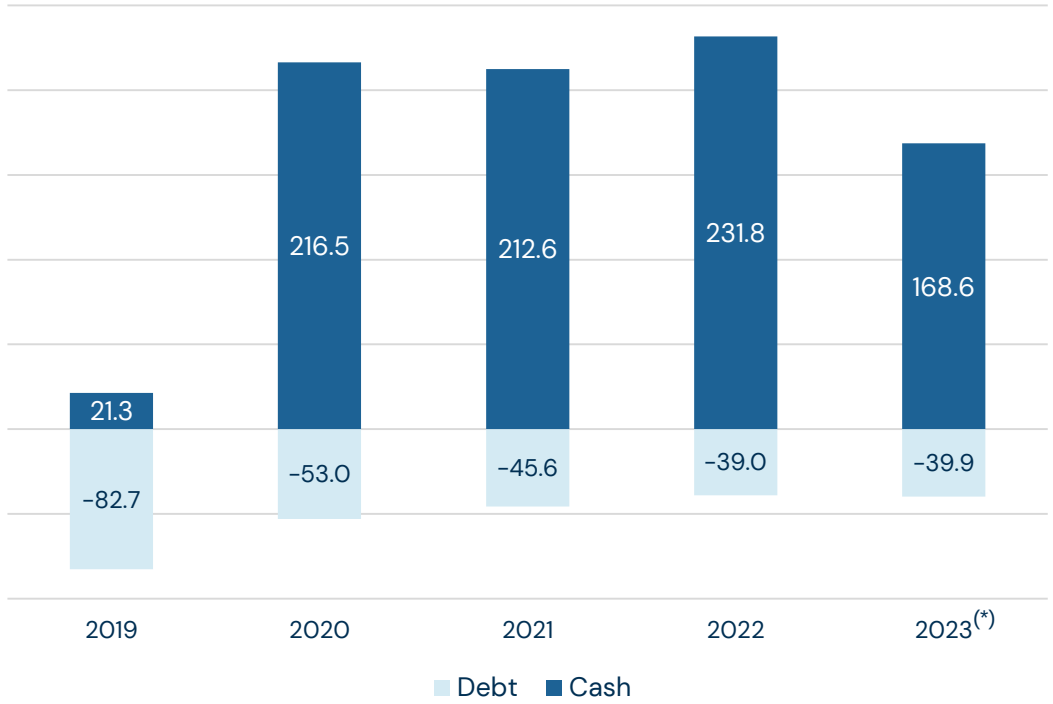
**Powered for OS**

(*) 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

# Financials

## Profitable and solid and stable financial position

### Robust cash position *(€ mn)*




### Historical revenues evolution *(€ mn)*

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

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


# 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 | 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

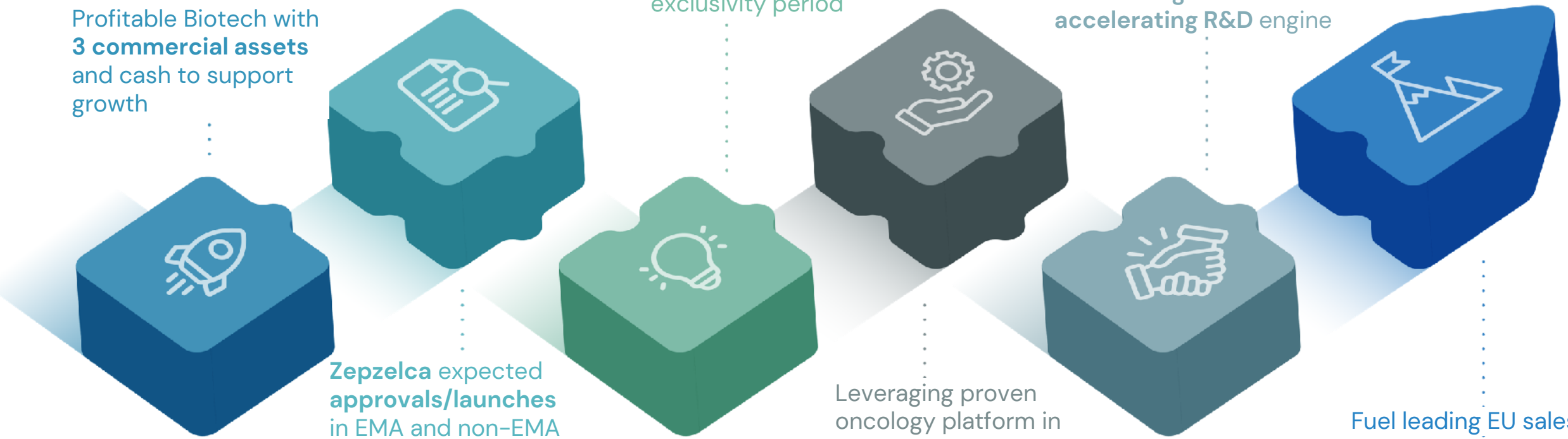
**Zepzelca** expected **approvals/launches** in EMA and non-EMA countries

Strong Zepzelca **I.P** exclusivity period

Leveraging proven oncology platform in **new indications**

**Financial** strength allows **broadening and accelerating R&D** engine

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

Pharma Mar


www.pharmamar.com