

Comisión Nacional del Mercado de Valores
Att. Director del Área de Mercados
C/Edison núm. 4
28006 Madrid

Colmenar Viejo (Madrid), a 10 de enero de 2017

De conformidad con lo previsto en el artículo 228 del Texto Refundido de la Ley de Mercado de Valores, por la presente se procede a comunicar el siguiente **HECHO RELEVANTE**:

“Se adjunta presentación corporativa en inglés que estará disponible a partir de la tarde de hoy también en la página web de la Compañía www.pharmamar.com.”



CORPORATE PRESENTATION

January 2017

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

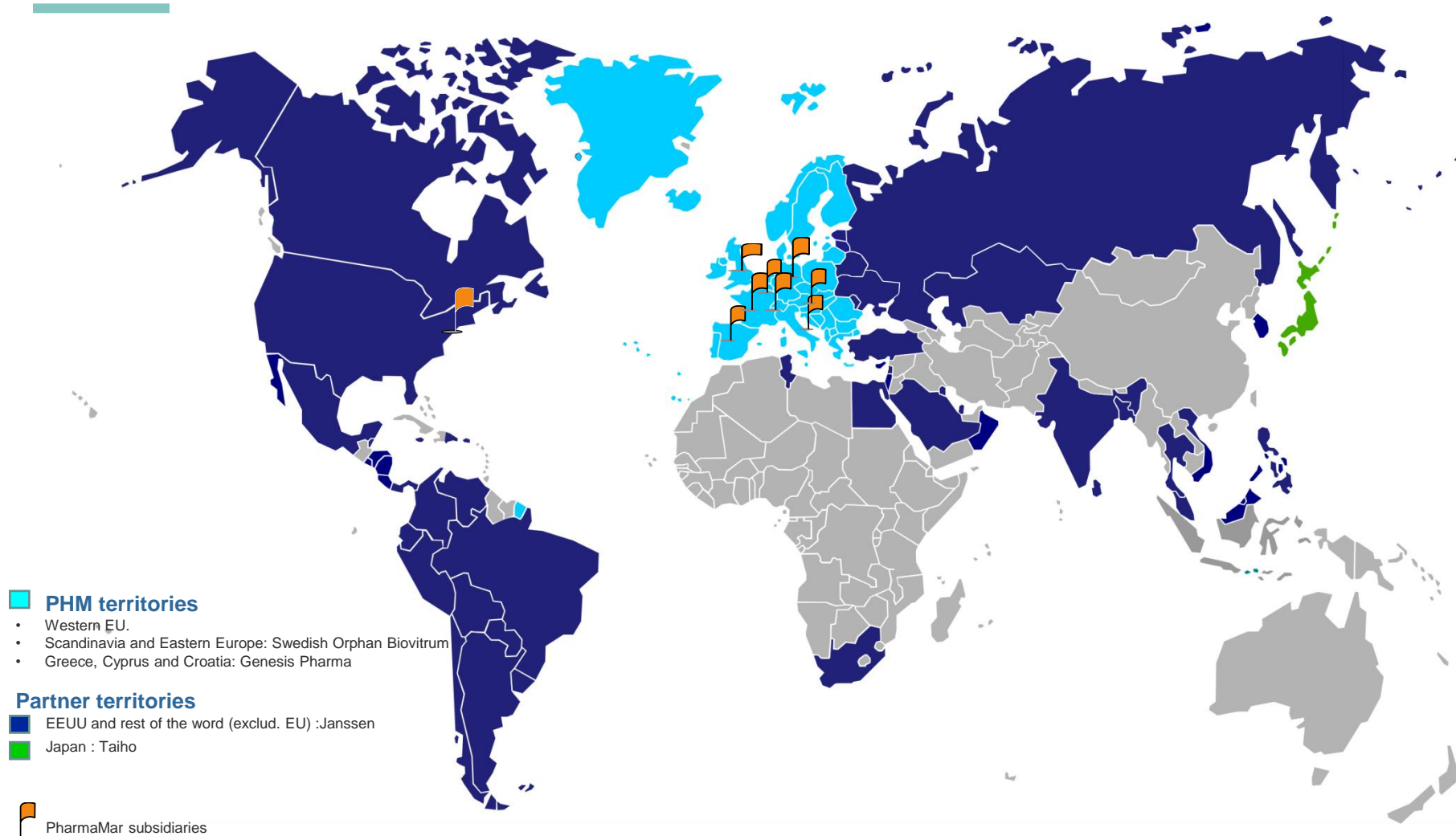
A leader in the development & commercialization of marine-derived oncology drugs



- **Multinational biotechnology company developing marine-derived and novel MoA oncology drugs**
 - Fully integrated biotechnology company – from discovery to commercialization
 - Highly productive R&D organization (1 approved drug and 2 in late stage development)
- **Established oncology sales force in Europe:**
 - Strong partners in the US (Janssen), Europe (Chugai), and Japan (Taiho, Chugai)
- **Late stage development pipeline driving future value**
 - Lurbinectedin (PM1183): Next generation Yondelis®
 - Aplidin®: Positive pivotal data in Multiple Myeloma with an EMA NDA filed in Sept 2016
- **Track record of operational excellence with a strong financial position**
 - Company with growing revenues and robust cash flow
 - Headquartered and traded in Madrid
 - C. €620m market cap (as of 12/21/16)
 - €63.5m in cash and cash equivalents (9 months 2016)*
 - €16m operating cash burn + debt service (9 months 2016)

* Proforma for Chugai Lurbinectedin partnership, €30mn upfront, announced Dec 22nd 2016

Yondelis® - Commercial expansion worldwide



Unique fully integrated platform

Fully integrated capabilities

Marine expeditions →

Sample library →

Screening & Synthesis →

Clinical Trials →

Commercialization



- Marine derived products
- Global expeditions

- New drug candidates
- Molecule optimization
- c.200,000 samples

- Patent protection
- Synthesis
- FDA approved production facility

- Pre-clinical trials
- Clinical trials
- Phase IV supportive trials

- Oncology-focused sales force in Europe (~ 65 people)
- Geographic licensing & partnering with experienced companies.

Marine-derived compounds with novel mechanisms of action

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

The Plan for Growth

Potential to commercialize new oncology products in more indications

PharmaMar today

- 1 marketed product
- 2 indications

- **Yondelis[®]**
 - Soft Tissue Sarcoma
 - R/R Ovarian Cancer

PharmaMar tomorrow

- 2 marketed products
- 3 indications

- **Aplidin[®]**
 - R/R multiple myeloma

PharmaMar in the near future

- 3 marketed products
- ≥ 5 indications

- **Lurbinectedin (PM1183)**
 - Small Cell Lung Cancer
 - Platinum resistant ovarian cancer
 - BRCA-2 Breast cancer

A Balanced portfolio of product candidates

Overview

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						
Aplidin®								
R/R multiple myeloma 4 th line;	Aplidin® + Dexameth.	EU/Others					Chugai/ Regionals	2H'17
R/R T-cell lymphoma (Pivotal)	Single agent	EU/Others						Ongoing
R/R multiple myeloma	Aplidin® + Bortezom+ Dexameth.	EU/Others						Ongoing
Lurbinectedin (PM1183)						Chugai (Japan)		
Plat. Resistant ovarian cancer	Single agent	Global						2H'17
SCLC 2 nd line	Lurbinec + Doxo	Global						2019
BRCA 1/2 Breast cancer	Single agent	Global						Initiating
Basket trial	Single agent	Global						Ongoing
Solid tumors	Combinations	Global						Ongoing
PM184								
Advanced Breast Cancer 3 rd /4 th line	Single agent	Global						Ongoing
Solid tumors	Single agent and combinations	Global						Ongoing

Pipeline – Lurbinectedin (PM1183)

Targeted transcription Inhibitor as a cancer therapeutic



- Cancer cells aberrantly deregulate specific gene expression programs with critical functions in cell differentiation, proliferation and survival (Hoadley et al 2014)
- These altered gene programs in cancer cells have a striking dependence on continuous active transcription (transcription addiction)
- Lurbinectedin only affects activated transcription. Does not affect basal transcription*.
- Examples of tumors with transcription addiction:
 - Small Cell Lung Cancer (SCLC) cells are addicted to lineage-specific and proto-oncogenic transcription factors that support their growth (Christensen et al 2015)
 - Soft Tissue Sarcomas (STS) bearing translocations.
 - Effect on tumor microenvironment: Lurbinectedin inhibits the activated transcription of certain cytokines as IL-6, IL-8, CCL2 and PTX3

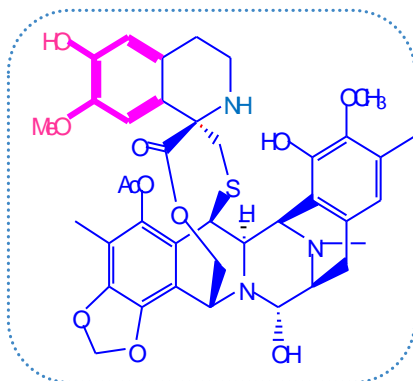
* **Source: Molecular Cancer Therapeutics 2016 Oct;15(10):2399-2412.** Lurbinectedin Specifically Triggers the Degradation of Phosphorylated RNA Polymerase II and the Formation of DNA Breaks in Cancer Cells.

Lurbinectedin (PM1183):

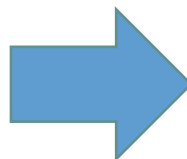
Key oncology compound – accelerating growth

Lurbinectedin, a second generation Yondelis®, with improved PK and other attributes

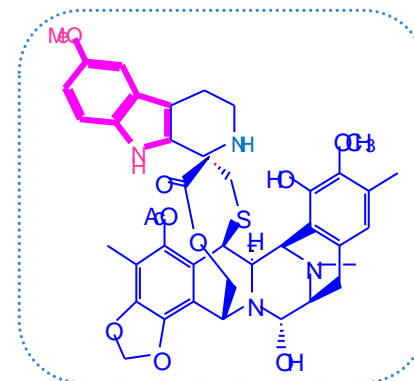
YONDELIS®



IMPROVED PK PROFILE



Lurbinectedin



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

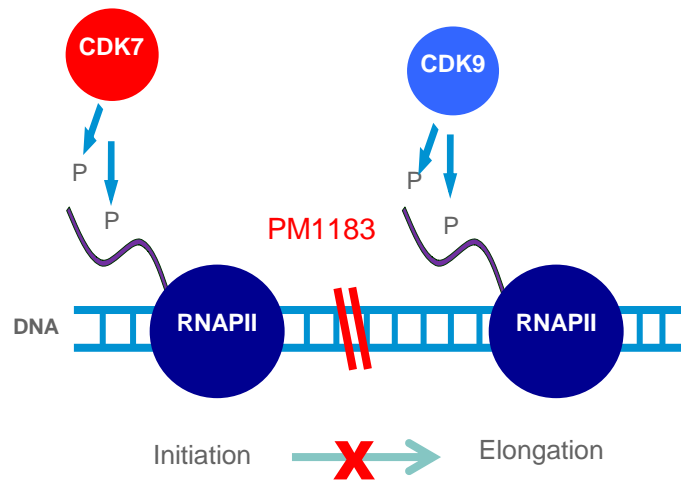
- 4x tolerated dose.
- 15x exposure at RD.
- Less toxicity
- More oncology “office practice” friendly.

Pipeline – Lurbinectedin (PM1183)

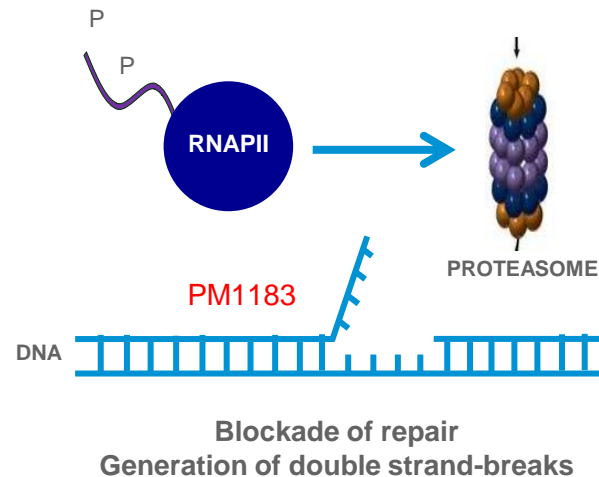
Key oncology compound – accelerating growth

- Inhibition of trans-activated transcription but not of basal transcription.
- Induction of the degradation of RNA Pol II but not of RNA Pol I or III.

RNA POL II INHIBITION



RNA POL II DEGRADATION



Source: Molecular Cancer Therapeutics 2016 Oct;15(10):2399-2412. Lurbinectedin Specifically Triggers the Degradation of Phosphorylated RNA Polymerase II and the Formation of DNA Breaks in Cancer Cells.

Pipeline – Lurbinectedin (PM1183)

Development strategy



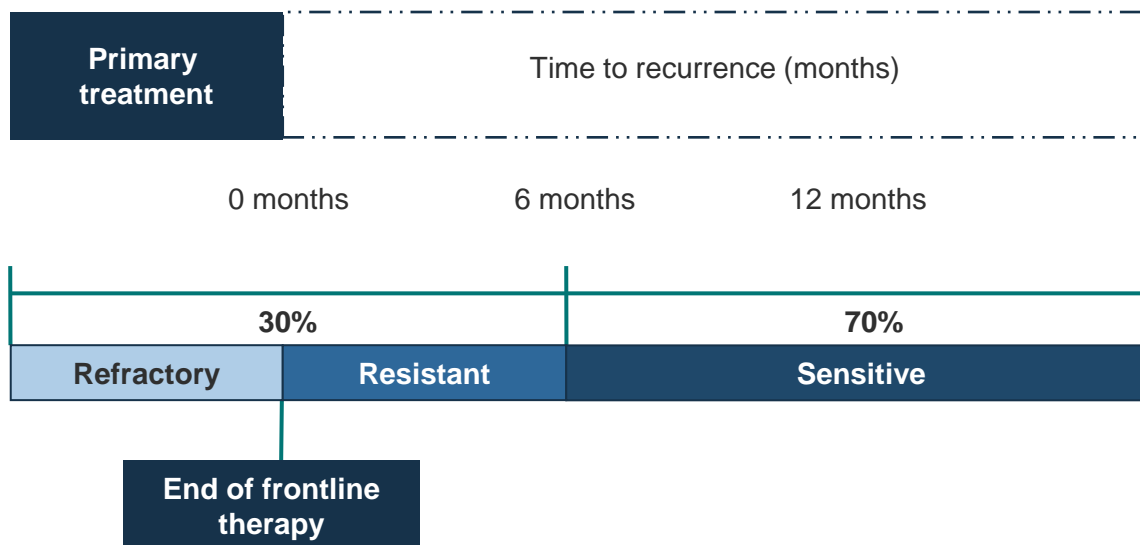
CLINICAL PROGRAM/ INDICATION		PHASE I	PHASE II	PHASE III	MARKET	PARTNERS
Lurbinectedin PM1183[®]						Chugai (Japan)
Plat. Resistant ovarian cancer 2 nd /3 rd line	Single agent	▶				
SCLC 2 nd line	Combo Doxorubicin	▶				
BRCA2 Breast cancer* 2 nd /3 rd line	Single agent	▶				
Basket Trial	Single agent	▶				
Combination Studies	Solid Tumors	▶				

* Subsequent to FDA meeting December 2016; subject to finalization in 2017

Lurbinectedin – Platinum Resistant Ovarian Cancer

Market overview: Orphan Indication US/EU

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



Source: Estimated ovarian cancer incidence and mortality, all ages. GLOBOCAN 2012 and PharmaMar market research studies

Standard of care for Ovarian Cancer (per labels)

Lurbinectedin: Competitive Landscape

- PARP inhibitors work by blocking the action of poly (ADP-ribose) polymerase, a DNA repair enzyme; they are used after DNA damaging drugs which are *highlighted below*

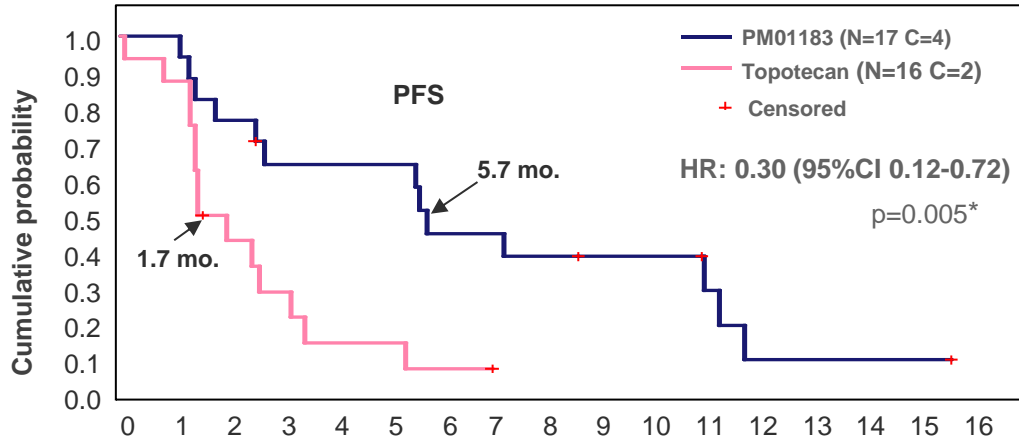
Front Line	Second line	3L and beyond
<ul style="list-style-type: none"> <i>Platinum/Taxane</i> 	<p><u>Sensitive</u></p> <ul style="list-style-type: none"> Same as 1L Yondelis/PLD (EU) Avastin Olaparib maintenance (EU) <p><u>Resistant</u></p> <ul style="list-style-type: none"> <i>PLD</i> <i>Topotecan</i> Lurbinectedin* <p><u>Refractory</u></p> <ul style="list-style-type: none"> Same as resistant 	<ul style="list-style-type: none"> Olaparib, (US) germline BRCAm, after 3 or more lines of chemo Rucaparib (US) BRCAm after 2 or more lines of chemo

* Investigational drug; not approved

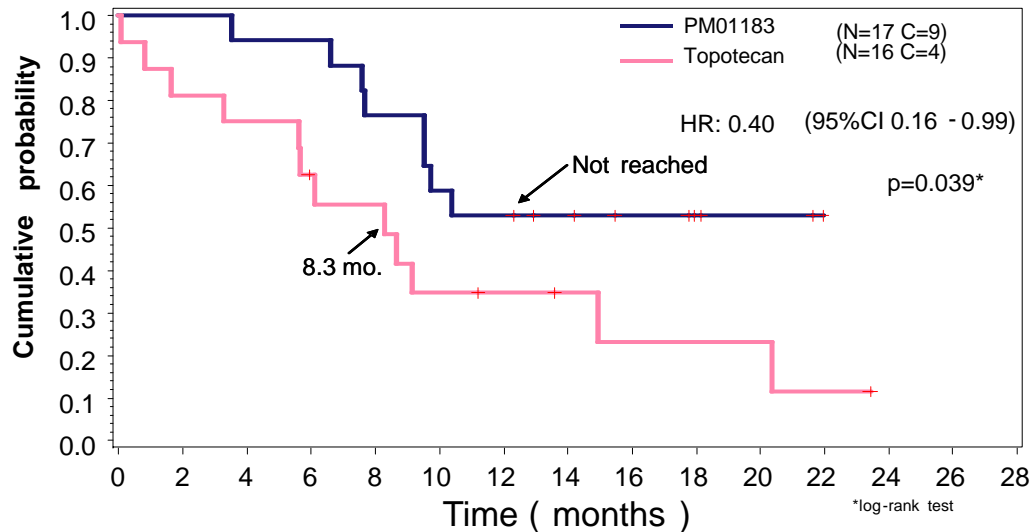
Lurbinectedin:Phase II Platinum Resistant Ovarian Cancer



Trial results



Superior PFS

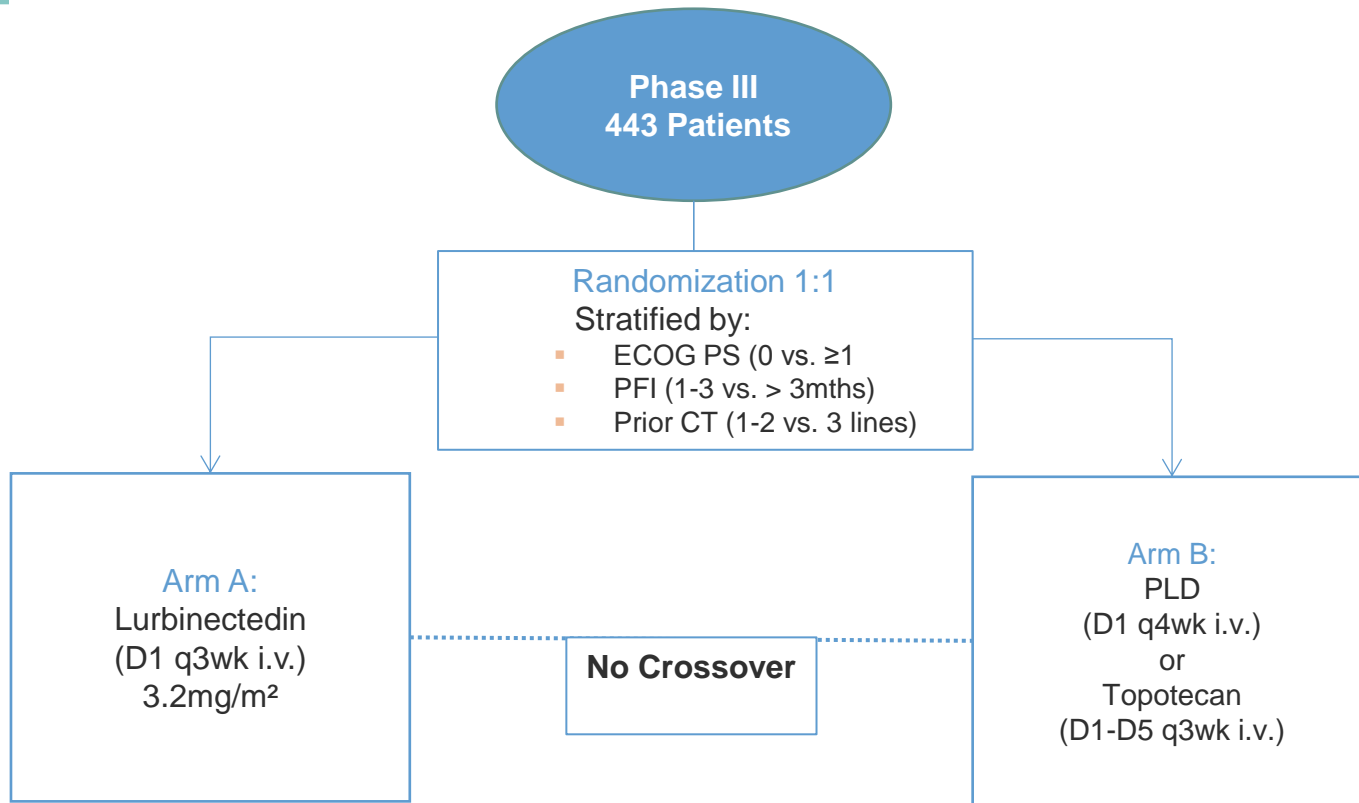


Superior OS

Source: ASCO 2014 Poveda et al.

Lurbinectedin:Phase III 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 patients
Interim analysis: @ 210 patients, summer '16

Patient recruitment completed: October 2016; Data expected 2H17

Lurbinectedin: Small Cell Lung Cancer (SCLC)

Market overview. Orphan Indication US/EU



In the US per annum:

- ~ 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:

- ~ 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.
- SOC: Topotecan, CAV (off label)
- Last FDA approval, Topotecan, October 2007
- Last EMA approval, Topotecan, August 2009

Standard of care for Small Cell Lung Cancer

Lurbinectedin: Competitive Landscape

- First line treatment. Platinum/Etoposide

2 nd line	3 rd line	N	ORR (%)	Notes
Lurbinectedin/Doxo		21	67	ASCO 2015
Paclitaxel		Literature	29	Nature Reviews Glisson, 2011
Topo		Literature	24	Glisson, 2011
CAV		Literature	19	Glisson, 2011
Nivo	Nivo	98	11	2 nd /3 rd line
Nivo/Ipi	Nivo/Ipi	61	25	2 nd /3 rd line
Pembro	Pembro	24	33	'heavily pre-treated'
Rova-T	Rova-T	61	18	2 nd and 3 rd line
Rova-T	Rova-T	48	38	DLL3 'high'

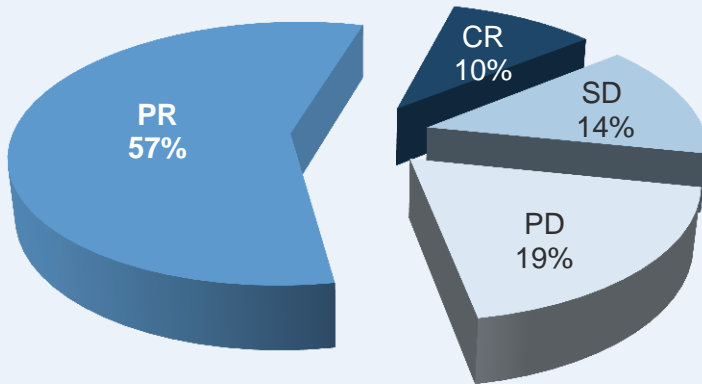
For information purposes, not head to head data

Lurbinectedin: Phase I/II Small Cell Lung Cancer

Trial results – Active treatment as second-line therapy with Doxorubicin

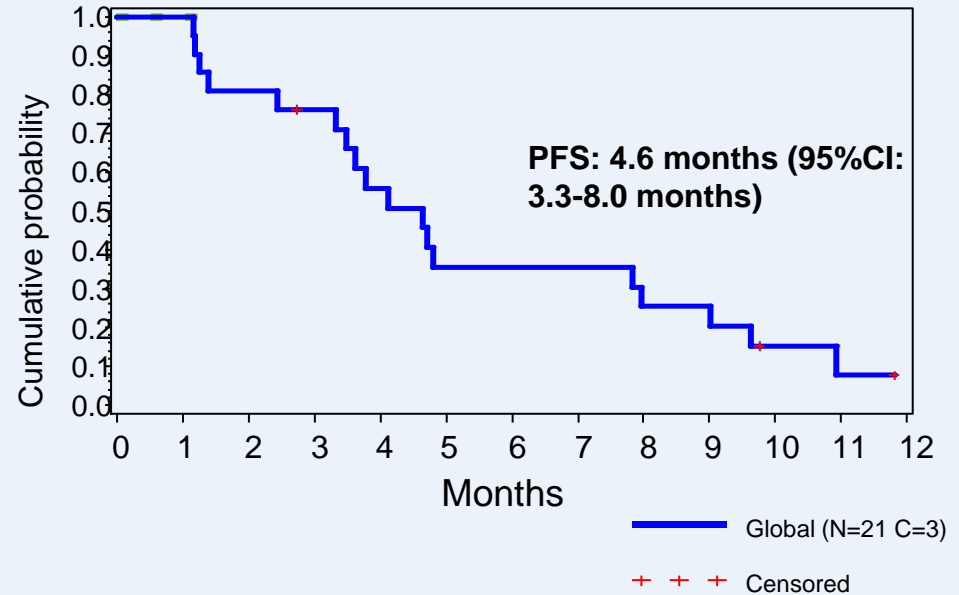
Best RECIST v.1.1 overall response during treatment (n=21)

ORR: 67 %
(95%CI: 43-85)



M. Forster et al. ASCO 2015

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



Other examples ORR in SCLC:

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

PFS reported in registration Topotecan trial study :

- Topotecan : 3 months
- CAV : 2.8 months

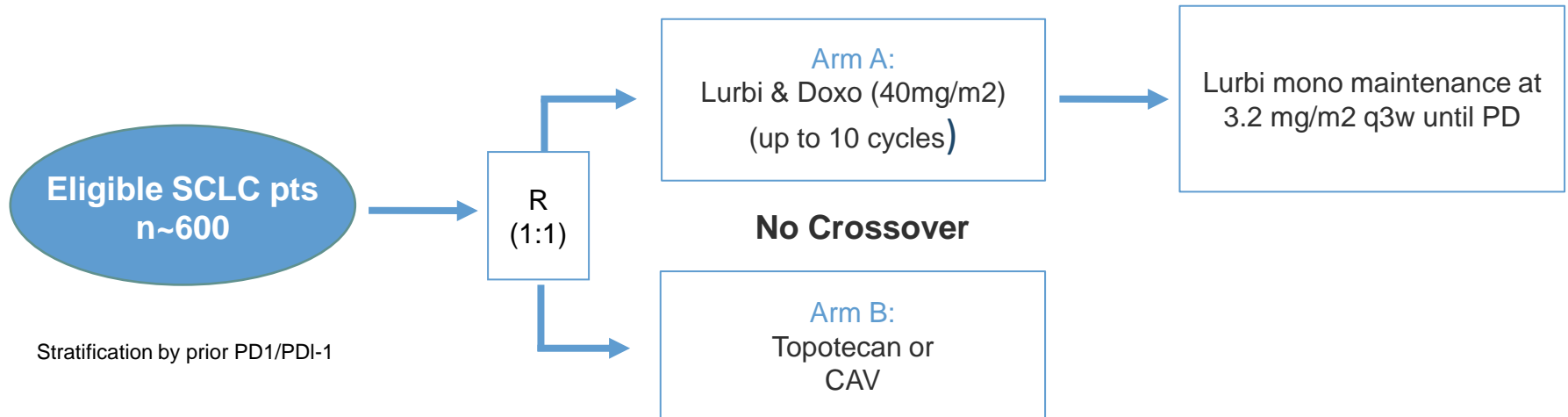
Source: Nature Reviews 2011;8:611-19. William N, Glisson

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

Lurbinectedin: Phase III 2nd line Small Cell Lung Cancer

ATLANTIS Trial Design SCLC (Trial initiated August 2016)

- Primary endpoint: median PFS
 - HR ≤ 0.7 in PFS with 90% power;
 - Futility analysis planned at n=150 events approximately
- Key secondary endpoints:
 - OS
- Registration Strategy
 - Trial supported by ongoing n=50 monotherapy trial
 - Factorial synergy supported by CAV control arm (includes Anthracycline ~ Doxo)



Lurbinectedin: Phase IIb in BRCA 1/2- Breast Cancer

Clinical efficacy: Progression Free Survival (PFS) and Overall Survival OS

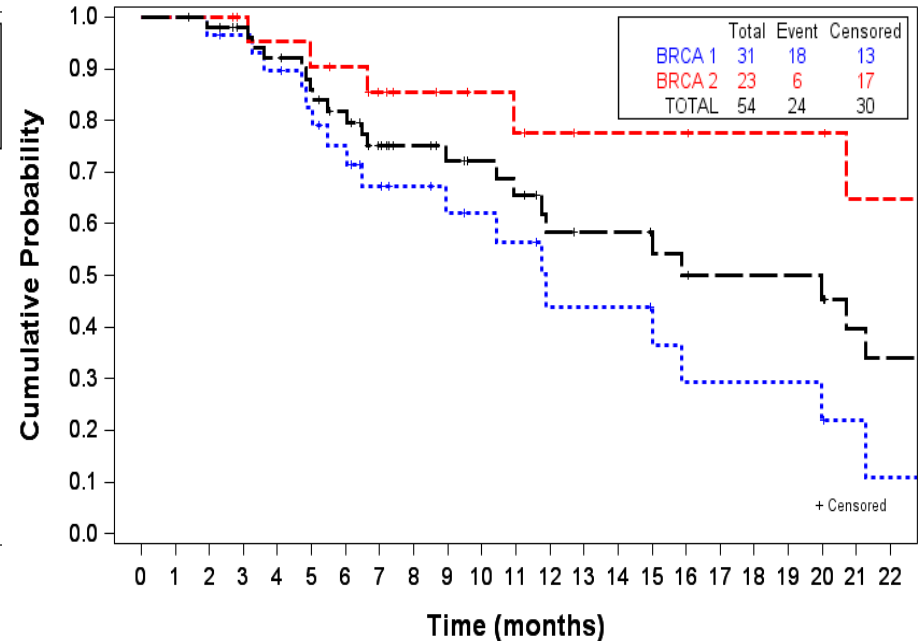
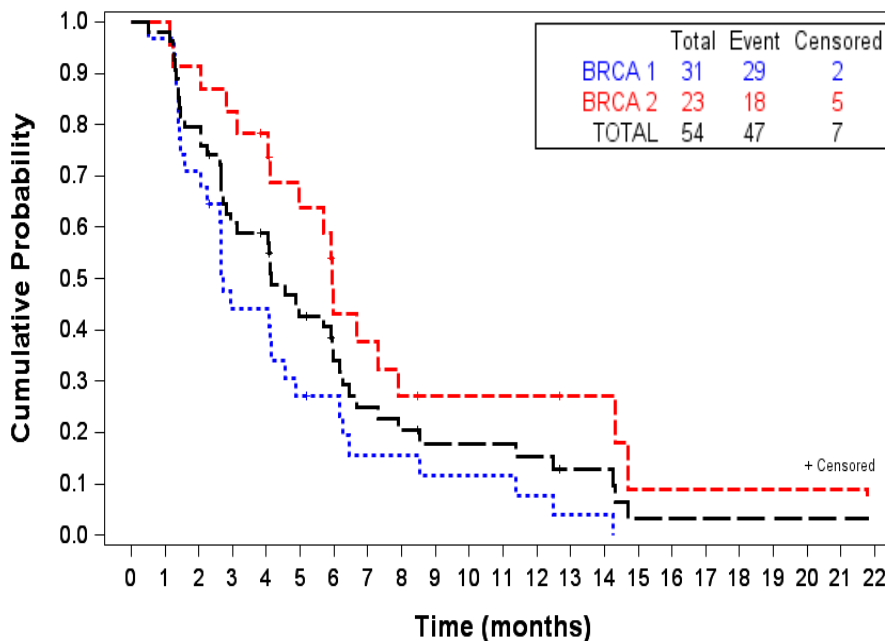


Median PFS BRCA 1/2:
4.1 months 95% CI (2.8-5.9)

BRCA 1: 2.7 95% CI (2.1-4.6)
BRCA 2: 5.9 95% CI (4.1-7.9)

Median OS BRCA 1/2:
20.0 months 95% CI (10.9-31.8)

BRCA 1: 11.8 95% CI (6.5-20.0)
BRCA 2: 31.8 95% CI (20.7-38.9)



Source: ESMO 2016

Lurbinectedin – 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)
ORR (95% CI)	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)
Duration of Response (95% CI)	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)
Disease control rate	25 (93%)	19 (70%)	23 (74%)	22 (96%)	45 (83%)	26 (79%)	19 (90%)	27 (87%)	18 (78%)
Clinical benefit (CR+PR+SD ≥ 3 mo)	19 (70%)	14 (52%)	14 (45%)	19 (83%)	33 (61%)	29 (88%)	14 (67%)	21 (68%)	12 (52%)

* Includes
2 pts also
HER-2 +

Source: ESMO 2016

Lurbinectedin: Registrational trial BRCA 2- Breast Cancer

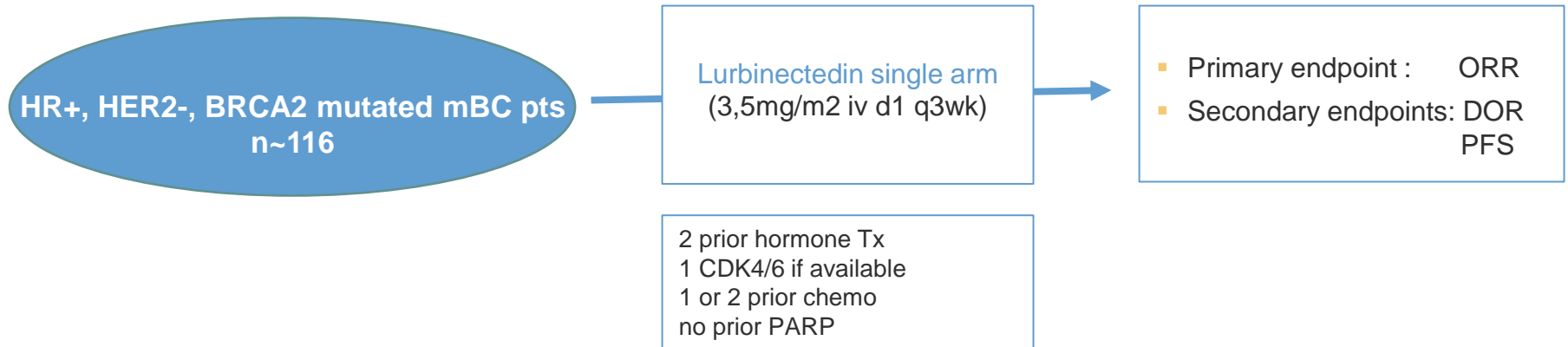
Subject to finalization and changes

In the US per annum:

- ~ 10,300 new cases of BRCA 2- Breast cancer

In the EU-28 per annum:

- ~ 14,500 new cases of BRCA 2- Breast cancer



Expect to open first center 2H 2017

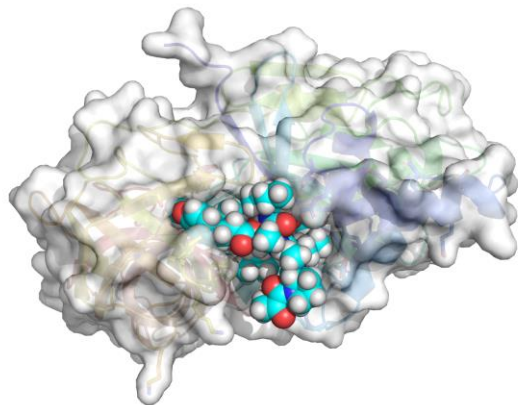
Pipeline - Aplidin®

First in class drug with a novel mechanism of action

Aplidium albicans

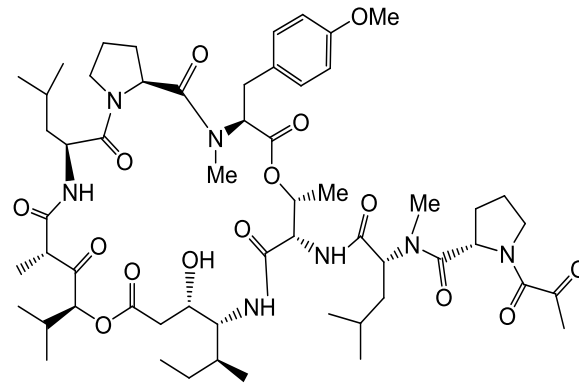


eEF1A2



Aplidin®

PLITIDEPSIN



MECHANISM OF ACTION

- Targets eEF1A2
- Proto-oncogene over-expressed in different tumor types e.g. multiple myeloma

Non-canonical functions of eEF1A2:

- Regulation of oxidative stress (e.g. peroxiredoxin-1, etc.)
- Regulation of apoptosis (e.g. esfingosina-1 quinasa)

Source: **Scientific Reports. 2016 Oct 7;6:35100.** Translation Elongation Factor eEF1A2 is a Novel Anticancer Target for the Marine Natural Product Plitidepsin.

Pipeline – Aplidin®

First in class drug with a novel mechanism of action



CLINICAL PROGRAM/ INDICATION		PHASE I	PHASE II	PHASE III	REGISTRATION APPLICATION	MARKET	PARTNERS	
Aplidin®								
R/R multiple myeloma 4 th line; EU/others	Aplidin® + Dexameth							CHUGAI
R/R T-cell lymphoma	Single agent							
R/R multiple myeloma	Aplidin® + Bortezomib+ Dexameth							

Partnered with Roche's Chugai in 8 European countries



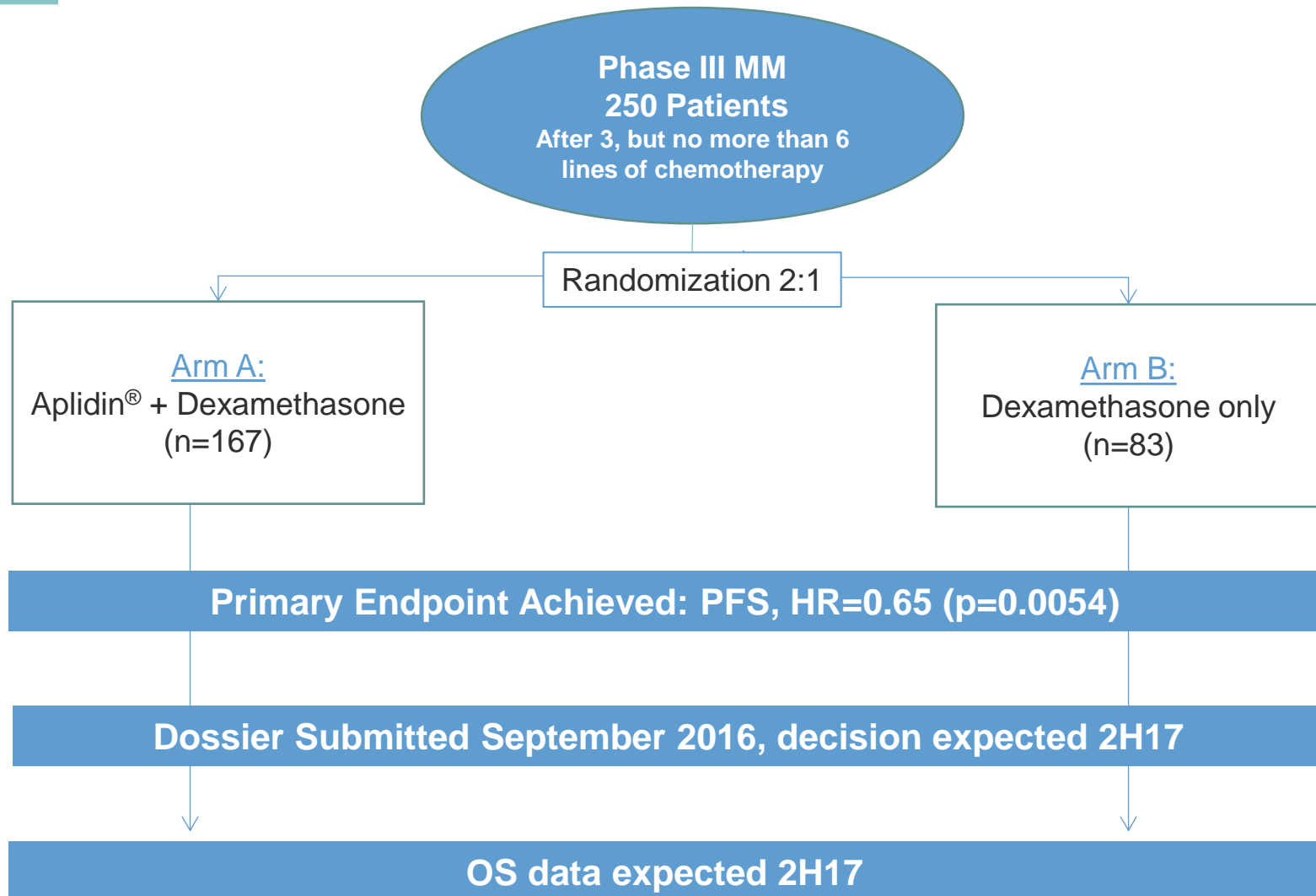
Other partners for Aplidin®



Commercial opportunity for Europe in M.M. estimated at c.€300mm

Aplidin[®] - ADMYRE Trial

Phase III in Relapsed / Refractory Multiple Myeloma



Key Events

Transformative times for Pharma Mar; catalyst rich 2017

-
- ✓ ■ Yondelis® approved in Japan for STS (9/2015); approved in the US for STS (10/2015)
 - ✓ ■ Lurbinectedin Phase III pivotal trial initiated for SCLC (Aug. 2016)
 - ✓ ■ Lurbinectedin interim activity analysis Phase III in platinum-resistant ovarian cancer (Aug`16)
 - ✓ ■ Aplidin® positive data for Phase III for multiple myeloma and dossier submitted (Sept. 2016)
 - ✓ ■ Lurbinectedin data for Phase II metastatic breast cancer (Sept. 2016)
 - ✓ ■ Lurbinectedin Phase III in platinum-resistant ovarian cancer: recruitment completed (Oct`16)
 - ✓ ■ Lurbinectedin license agreement in Japan (Chugai, Dec`16)
 - Update Breast cancer trial, following FDA meeting
 - Yondelis INNOVATYON (IST) interim analysis relapsed OC (2q`17)
 - Aplidin® CHMP recommendation in multiple myeloma (2H 2017)
 - Lurbinectedin Phase III data in platinum-resistant ovarian cancer (2H 2017)
 - Aplidin® OS data Phase III for multiple myeloma expected 2H17
 - Lurbinectedin potential start of Phase III BRCA
 - Lurbinectedin expected publication of Phase II data as a single agent in SCLC



For more information: www.pharmamar.com