



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

Colmenar Viejo (Madrid), June 12, 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".

June 2018



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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) and Australia (STA).



Late stage pipeline driving future value; 1 Phase III ongoing, other indications Phase II

- **Zepsyre®** (lurbinectedin).



Track record of operational excellence.

- Revenue generating and cash flow.
- 2017 revenues €179mm; Q1 '18 €45mm
- C. €365market cap.
- €24mm in cash and cash equivalents (Q1 2018)
- Headquartered and traded in Madrid.

YONDELIS® - COMMERCIAL EXPANSION WORLDWIDE



Yondelis Sales 2017: €132,5MN

EU (PHM): €85MN

ROW: €48MN

● PHM Territories /

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

● Partner Territories /

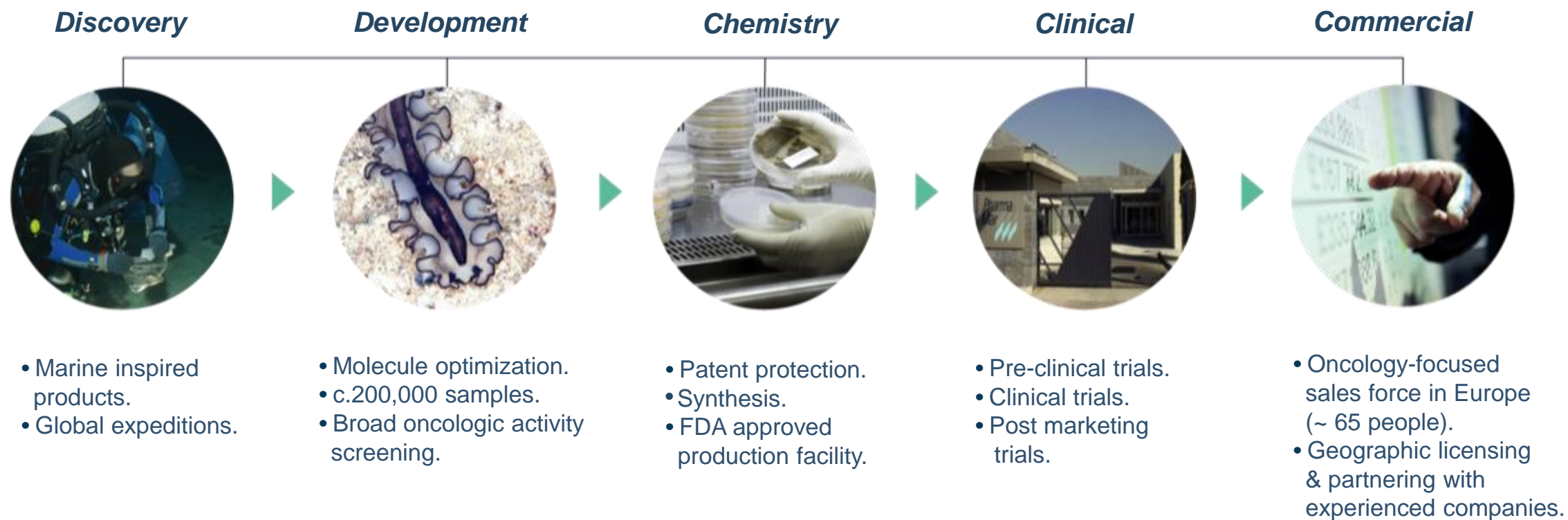
- USA and rest of the world (exclud. EU): Janssen.
- Sarcoma

● 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

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FURTHER IN THE FUTURE

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IN THE NEAR FUTURE

• **2 marketed products**

PM184
PM14

- 2 or more clinical products.
- Multiple indications.

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TODAY

- **1 marketed product**
- **2 indications**

Zepsyre®
(Lurbinectedin)

- **Small Cell Lung cancer.**

Yondelis®

- **Soft Tissue Sarcoma.**
- **R/R Ovarian Cancer (EU)**

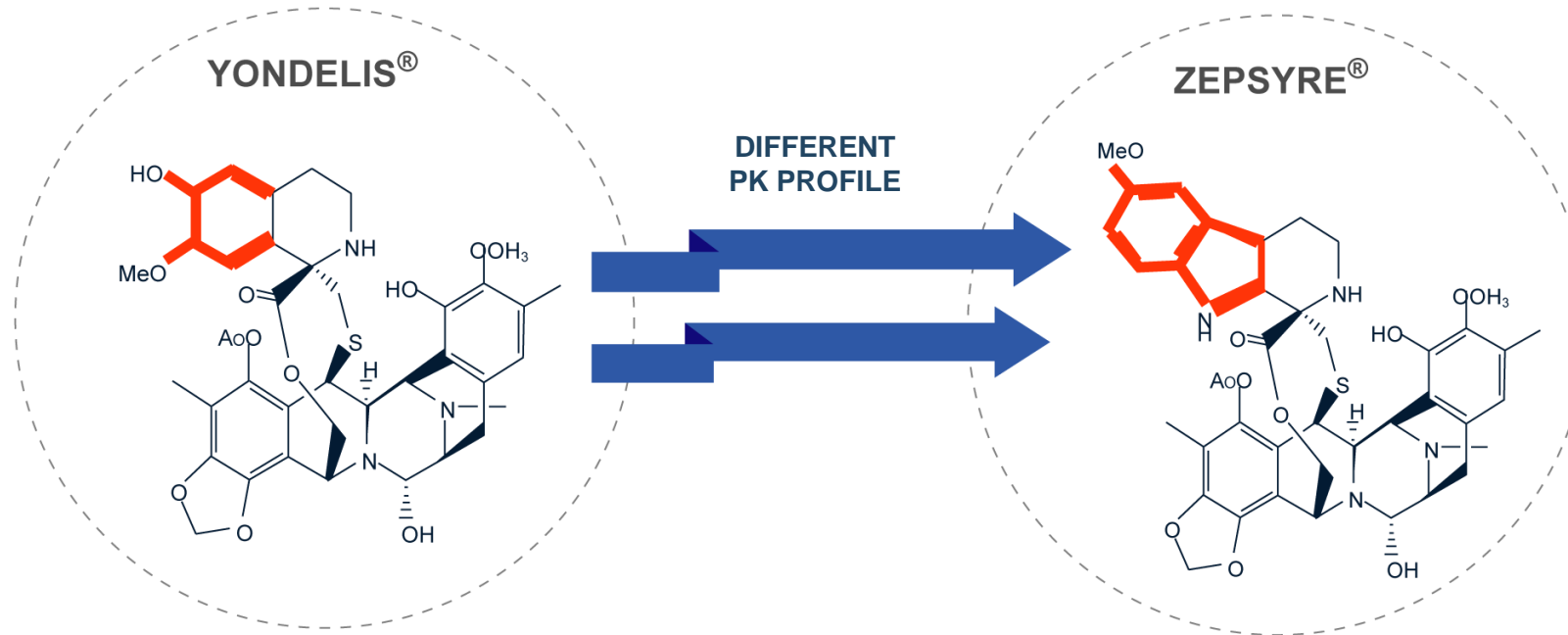
OUR ONCOLOGY PORTFOLIO:

	Clinical Program / Indication		Phase I	Phase II	Phase III	Market	Partner	Data timing
Yondelis®	Soft Tissue Sarcoma 2 nd /3 rd line	Single agent	EU, US, Japan				J&J (US) Taiho (Japan)	
	Ovarian Cancer 2 nd /3 rd line	Yondelis®+Doxil	EU/Others					
Zepsyre® Lurbinectedin	SCLC Relapsed	Zepsyre®+Doxo	Global					2H 2019
	Basket trial	Single agent	Global					Ongoing
PM184	Colorectal Cancer 3 rd line	Single agent	Global					FPI 1H '18
	Solid tumors	Single agent and combinations	Global					Ongoing
PM14	Solid tumors	Single agent and combinations	Global					Ongoing

ZEPSYRE[®] (Lurbinedin)

Key oncology compound– accelerating growth

Zepsyre, a second generation Yondelis[®], with improved PK, absorption and other attributes.



- Zepsyre is administered as a 1h peripheral infusion versus 24h continuous central catheter infusion with Yondelis[®].
- Zepsyre linear PK profile.

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

MoA- ZEPSYRE® (Lurbinectedin)

Targeted transcription Inhibitor as a cancer therapeutic

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

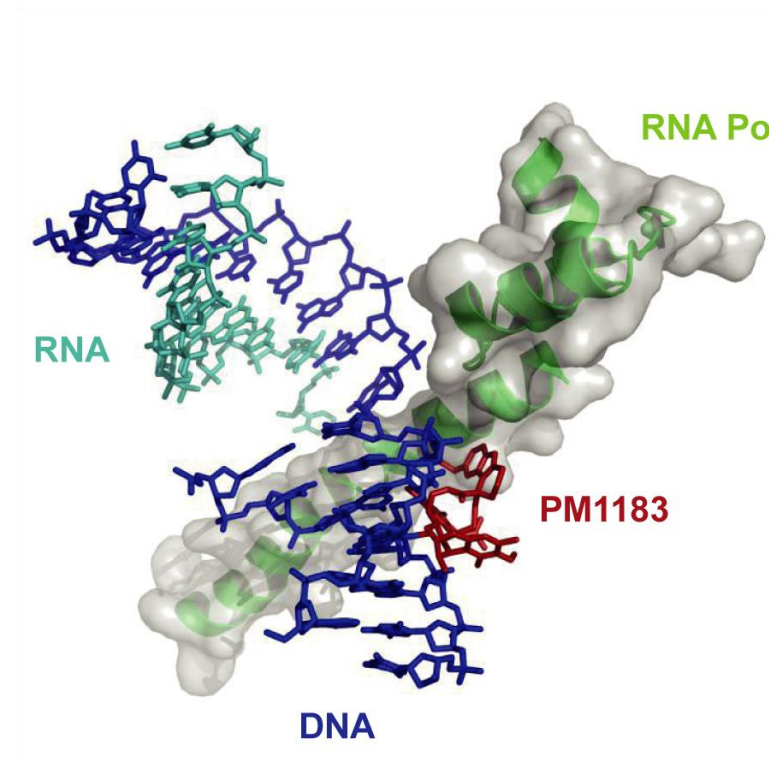
Generates double strand DNA breaks.

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.

PIPELINE- ZEPSYRE® (Lurbinectedin)

Development and commercial strategy

Clinical Program / Indication		Phase I	Phase II	Phase III	Market	Data timing
ZEPSYRE®						
SCLC Relapsed	Combo Doxorubicin	▶				2H 2019
Basket trial	Single agent	▶				Ongoing
Combination Studies	Solid Tumors	▶				Ongoing

Commercial Plans:

- EU: Utilize existing Yondelis sales force
- US: Self commercialize; build out commercial infrastructure
- ROW: regional partnerships

ZEPSYRE®: SMALL CELL LUNG CANCER (SCLC)

Market overview: Orphan Indication US/EU ¹



In the US per annum ²:
~ 33,200 new cases of small cell lung cancer
~ 24,040 deaths from small cell lung cancer

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

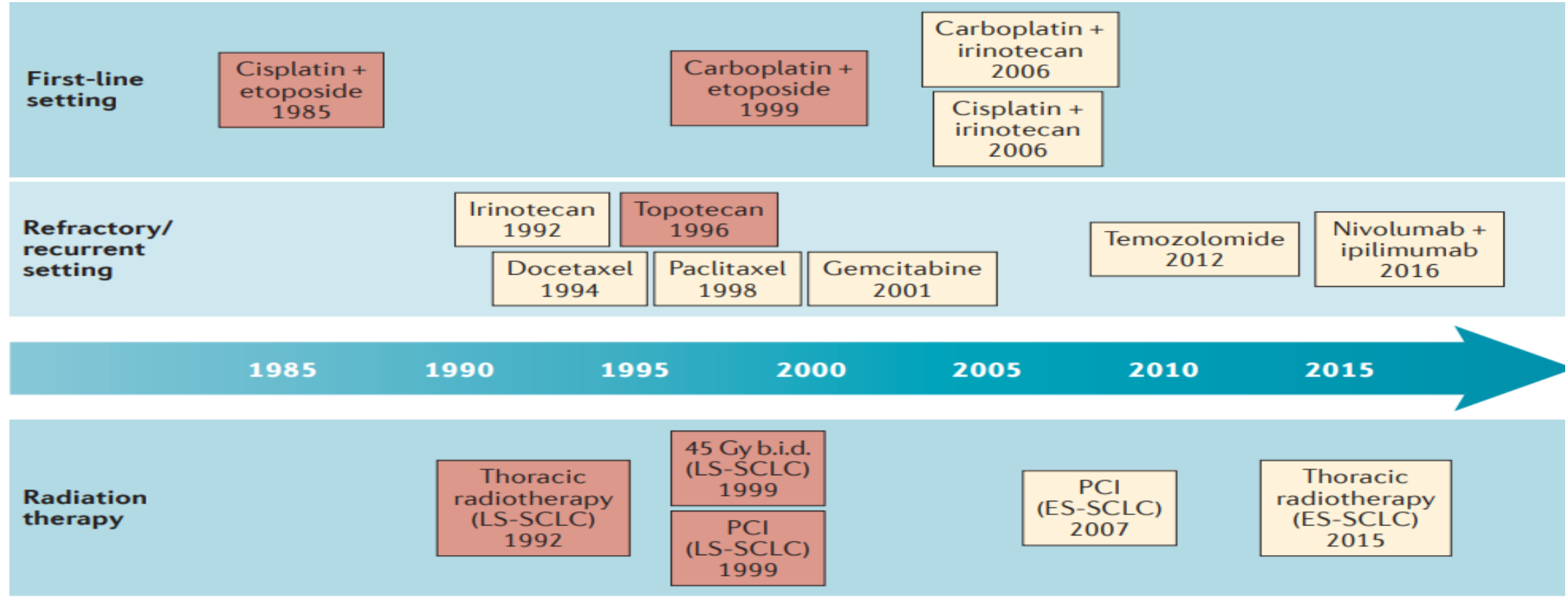
- SCLC represents a significant unmet medical need with limited late stage options.
- The 5-year survival rate is about 5% ³
- SOC: Topotecan, CAV (off label)
- Last FDA approval, Topotecan, 1996.

Sources:

1, 2 American Cancer Society, Decision Resources, Inc.

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

Small Cell Lung Cancer over the years¹; it's not NSCLC!



N
S
C
L
C
IO
EGFR
TKI

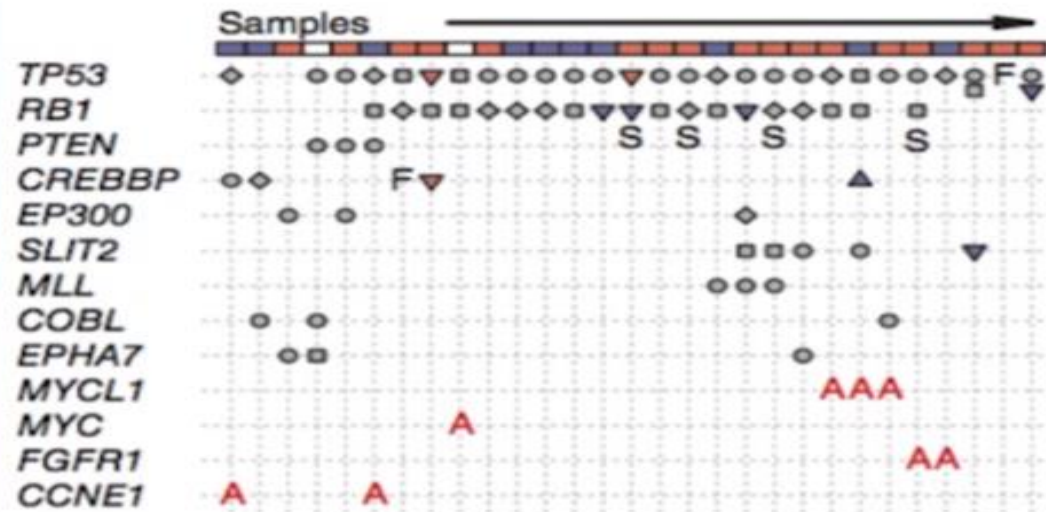
Alkylating
 Antimetabolites
 Antiangiogenesis
 Microtubule

CARBOplatin
 GEMZAR
 ALIMTA®
 AVASTIN®
 CYRAMZA®
 Abraxane®
 OPDIVO® KEYTRUDA® TECENTRIQ® IMCINZI®
 TAGRISSO® osimertinib
 XALKORI®
 Portrazza™
 ALUNBRIG™

Taxol
 TAXOTERE®
 IRESSA® Tarceva®

Source; Sabari et al, Clinical Oncology; September 2017

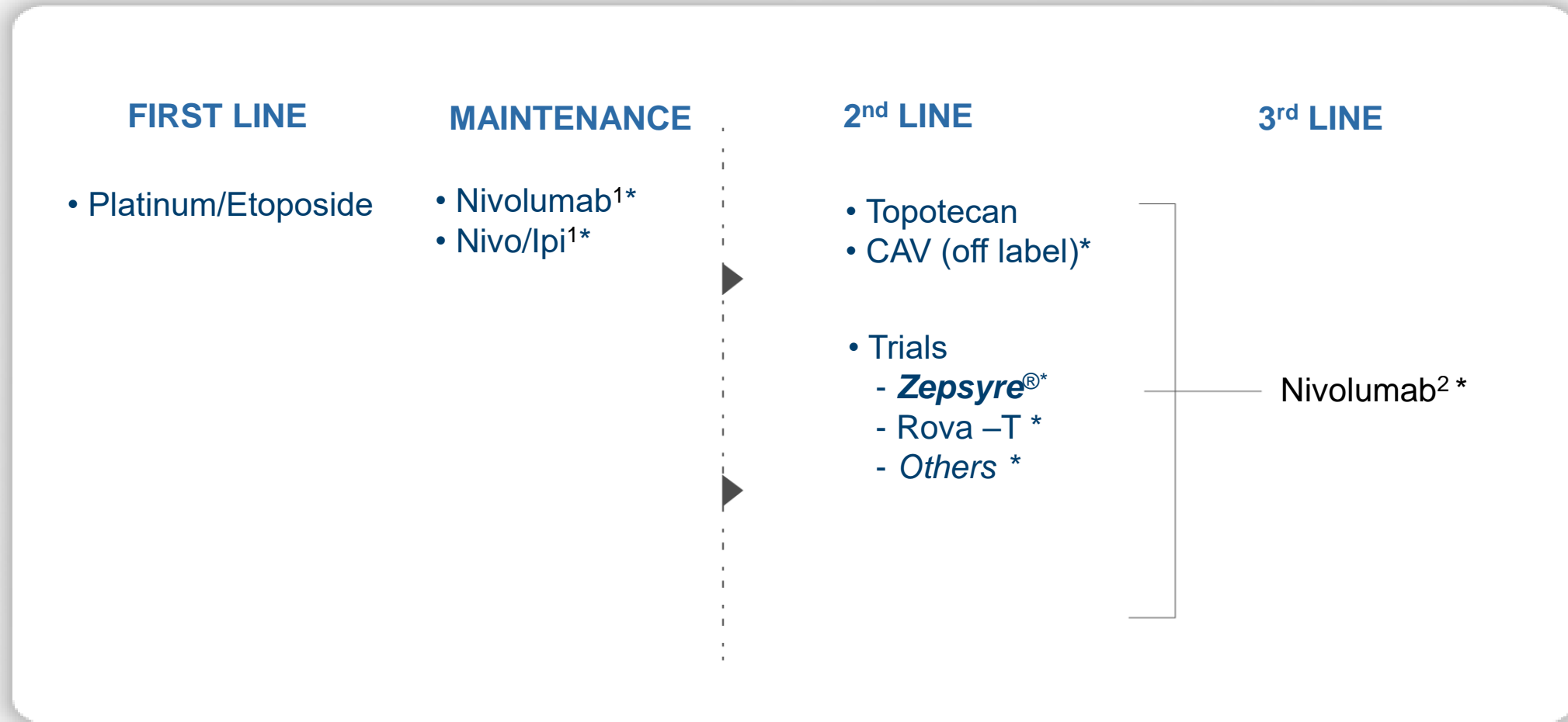
Why is SCLC so hard to target?



- + Most common genomic alterations are in tumor suppressor genes
- + Turning off an "off switch" is a real challenge

ZEPSYRE®: SMALL CELL LUNG CANCER

Current and Emerging treatment paradigm



* Investigational drug or not approved for this indication

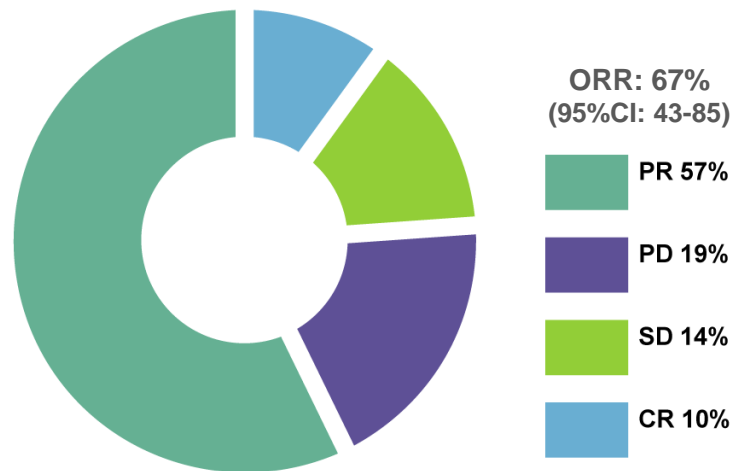
1. Not approved; however both included in NCCN guidelines

2. Nivo filed for 3rd line SCLC with FDA; PDUFA August 6 2018

ZEPSYRE®: PHASE I/II RELAPSED SMALL CELL LUNG CANCER

Cohort A: ASCO 2015 n=21

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



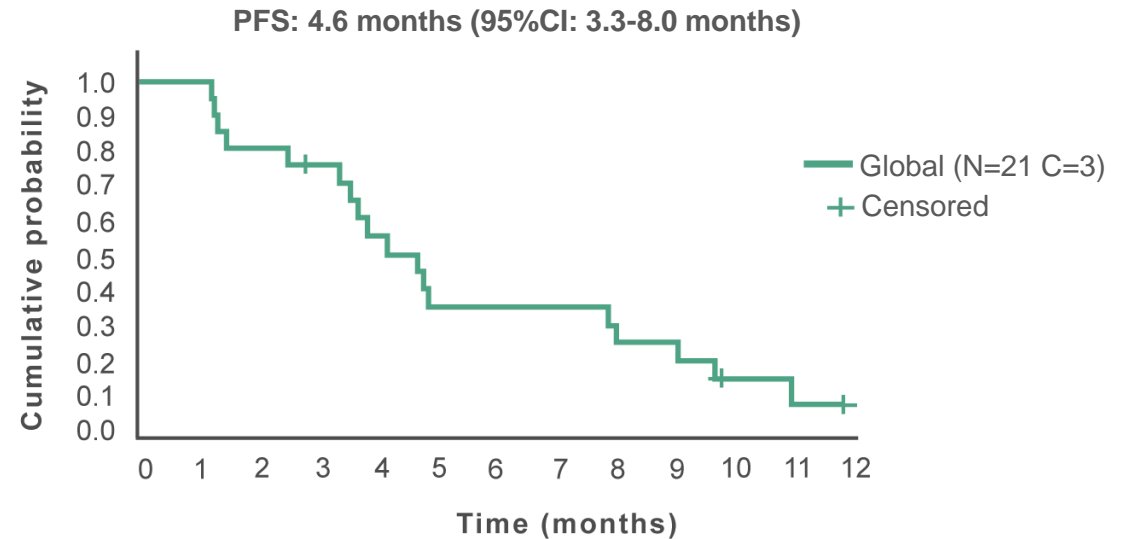
M. Forster et al. ASCO 2015

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:

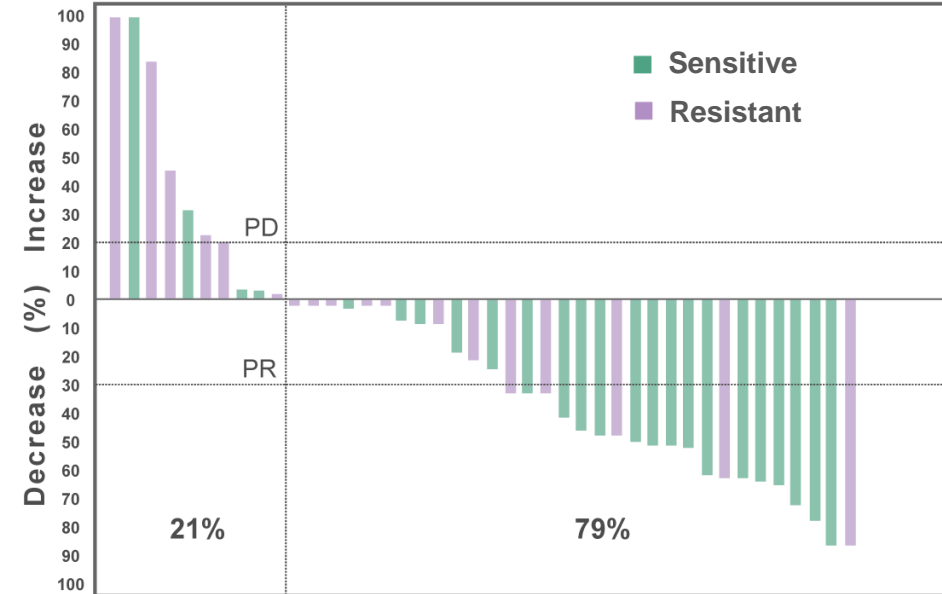
- CAV: 2.8 months
- Topotecan 3 months

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

ZEPSYRE®: PHASE I/II 2nd LINE SMALL CELL LUNG CANCER

Combo and Monotherapy latest data

EFFICACY			
RESPONSE EVALUABLE PATIENTS	Lurbinectedin +DOX (q3wk)		Lurbinectedin single-agent (q3wk)
	Cohort A L 3-5 mg FD D1 + DOX 50 mg/m ² D1 (n=21)	Cohort B L 2 mg/m ² D1 + DOX 40 mg/m ² D1 (n=27)	L 3.2 mg/m ² D1 n=61
CR	2 (10%)	1 (4%)	-
PR	12 (57%)	9 (33%)	24 (39%)
ORR	14 (67%)	10 (37%)	24 (39%)
SD	3 (14%)	9 (33%)	21 (34%)
PD	4 (19%)	8 (30%)	16 (26%)
DCR	17 (81%)	19 (70%)	45 (74%)
DOR (mo)	4.5	5.2	6.2
PFS (mo) CTFI >30d*	4.7	5.3	-
PFS (mo) Platinum-sensitive	5.8	6.2	n.a
PFS (mo) median	n.a	n.a	4.1
OS	n.a	n.a	11.8



Combined Cohorts A&B¹
N=48

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

Phase III regimen and endpoint

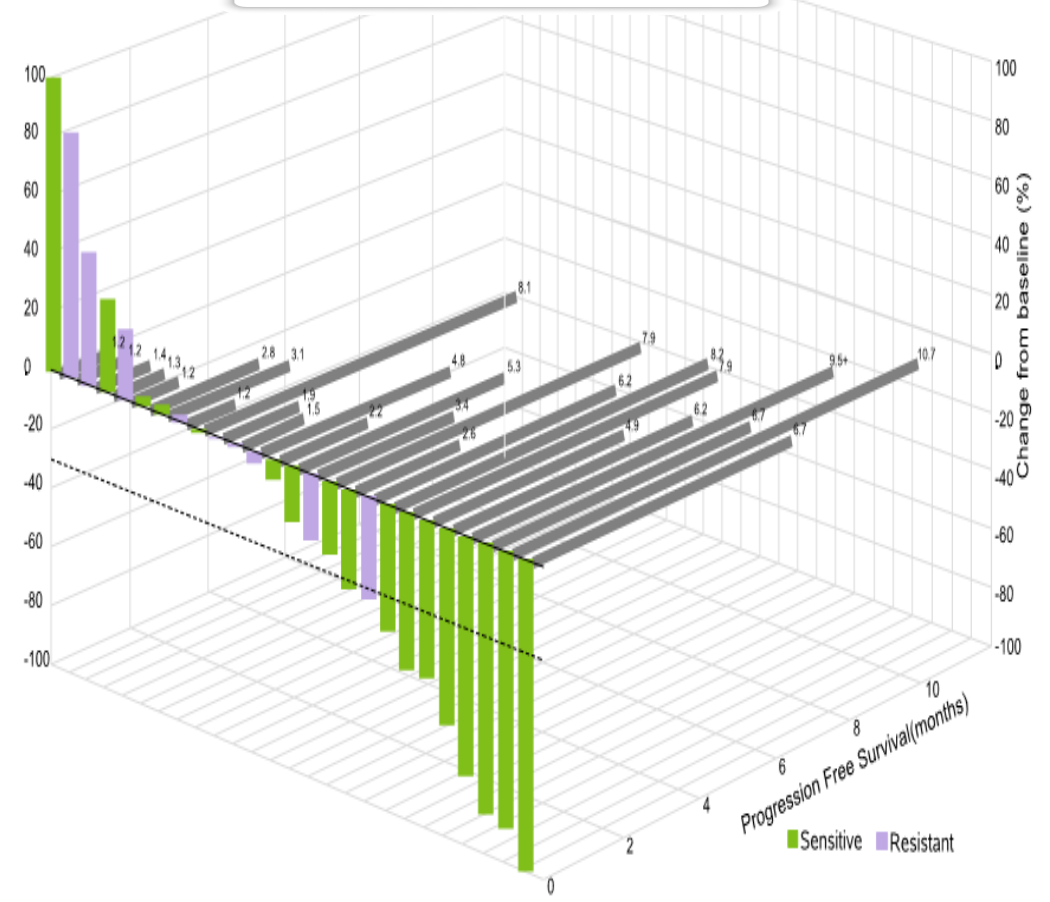
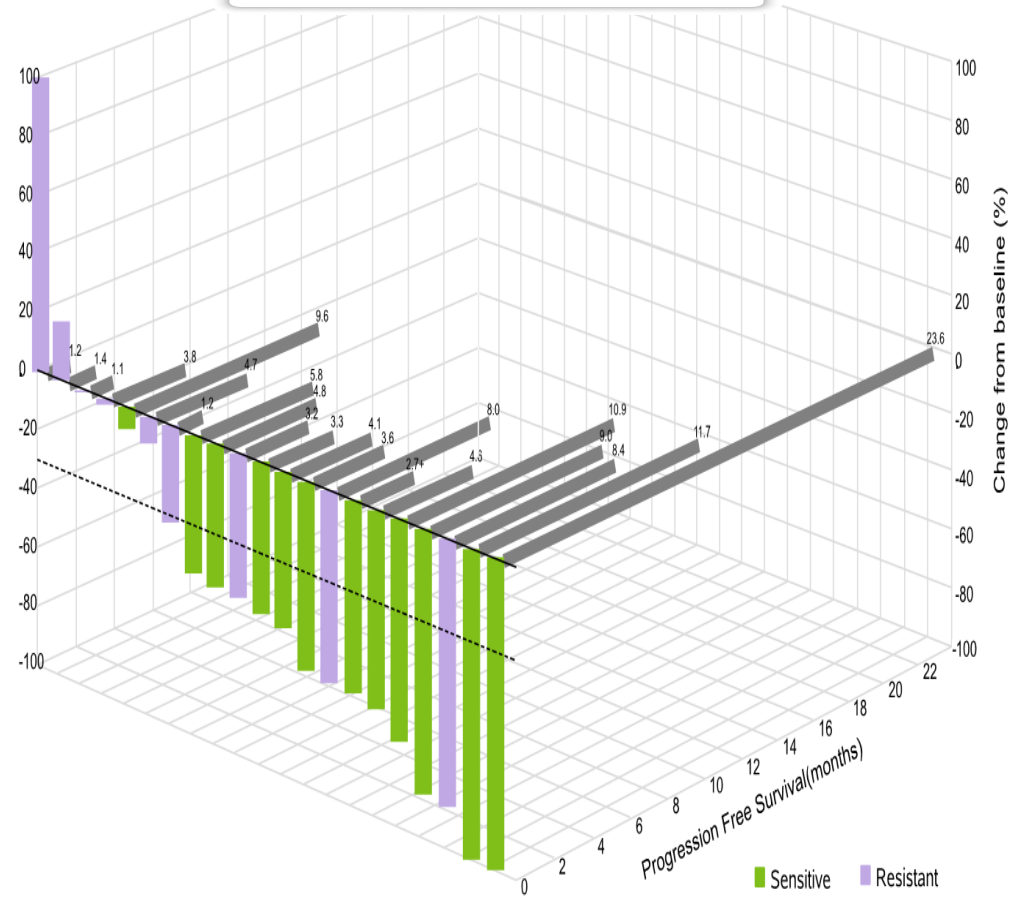
1. Cohort A as ASCO 2015, Cohort B as ESMO 2017 and mono as ASCO 2018.

ZEPSYRE®: PHASE I/II 2nd LINE SMALL CELL LUNG CANCER

Cohorts A & B, maximal tumor reduction according to CTFI and PFS (n=21, 27)

PFS: 4.7m
Median DOR:4.5mo

PFS: 5.3m
Median DOR:5.2mo



WHAT DOES OVARIAN PHASE III TELL US RE SCLC?

OVARIAN:

- Drug is active
- Drug is tolerated
- Phase III BSA DOSE ~75% OF Phase II Fixed Dose
- Rescue G-CSF
- Weekly scanning
- Lab abnormalities grade 3-4 stat sig better for anemia, neutropenia, thrombocytopenia vs. control

SCLC:

- Monotherapy also shows activity, could offer alternative, especially for older/frailer or with cardio co-morbidities
- Phase III BSA DOSE ~90% OF Phase II Fixed Dose
- Prophylaxis G-CSF
- Bi-weekly scanning
- Data showing neutropenia inc. FN and thrombocytopenia are mainly early cycle, transient, and successfully managed with dose modifications/GCSF.

NON HEAD-TO-HEAD COMPARISONS

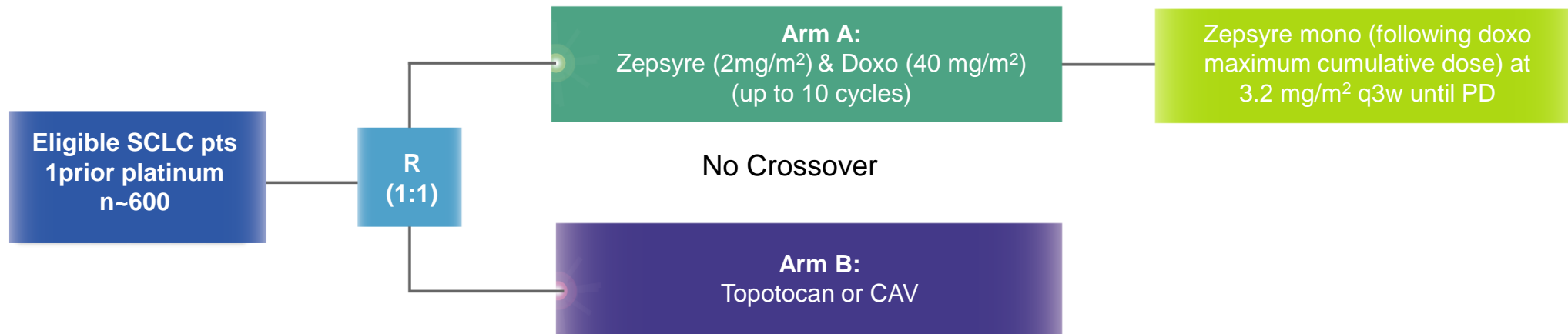
	Cohort A, n=21 FD combo doxo	Cohort B, n=27 BSA combo doxo	Monotherapy n=61	Topotecan label N=107	CAV (from Topo label), n=104
ORR	67%	37%	39%	24%	18%
DCR	81%	70%	74%		
PFS CTFI>30d	4.7m (CTFI>30d)	5.3m (CTFI>30d)	4.1m	3.1m	2.8m
OS		World Lung 2018	11.8m	5.8	5.7m
FN Gr 3-4	36%	12%	9%	28%	26%
Anemia Gr 3-4	46%	25%	6%	42%	20%
Thrombocytopenia G3-4	32%	22%	8%	29% (G4)	5% (G4)
Neutropenia G3-4	96%*	93%*	39%*	70% (G4)	72% (G4)

* G-CSF give as rescue in 71%, 43% and 18% respectively, Phase III using prophylaxis

ZEPSYRE®: PHASE III RELAPSED SMALL CELL LUNG CANCER

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

- **Primary endpoint: median OS HR \leq 0.75 with 90% power (10m vs. 7.5m)**
- **Key secondary endpoints:**
 - PFS
- **Registration Strategy**
 - Interim analysis passed @n=150 after 2 cycles (NOV'17).
 - Interim analysis passed @n=500 (May'18).
 - Trial supported by ongoing monotherapy trial (n=61 at ASCO 2018).
 - Trial will complete enrolment ~Q3 2018



Stratification by prior PD1/PDI-1 and brain mets.

ZEPSYRE®: ATLANTIS TRIAL

Change primary endpoint from PFS to OS

- PharmaMar recently received the OS analysis for cohort B of the combo Phase I/II (submitted to IASLC World conference on Lung Cancer) which prompted the change
 - Regulators prefer OS vs. surrogate endpoints, especially in an aggressive and fatal disease such as SCLC
 - Greater chance of approval and uptake
-
- The change adds a modest ~6-8m to the data read out timing

KEY IP AND BARRIERS TO ENTRY

■ Yondelis:

- EU: Sarcoma orphan expired 9/17, ovarian orphan 2019, use 2022, formulation 2025#
- US: Sarcoma orphan 2022, formulation 2025#
- Japan: Sarcoma orphan 2022, formulation 2025#. Ovarian 10 years from approval orphan
- Manufacturing US/EU/Japan 2031

■ Zepsyre

- All indications orphan US/EU/JP (7/10/10yrs)
- Composition 2024 (US)*, 2022 (EU)*
- SCLC combo doxorubicin 2031

■ All indications: Chemistry/synthesis/manufacturing know how

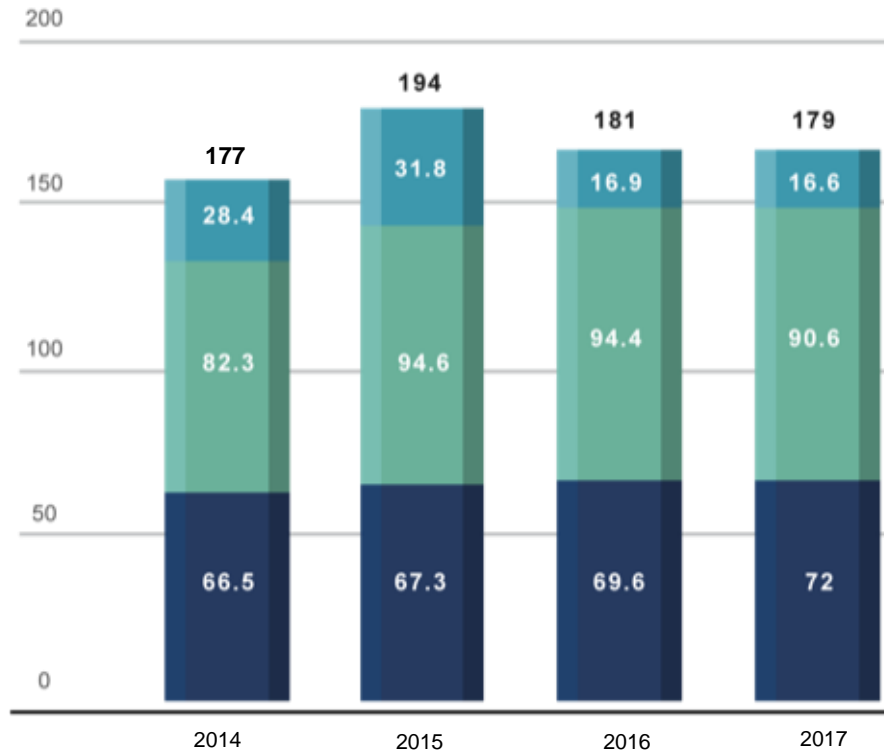
* Subject to potential patent term extension

patent pending

GROUP REVENUES AND R&D EXPENSES

Revenues

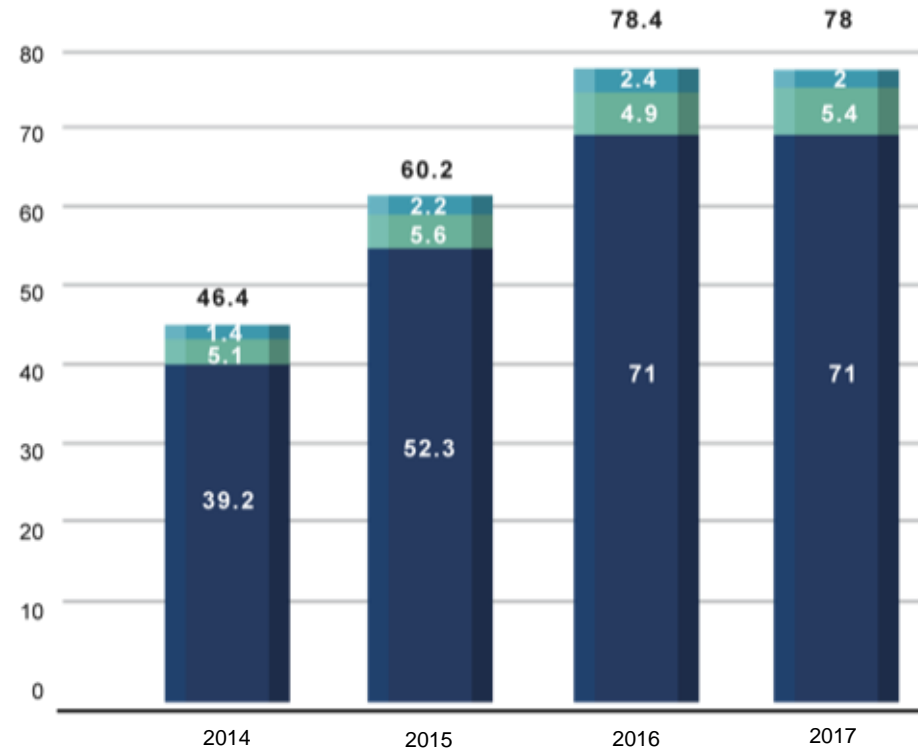
€ millions



■ ROYALTIES & MILESTONES BIOPHARMA
■ SALES BIOPHARMA
■ SALES CONSUMER CHEM.

R&D

€ millions

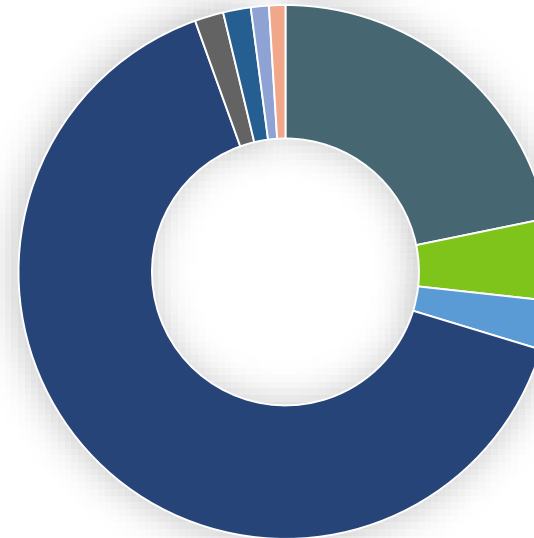


■ DIAGNOSTIC
■ RNAI
■ ONCOLOGY

KEY FACTS AND CURRENT SHAREHOLDERS

KEY FACTS

- Ticker: PHM SM
- Market Cap*: C. € 330 million
- 2017 Total Income: € 179 million
- 2017 EBITDA: € -7.4 million



- FERNÁNDEZ FAMILY 22%
- ROSP CORUNA PARTICIP. 5%
- BOARD MEMBERS/EMPLOYEES 3%
- FREE FLOAT 70%
- NORGES BANK 1.76%
- VANGUARD 1.69%
- DIMENSIONAL FUNDS 1.1%
- BLACKROCK 1%

Source: Bloomberg March 2nd 2018

KEY EVENTS

Transformative times for Pharma Mar; catalyst 2018

- ✓ • SCLC futility analysis
- ✓ • Zephyre® Phase III platinum-resistant ovarian cancer 1H '18; *primary endpoint not met*
- ASCO Zephyre® : Monotherapy SCLC, TiP ATLANTIS, Ewing's sarcoma
- Zephyre® SCLC ATLANTIS Phase III complete enrolment mid' 18
- Zephyre® PI/II cohort B OS data submitted to World Lung (September)
- Zephyre® CORAIL ovarian submission to ESMO (October)
- Zephyre® CORAIL OS data (Q4)
- Update(s) on Zephyre SCLC monotherapy trial, ESMO and others
- Protocol finalization and initiation of combos with Keytruda and Tecentriq
- Zephyre® ATLANTIS data (2H 19)



For more information: www.pharmamar.com

CONTEXTUAL COMPARATIVE DATA, READING ACROSS TRIALS.

STANDARD OF CARE FOR RELAPSED SMALL CELL LUNG CANCER

Competitive Landscape after first line treatment: Platinum/Etoposide

2 nd line	3 rd line	N	PFS (ORR%)	Notes
Zephyre/Doxo		48	5.0 (50%)	ASCO 2015/ ESMO 2017
Paclitaxel		Literature	(29)	Nature Reviews Glisson,2011 ¹
Topo		Literature	3.0 (24)	Glisson,2011 ¹
CAV		Literature	2.8 (19)	Glisson,2011 ¹
Nivo	Nivo	98	1.4 (11)	ASCO 2016-7 ESMO 2017
Nivo/Ipi	Nivo/Ipi	61	2.6 (23)	ASCO 2016-7 ESMO 2017
Pembro	Pembro	24	1.9 (33)	ESMO 2017
Pembro	Pembro	45	1.4 (12)	ESMO 2017
	Rova-T	177	(16)	3 rd line; "DLL 3 hgh" ²
Rova-T		48	4.3 (38)	2 nd line; DLL3 "high" ²
Sacituzumab	Saci	50	3.7 (14)	"Heavily pre-treated"

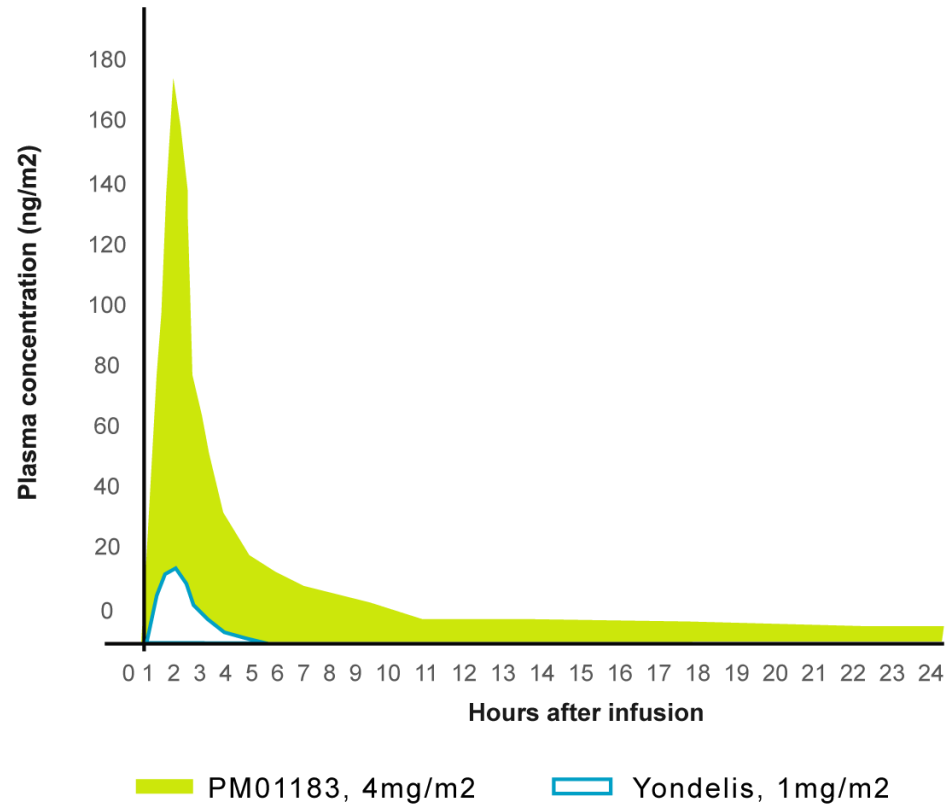
1. Source: Nature Reviews 2011;8:611-19. William N, Glisson, Lancet Oncology 6/4/16; Merck PR 12/6/16; Lancet Oncology 12/5/16
2. Source: AbbVie

SCLC: A history of failure

MoA	Drug	Study	Setting	N	Outcome
PARP	Olaparib	PII RDB vs. pbo	2L	220	Inferior to pbo
PARP	Veliparib	PI/II +/- Cis/Etop	Extensive	128	PFS 6.1 vs. 5.5 OS 10.3m vs. 8.9m
Aurora	Alisertib	PII solids	Refractory	48	ORR 21%
Aurora	Alisertib	PII +/- paclitax	2L	178	PFS 87d vs. 50d OS 186d vs. 165d
RAD51	Amivantinib	PII + carbo/etop	R/R	23	CBR 12%
Wee1	AZD1775	Phase I +chemo	Refractory solids	202	ORR 10%
NOTCH	Tarextumab	PII+etop/plat	Naïve extensive	145	“No difference”
DLL3	Rova-T	Open label PII	3L	349	16% ORR in “DLL3 high”
MoA	Drug	Study	Setting	N	Outcome
PARP	Olaparib	PII RDB vs. pbo	2L	220	Inferior to pbo
PARP	Veliparib	PI/II +/- Cis/Etop	Extensive	128	PFS 6.1 vs. 5.5 OS 10.3m vs. 8.9m

ZEPSYRE® vs YONDELIS®

Different pharmacological profile



Better safety profile

Percentage of patients

