

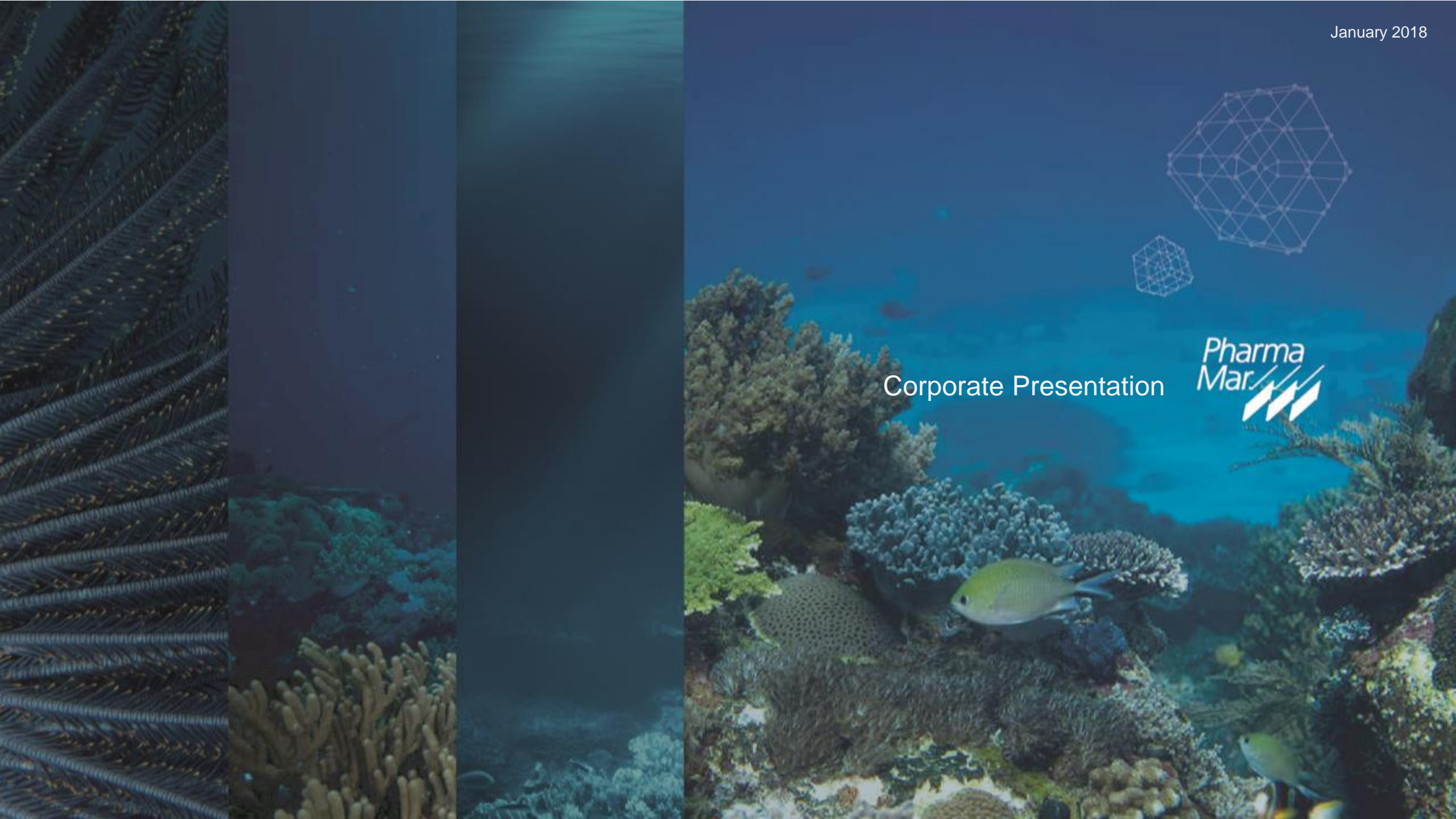


National Securities Market Commission  
Markets Directorate General  
c/ Edison núm. 4  
28006 Madrid

Colmenar Viejo (Madrid), January 9, 2018

Pursuant to article 228 of the consolidated text of the Spanish Securities Market Act, we hereby inform you of the following **SIGNIFICANT EVENT**:

"Please find attached corporate presentation (English version) which will be also available in the Company's web site [www.pharmamar.com](http://www.pharmamar.com)".



Corporate Presentation



## **Disclaimer\_**

This document includes only summary information and is not intended to be comprehensive. This document includes "forward-looking statements" that are based on Management's current expectations. Factors that could cause future results to differ materially from such expectations include, but are not limited to: the success of the Company's research strategy; the applicability of discoveries made therein; the difficulties inherent in the development of pharmaceuticals, including uncertainties as to the timing and results of preclinical studies; delayed achievements of milestones; reliance on collaborators; uncertainty as to whether the Company's potential products will succeed in entering human clinical trials and uncertainty as to the results of such trials;

uncertainty as to whether adequate reimbursement for these products will exist from the government, private healthcare insurers and third-party payers; and the uncertainties as to the extent of future government regulation of the pharmaceutical business. Therefore those statements involve risks and uncertainties beyond the Company's control and actual results may differ materially from those stated by such forward-looking statements. The Company expressly disclaims any obligation to review or update any forward-looking statements, contained in this document to reflect any change in the assumptions, events or circumstances on which such forward-looking statements are based unless so required by applicable law.

# INVESTMENT HIGHLIGHTS

*Leader in development & commercialization of marine-inspired oncology drugs*



**Global integrated biotech developing marine-inspired and novel MoA oncology drugs.**

- From discovery to commercialization.



**Established oncology sales force in Europe.**

- Strong partners in the US (Janssen), Japan (Taiho, Chugai) and Australia (STA).



**Late stage development pipeline driving future value; 2 Phase IIIs, soon 4.**

- **Zepsyre®** (lurbinectedin). First registrational data ~Q1 '18



**Track record of operational excellence with a strong financial position.**

- Revenue generating and robust cash flow.
  - 2017 1H revenues ~€97mm (+~5% y/o/y).
  - C. €585 market cap.
  - ~€32m in cash and cash equivalents (3Q2017)
- Headquartered and traded in Madrid.

# YONDELIS® - COMMERCIAL EXPANSION WORLDWIDE



## ● PHM Territories /

- WESTERN EU.
- Scandinavia and Eastern EUROPE:
- Swedish Orphan Biovitrum Greece, Cyprus and Balkans: Genesis Pharma
- Sarcoma and ovarian cancer.

## ● Partner Territories /

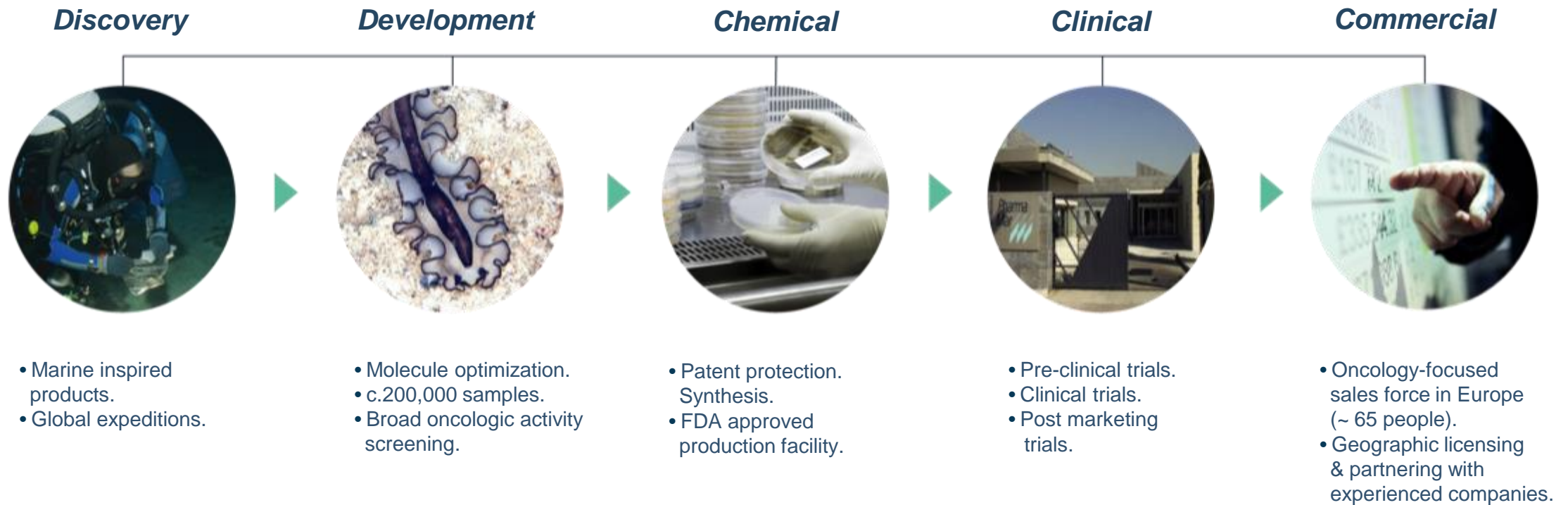
- USA and rest of the world (exclud. EU): Janssen.
- Sarcoma

## ● Partner Territories /

- JAPAN / Taiho
- Sarcoma

## ● PharmaMar Subsidiaries /

# UNIQUE FULLY INTEGRATED PLATFORM



**Regulatory inspections passed from FDA, AEMPS, PMDA (US, Spain/EU, Japan)**

# THE PLAN FOR GROWTH

*Potential to commercialize new oncology products in more indications*

Pharma  
Mar

## FURTHER IN THE FUTURE

**PM184**  
**PM14**

- 3 clinical products.
- Multiple indications.

Pharma  
Mar

## IN THE NEAR FUTURE

- 2 marketed products
- $\geq 4$  indications

Pharma  
Mar

## TODAY

- 1 marketed product
- 2 indications

**Zepsyre® (PM1183)**

- Platinum resistant ovarian cancer.
- Small Cell Lung cancer.
- BRCA 2 Breast cancer.
- Endometrial cancer.

**Yondelis®**

- Soft Tissue Sarcoma.
- R/R Ovarian Cancer.

# PORTFOLIO OF ONCOLOGY CANDIDATES

	Clinical Program / Indication		Phase I	Phase II	Phase III	Market	Partner	Data timing
<b>Yondelis®</b>	Soft Tissue Sarcoma 2 <sup>nd</sup> /3 <sup>rd</sup> line	Single agent	EU, US, Japan				J&J (US) Taiho (Japan)	
	Ovarian Cancer 2 <sup>nd</sup> /3 <sup>rd</sup> line	Yondelis®+Doxil	EU/Others					
<b>Zepsyre®</b> Lurbinectedin	Plat. Resistant ovarian cancer	Single agent	Global				Chugai (Japan)	Early 18
	SCLC Relapsed	Zepsyre®+Doxo	Global				Chugai (Japan)	2019
	BRCA 1/2 Breast cancer	Single agent	Global				Chugai (Japan)	Finalizing protocol
	Endometrial Cancer 2 <sup>nd</sup> line	Zepsyre®+Doxo	Global				Chugai (Japan)	Finalizing protocol
	Basket trial	Single agent	Global				Chugai (Japan)	Ongoing
<b>PM184</b>	Advanced Breast Cancer 3 <sup>rd</sup> /4 <sup>th</sup> line	Single agent	Global					Ongoing
	Solid tumors	Single agent and combinations	Global					Ongoing
<b>PM14</b>	Solid tumors	Single agent and combinations	Global					Ongoing



## MoA- ZEPSYRE® (Lurbinectedin)

### Targeted transcription Inhibitor as a cancer therapeutic

Zepsyre only affects activated transcription. Does not affect basal transcription\*

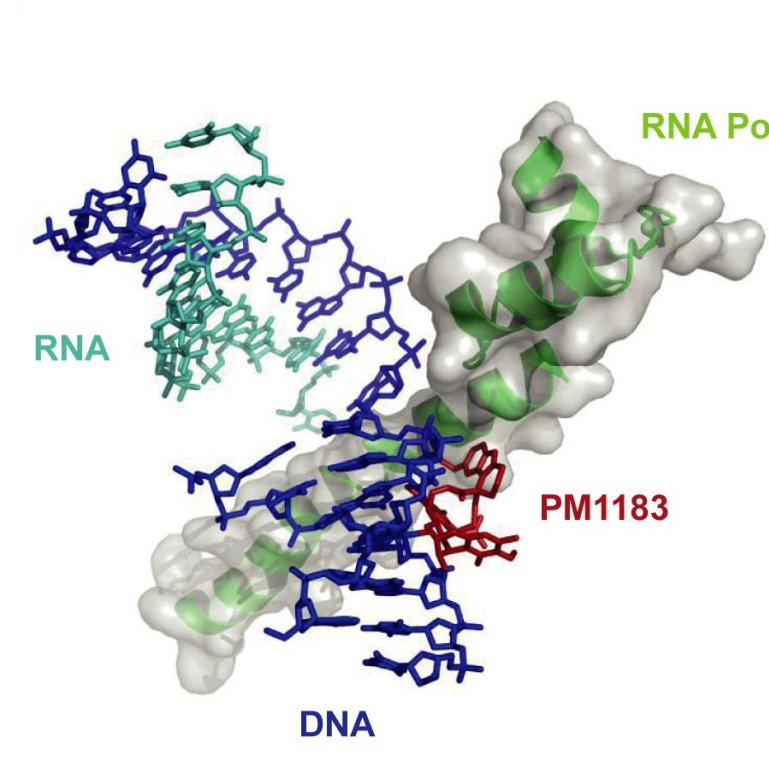
Generates double strand DNA breaks.

Some tumors are addicted to transcription (SCLC, Ovarian Cancer, etc...)

Effect on tumor microenvironment: Zepsyre inhibits the activated transcription of certain cytokines such as IL-6, IL-8, CCL2 and PTX3.

"Lurbinectedin...inhibits the transcription process through (i) its binding to CG-rich sequences, mainly located around promoters of protein-coding genes; (ii) the irreversible stalling of elongating RNA polymerase II (Pol II) on the DNA template and its specific degradation by the ubiquitin/proteasome machinery; and (iii) the generation of DNA breaks and subsequent apoptosis. The finding that inhibition of Pol II phosphorylation prevents its degradation and the formation of DNA breaks after drug treatment underscores the connection between transcription elongation and DNA repair. "

Santamaria et al, Mol Cancer Ther. 2016 Oct;15(10):2399-2412.

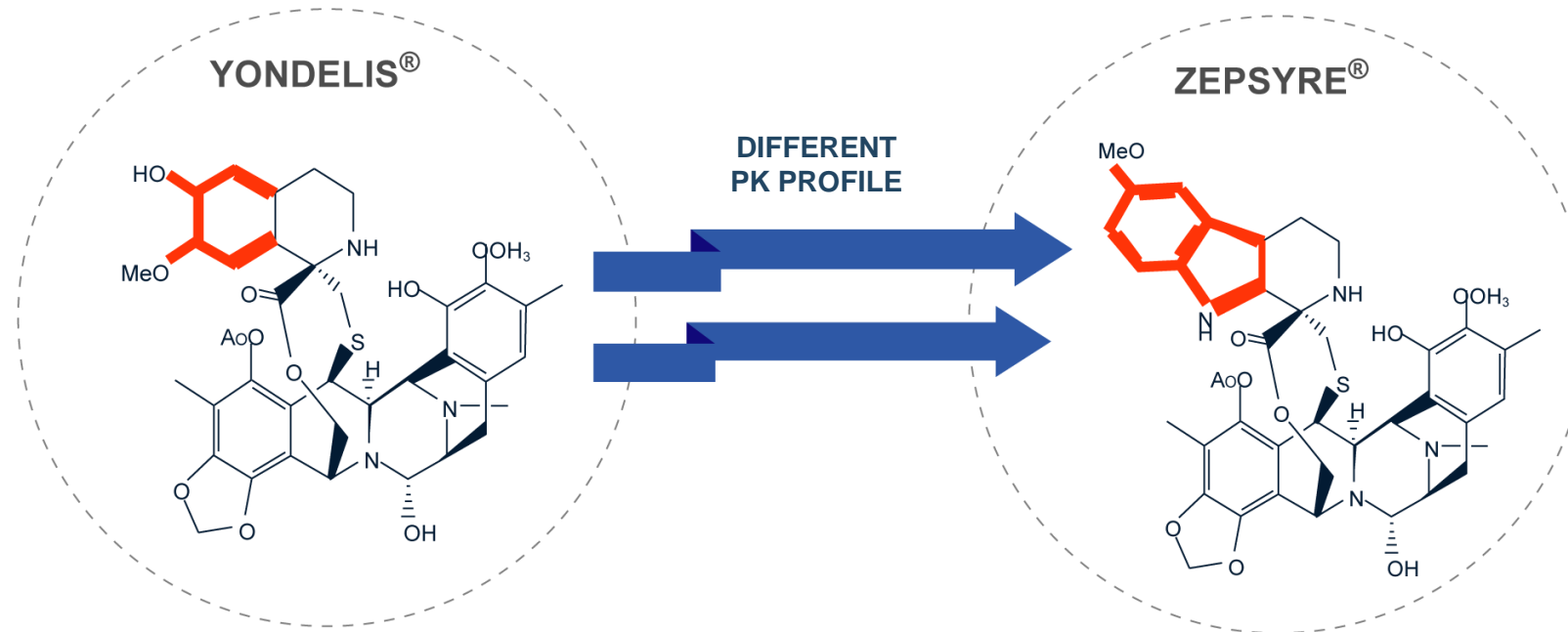


\*Source Molecular cancer Therapeutics 2016 Oct;15(10):2399-2412.

# ZEPSYRE<sup>®</sup> (Lurbinectedin)

*Key oncology compound– accelerating growth*

Zepsyre, a second generation Yondelis<sup>®</sup>, with improved PK, absorption and other attributes.



- Zepsyre is administered as a 1h peripheral infusion versus 24h continuous central catheter infusion with Yondelis<sup>®</sup>.
- Zepsyre linear PK profile.

- 4x tolerated dose.
- 15x exposure at RD.
- Better therapeutic window.
- Oncology “office practice” friendly.

# PIPELINE- ZEPSYRE® (Lurbinectedin)

## Development strategy

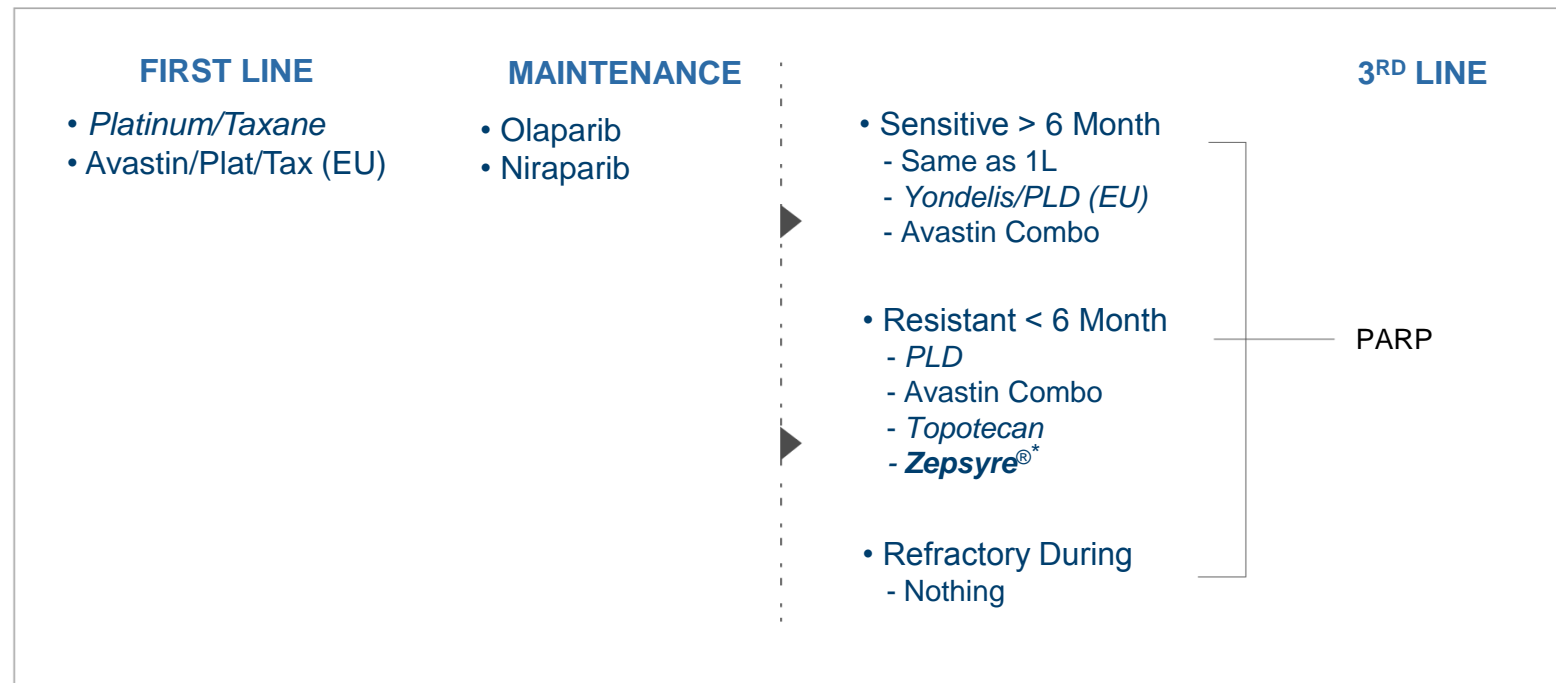
CLINICAL PROGRAM/ INDICATION		PHASE I	PHASE II	PHASE III	MARKET	DATA TIMING
<b>ZEPSYRE®</b>						
Plat. Resistant ovarian cancer	Single agent	▶				Early 2018
SCLC Relapsed	Combo Doxorubicin	▶				Data ~mid'19
BRCA 1/2 Breast cancer* 2nd /3rd line	Single agent	▶				Starting 1H'18
Endometrial* 2nd line	Combo Doxorubicin	▶				Starting 1H'18
Basket trial	Single agent	▶				Ongoing
Combination Studies	Solid Tumors	▶				Ongoing

\*Subject to finalization 1H'18

# ZEPSYRE®: PLATINUM RESISTANT OVARIAN CANCER

## Market overview: Orphan Indication US/EU <sup>1</sup>

- ~ 250,000 WW new cases of ovarian cancer.
- ~ 150,000 WW deaths from ovarian cancer.
- Platinum resistant patients account for ~15% of ovarian cancer.
- 80% relapse after first platinum.



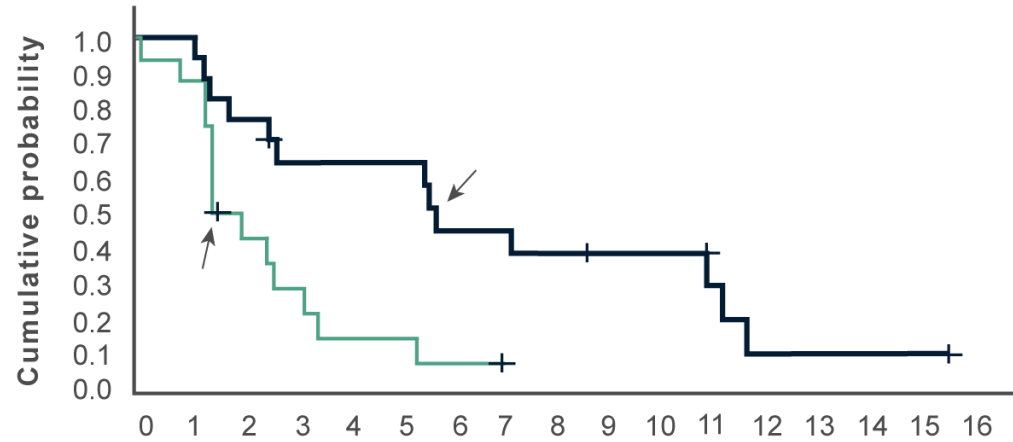
<sup>1</sup> **Source:** Estimated ovarian cancer incidence and mortality, all ages. GLOBOCAN 2012 and PharmaMar market research studies

\*Investigational drug-not approved in any jurisdictions

*Italics = DNA damaging agents*

# ZEPSYRE®: PHASE II PLATINUM RESISTANT OVARIAN CANCER

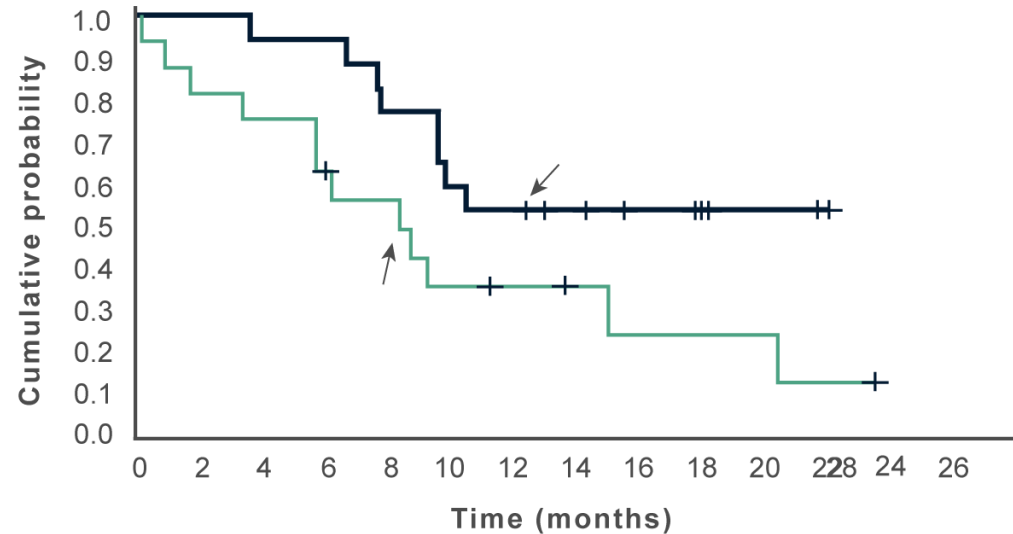
## ASCO 2014



### STAT SIG PFS

- PM01183 (N=17 C=4)
- Topotecan (N=16 C=2)
- + Censored

HR: 0.30 (95%CI 0.12-0.72)  
p=0.005\*



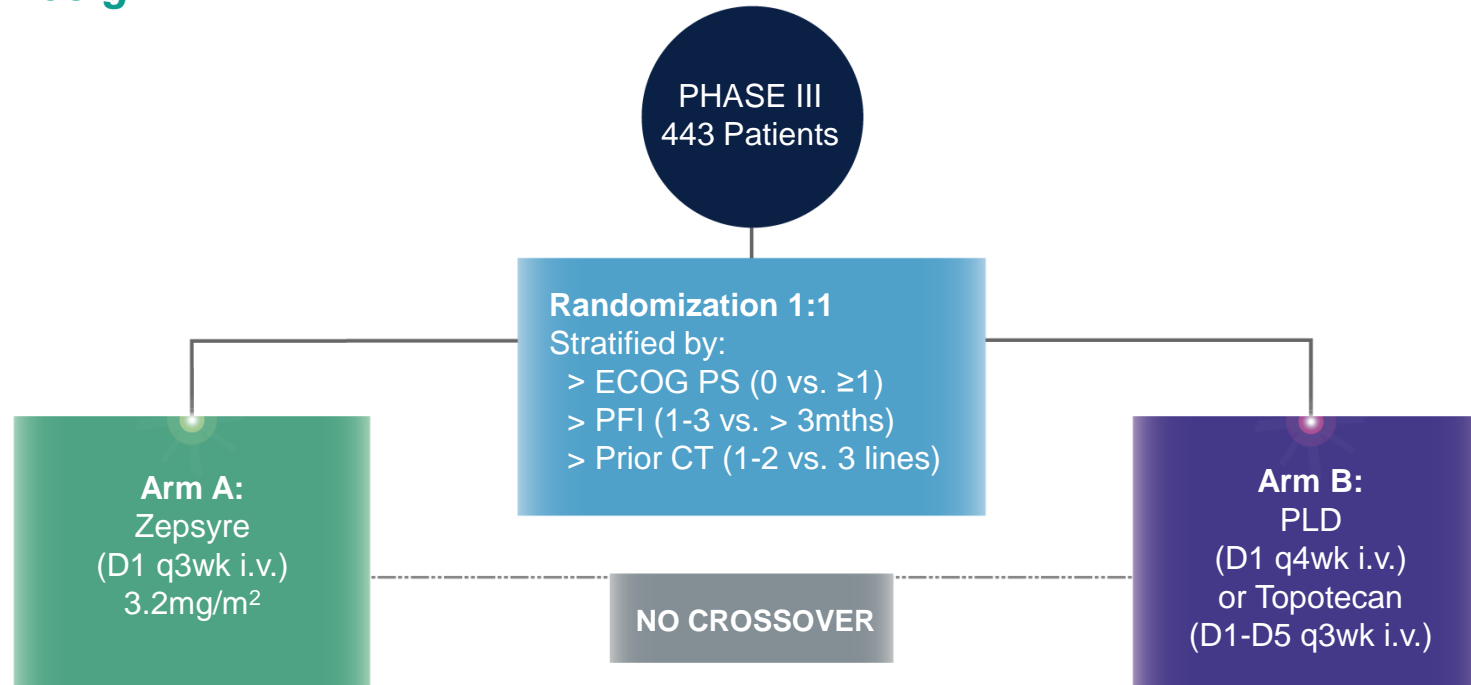
### STAT SIG OS

- PM01183 (N=17 C=9)
- Topotecan (N=16 C=4)
- + Censored

HR: 0.40 (95%CI 0.16-0.99)  
p=0.039\*

\*log-rank test

# ZEPSYRE®: PHASE II PLATINUM RESISTANT OVARIAN CANCER CORAIL Trial Design



**Primary Endpoint: PFS, 90% power for HR=0.7; p=0.025 (one-sided)**

**Interim safety analysis: passed @ 80 events  
Interim analysis : @ 210 patients, July 2016**

**Patient recruitment completed: October 2016; Data expected Q1 '18**

# ZEPSYRE®: SMALL CELL LUNG CANCER (SCLC)

*Market overview: Orphan Indication US/EU <sup>1</sup>*



**In the US per annum<sup>2</sup>:**  
~ 33,200 new cases of small cell lung cancer  
~ 24,040 deaths from small cell lung cancer  
(~ 27% of all cancer deaths)

**In EU-28 per annum<sup>2</sup>:**  
~ 46,645 new cases of small cell lung cancer  
~ 40,700 deaths from small cell lung cancer

- SCLC represents a significant unmet medical need with limited late stage options.
- The 5-year survival rate is about 5%<sup>3</sup>
- SOC: Topotecan, CAV (off label)
- Last FDA approval, Topotecan, 1996.

**Sources:**

1 American Cancer Society, Decision Resources, Inc.

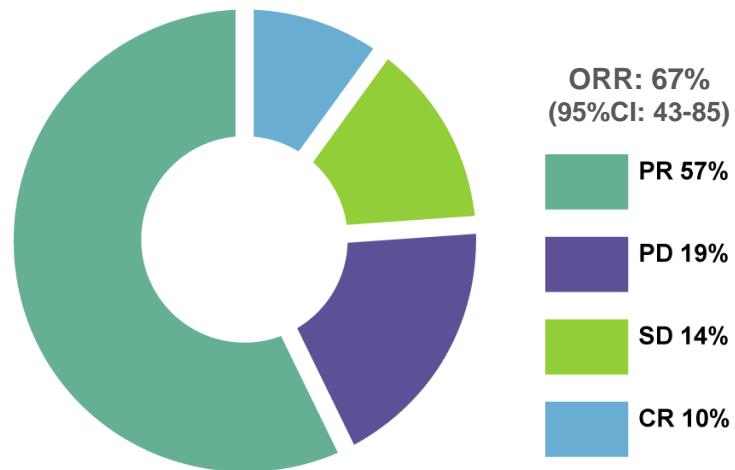
2 Triptych Health Partners held a Thoracic Oncology Strategic Advisory Board, June 2017

3 <http://www.cancer.gov/types/lung/hp/small-cell-lung-treatment-pdq>

# ZEPSYRE®: PHASE I/III RELAPSED SMALL CELL LUNG CANCER

*Cohort A: ASCO 2015 n=21*

Best RECIST v.1.1 overall response  
During treatment (n=21)



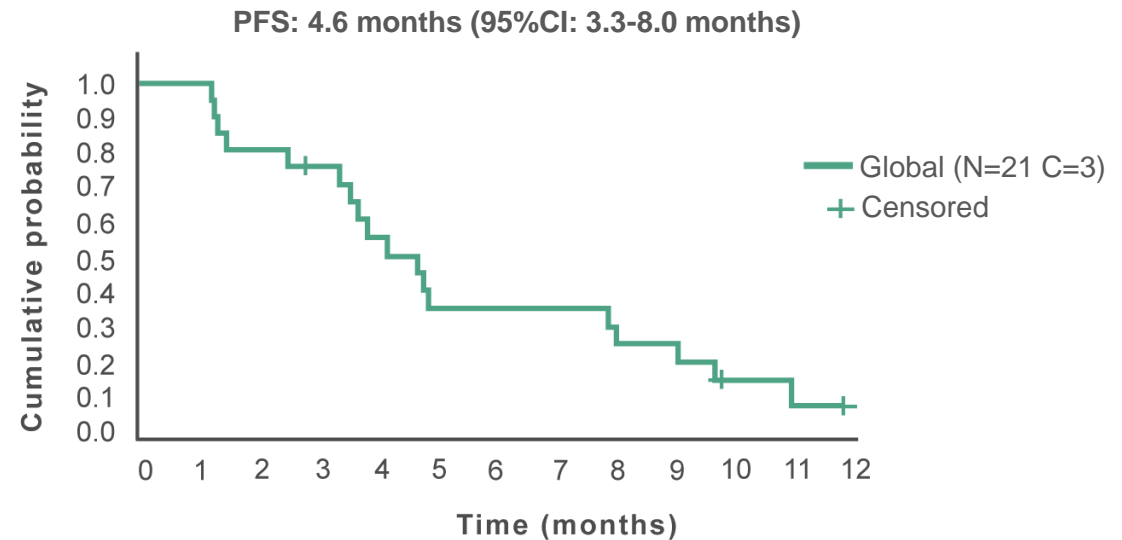
M. Forster et al. ASCO 2015

Other examples ORR in SSLC:

- CAV 19%
- Topotecan 24%
- Paclitaxel 29%
- Gemcitabine 12%
- Vinorelbine 12%

Source: Nature Reviews 2011;8;611-19 William N.Glisson.

Kaplan-Meier global PFS and according to CTFI (n=21)



PFS reported in registration Topotecan trial study:

- CAV: 2.8 months
- Topotecan 3 months

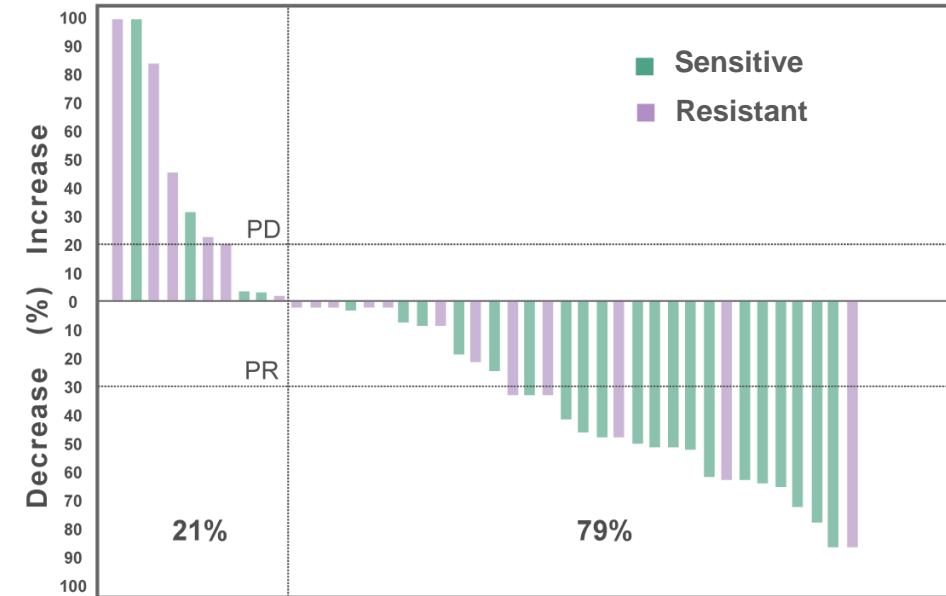
Source: J Clin Oncol, 1999, Von Pawel et al.



# ZEPSYRE®: PHASE I/III 2ND LINE SMALL CELL LUNG CANCER

Cohort B: ESMO 2017; n=27

EFFICACY				
RESPONSE EVALUABLE PATIENTS	Lurbinectedin +DOX (q3wk)		Lurbinectedin +TAX (q3wk)	Lurbinectedin single-agent (q3wk)
	Cohort A L 3-5 mg FD D1 + DOX 50 mg/m <sup>2</sup> D1 (n=21)	Cohort B L 2 mg/m <sup>2</sup> D1 + DOX 40 mg/m <sup>2</sup> D1 (n=27)	L 2 mg/m <sup>2</sup> D1 + TAX 80 mg/m <sup>2</sup> D1 & D8 (n=7)	L 3.2 mg/m <sup>2</sup> D1 (n=36)
CR	2 (10%)	1 (4%)	1 (4%)	-
PR	12 (57%)	9 (33%)	4 (57%)	13 (36%)
ORR	14 (67%)	10 (37%)	5 (71%)	13 (36%)
SD	3 (14%)	9 (33%)	-	14 (39%)
PD	4 (19%)	8 (30%)	2 (29%)	9 (25%)
DCR	17 (81%)	19 (70%)	5 (71%)	27 (75%)
DOR (mo)	4.5	5.2	2.3	6.2+
PFS (mo) CTFI >30d*	4.7	5.3	3.9	3.1+
CR	5.8	6.2	3.9	4.6+



Combined Cohorts A&B<sup>1</sup>  
N=48

CR 6%  
PR 44%  
ORR 50%  
PFS 5.0m

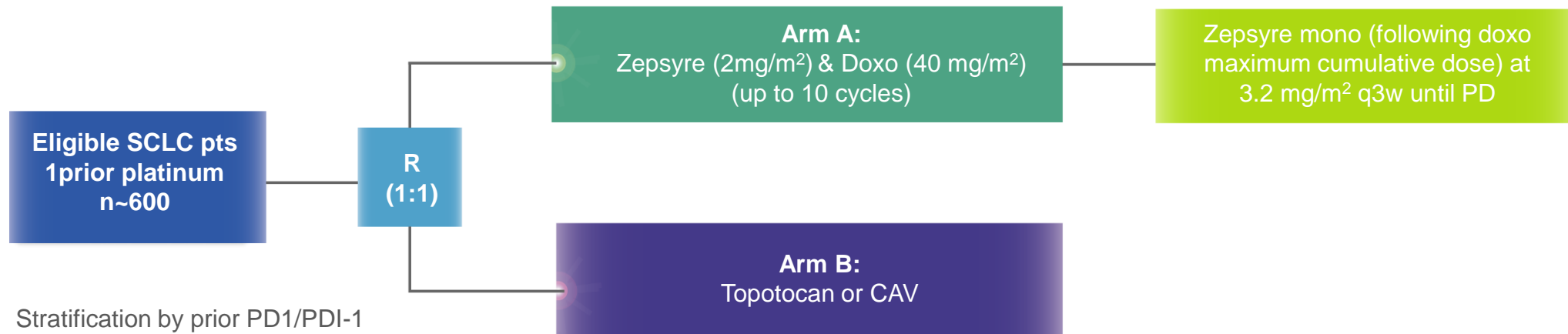
Phase III regimen

1. Extrapolation from cohorts A & B for illustrative purposes only. Not presented at ESMO.

# ZEPSYRE®: PHASE III RELAPSED SMALL CELL LUNG CANCER

*ATLANTIS Trial Design SCLC (Trial initiated August 2016); Anticipate data 2019*

- **Primary endpoint:** median PFS HR  $\leq 0.7$  in PFS with 90% power
- **Key secondary endpoints:**
  - OS
- **Registration Strategy**
  - Futility analysis passed @n=150 after 2 cycles (NOV'17).
  - Trial supported by ongoing monotherapy trial (n=36 at ESMO 2017).
  - Trial greater than 50% enrolled (OCT'17).



# ZEPSYRE®: 2ND LINE ENDOMETRIAL CANCER

*Market overview<sup>2</sup>: Orphan Indication US/EU <sup>1</sup>*



**In the US per annum:  
~ 50,000 new cases of endometrial cancer**

**In EU-28 per annum:  
~ 70,000 new cases of endometrial cancer**

- 2nd line chemo naïve patients ~ 25%.
- The most common gynaecologic cancer in developed countries, mainly afflicting those >50.
- SOC first line: Type 1 (80%): Hormone therapy, Type 2: Doxorubicin, paclitaxel, cisplatin (TAP). ORR 57%, OS 15.3m.
- 72% of endometrial cancer diagnosed early; 15% to 20% will recur<sup>1</sup>.
- There have not been any drug approvals for endometrial cancer over decades.

<sup>1</sup> Systemic treatment of endometrial cancer: Are there any new agents in sight? Andres Poveda. 2017 Progress and controversies in Gynaecology Oncology Conference.

<sup>2</sup> Source: Globocan 2012

# ZEPSYRE<sup>®</sup>: PHASE Ib IN 2L ENDOMETRIAL CANCER

## ASCO 2017 Abstract 5586

RESPONSE EVALUABLE PATIENTS	L+DOX (q3wk)		L+TAX (q3wk)	L alone (q3wk)
	Cohort A	Cohort B	L 2,2 mg/m <sup>2</sup> D1 + TAX 80 mg/m <sup>2</sup> D1 & D8 (n=11)	L 3.2 mg/m <sup>2</sup> D1 (n=40)
	L 3-5 mg FD D1 + DOX 50 mg/m <sup>2</sup> D1 (n=14)	L 2 mg/m <sup>2</sup> D1 + DOX 40 mg/m <sup>2</sup> D1 (n=18)		
CR	2 (14%)	-	-	1 (3%)
PR	2 (14%)	8 (44%)	3 (27%)	4 (10%)
ORR	4 (28%)	8 (44%)	3 (27%)	5 (12,5%)
SD	8 (57%)	7 (39%)	2 (18%)	15 (38%)
PD	2 (14%)	3 (16%)	6 (55%)	20 (50%)
DCR	9 (85%)	15 (83%)	5 (45%)	20 (50%)
DOR (mo)	19.5	6.8	6.1	4.3+
PFS (mo)	7.8	7.8	1.9	2.5+

CR, complete response; D, day; DCR, disease control rate; DOR, duration of response; DOX, doxorubicin; FD, flat dose; mo, months; ORR, overall response rate; PD, progressive disease; PFS, progression free survival; PM, PM1183, PR, partial response; q3wk, every 3 weeks; SD, stable disease; TAX, paclitaxel.

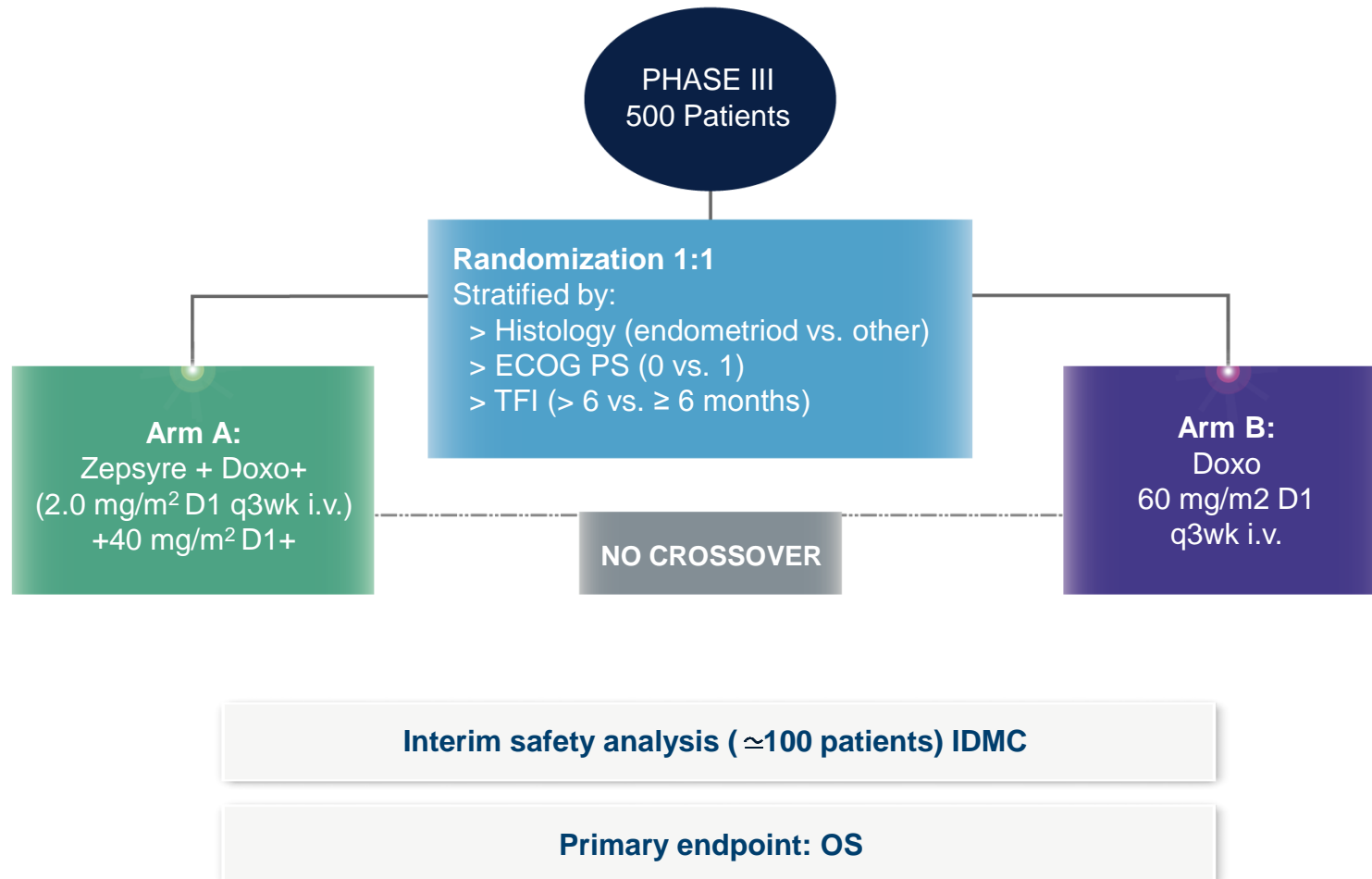
Phase III regimen

Combined Cohorts A&B  
N=32<sup>1</sup>  
CR 6%  
PR 31%  
ORR 38%  
PFS 7.8m

1. Extrapolation from cohorts A & B for illustrative purposes only. Not presented at ASCO

# ZEPSYRE®: PLANNED PHASE III 2ND LINE ENDOMETRIAL CANCER

*Subject to finalization and changes. Planning to start in 1H 2018*



\*With prophylactic G-CFS

# ZEPSYRE® \_ PHASE IIB IN BRCA 1/2-BREAST CANCER

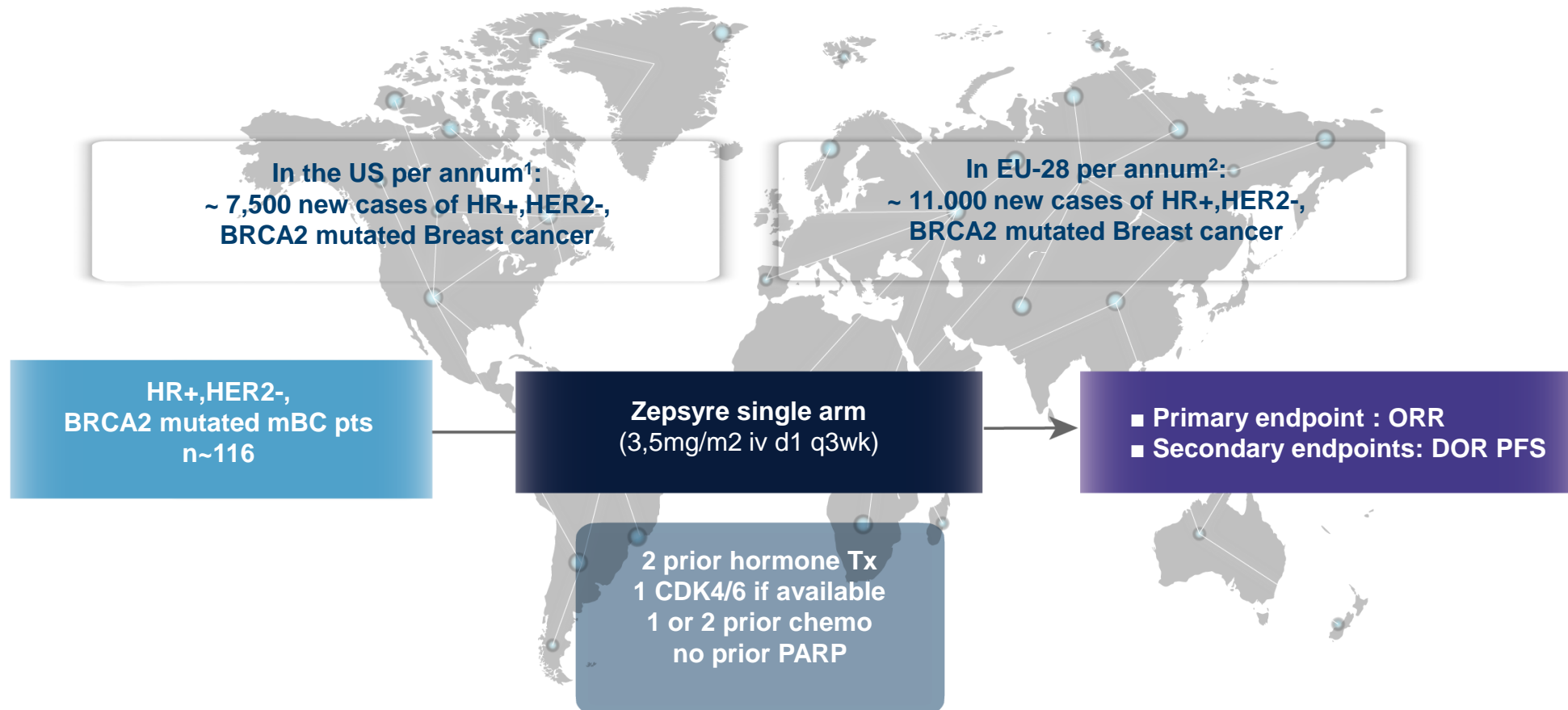
*Best ORR in specific subpopulations*

	Prior Platinum		BRCA			Hormone Status		Prior advanced CT lines	
	No (n: 27)	Yes (n: 27)	1 (n: 31)	2 (n: 23)	1/2 (n: 54)	Triple Negative (n: 33)	HR+ (n: 21*)	0-1 (n: 31)	2-3 (n: 23)
<b>ORR (95% CI)</b>	56% (35.3-55.6)	26% (11.1-25.9)	26% (11.9-25.8)	61% (38.5-60.9)	40.7% (27,6-55,0)	36% (13.3-27.3)	48% (38.4-81.9)	52% (33.1-69.9)	26% (10.2-48.4)
<b>Duration of Response (95% CI)</b>	10.2 m (3.0-13.5)	5.9 m (2.8-12.8)	6.6 m (2.8-12.8)	6.7 m (3.4-13.5)	6.7 m (3.0-13)	7.7 m (2.8-12.8)	6.7 m (2.8-13.4)	8.5 m (3.0-12.8)	3.4 m (2.8-20.5)
<b>Disease control rate</b>	25 (93%)	19 (70%)	23 (74%)	22 (96%)	45 (83%)	26 (79%)	19 (90%)	27 (87%)	18 (78%)
<b>Clinical benefit (CR+PR+SD ≥ 3 mo)</b>	19 (70%)	14 (52%)	14 (45%)	19 (83%)	33 (61%)	29 (88%)	14 (67%)	21 (68%)	12 (52%)

\*Includes 2 pts also HER-2 +

# ZEPSYRE®: PLANNED REGISTRATIONAL TRIAL<sup>2</sup> BRCA 2M BREAST

*Orphan Indication US/EU*

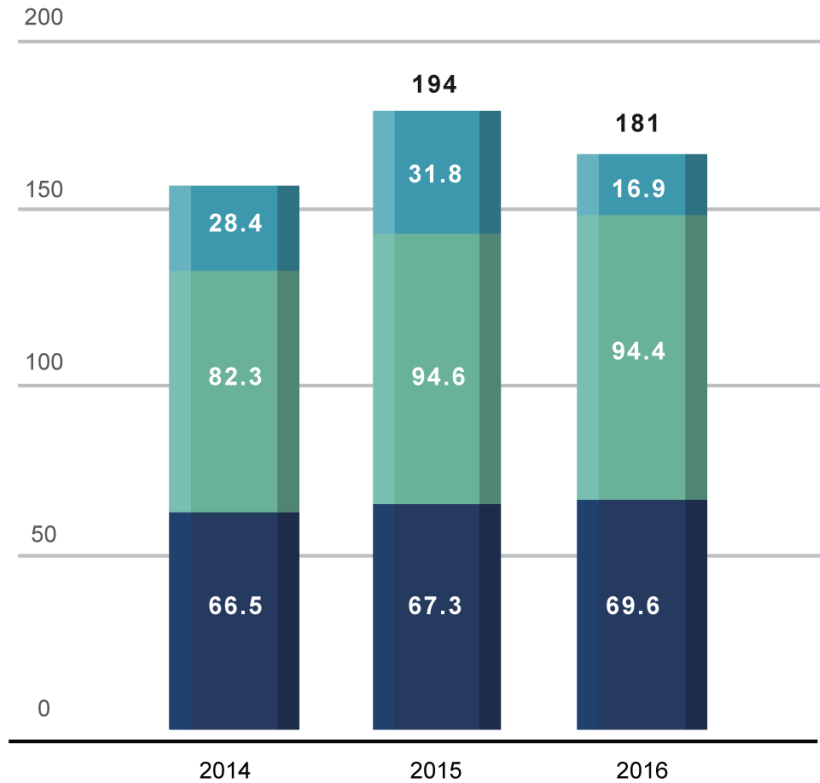


1. Source: US: seercancer.gov , EU28: Globocan2012, Oral poly(ADP-ribose) polymerase inhibitor olaparib in patients with BRCA1 or BRCA2 mutations and advanced breast cancer: a proof-of-concept trial. Andrew Tutt et al. Lancet 2010; 376: 235–44  
2. Subject to finalization and changes

# GROUP REVENUES AND R&D EXPENSES

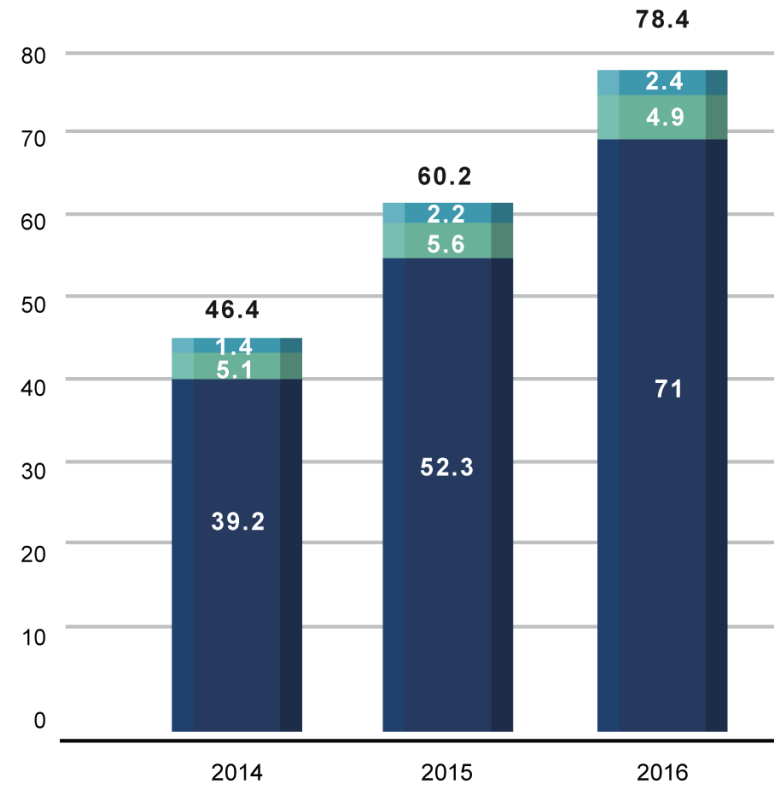
## Revenues

€ millions



## R&D

€ millions







For more information: [www.pharmamar.com](http://www.pharmamar.com)