Disclaimer

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**Investment Highlights**

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

- **Global biotech developing marine-derived and novel MoA oncology drugs**
  - Fully integrated biotechnology company – from discovery to commercialization

- **Established oncology sales force in Europe**
  - Strong partners in the US (Janssen) and Japan (Taiho, Chugai)

- **Late stage development pipeline driving future value; 2 Phase IIIls, soon 4**
  - Zepsyre® (lurbinectedin (PM1183))

- **Operating track record with a strong financial position**
  - Growing revenues and robust cash flow; total revenues 2016 of €181mm; Yondelis® sales & royalties ~€100mm
  - C. € 530 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

**Partner territories**
- EEUU and rest of the world (exclude. EU) : Janssen
- Japan : Taiho

PharmaMar subsidiaries
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)
## A Balanced portfolio of product candidates

<table>
<thead>
<tr>
<th>Clinical Program / Indication</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Market</th>
<th>Partner</th>
<th>Data timing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Yondelis®</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soft Tissue Sarcoma 2nd/3rd line</td>
<td>Single agent</td>
<td>EU, US, Japan</td>
<td>J&amp;J (US) Taiho (Japan)</td>
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<td></td>
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<tr>
<td>Ovarian Cancer 2nd/3rd line</td>
<td>Yondelis®+Doxil</td>
<td>EU/Others</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Aplidin®</strong></td>
<td></td>
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</tr>
<tr>
<td>R/R multiple myeloma 4th line;</td>
<td>Aplidin® + Dexameth.</td>
<td>EU/Others</td>
<td>Chugai/Regionals</td>
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<tr>
<td>R/R Angioimmunoblastic T-cell lymphoma</td>
<td>Single agent (Pivotal)</td>
<td>EU/Others</td>
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<tr>
<td>R/R multiple myeloma</td>
<td>Aplidin® + Bortezom + Dexameth.</td>
<td>EU/Others</td>
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<td>R/R multiple myeloma</td>
<td>Aplidin® + Pomalid. + Bortezom+ Dexameth.</td>
<td>EU/Others</td>
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<tr>
<td><strong>Zepsyre®</strong> Lurbinectedin PM1183</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Plat. Resistant ovarian cancer</td>
<td>Single agent</td>
<td>Global</td>
<td>Chugai (Japan)</td>
<td>January 18</td>
<td></td>
<td></td>
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<tr>
<td>SCLC Relapsed</td>
<td>Zepsyre+ Doxo</td>
<td>Global</td>
<td>Chugai (Japan)</td>
<td>2019</td>
<td></td>
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<tr>
<td>BRCA 1/2 Breast cancer</td>
<td>Single agent</td>
<td>Global</td>
<td>Chugai (Japan)</td>
<td>Finalizing protocol</td>
<td></td>
<td></td>
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<tr>
<td>Endometrial Cancer 2nd line</td>
<td>Zepsyre + Doxo</td>
<td>Global</td>
<td>Chugai (Japan)</td>
<td>Finalizing protocol</td>
<td></td>
<td></td>
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<tr>
<td>Basket trial</td>
<td>Single agent</td>
<td>Global</td>
<td>Chugai (Japan)</td>
<td>Ongoing</td>
<td></td>
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<tr>
<td><strong>PM184</strong></td>
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<tr>
<td>Advanced Breast Cancer 3rd/4th line</td>
<td>Single agent</td>
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<tr>
<td>Solid tumors</td>
<td>Single agent and combinations</td>
<td>Global</td>
<td></td>
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<td><strong>PM14</strong></td>
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<td></td>
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<tr>
<td>Solid tumors</td>
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</tbody>
</table>
Pipeline – Zepsyre® (PM1183)
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.

Zepsyre® (PM1183):
Key oncology compound – accelerating growth

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

Yondelis®

IMPROVED PK PROFILE

Zepsyre®

- 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.
### Pipeline – Zepsyre® (PM1183)

**Development strategy**

<table>
<thead>
<tr>
<th>CLINICAL PROGRAM/INDICATION</th>
<th>PHASE I</th>
<th>PHASE II</th>
<th>PHASE III</th>
<th>MARKET</th>
<th>PARTNERS</th>
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<tr>
<td>Zepsyre</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Chugai (Japan)</td>
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<tr>
<td>Plat. Resistant ovarian cancer</td>
<td>Single agent</td>
<td></td>
<td></td>
<td></td>
<td>Data q1 ‘18</td>
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<tr>
<td>SCLC Relapsed</td>
<td>Combo Doxorubicin</td>
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<td>Data ~mid ‘19</td>
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<tr>
<td>BRCA2 Breast cancer*</td>
<td>Single agent</td>
<td></td>
<td></td>
<td></td>
<td>Starting Q4’17/Q1’18</td>
</tr>
<tr>
<td>2nd/3rd line</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endometrial**</td>
<td>Combo Doxorubicin</td>
<td></td>
<td></td>
<td></td>
<td>Starting 1H ‘18</td>
</tr>
<tr>
<td>2nd line</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Basket Trial (SCLC, Endometrial, Ewing...)</td>
<td>Single agent</td>
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<td></td>
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<td>Ongoing</td>
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<tr>
<td>Combination Studies</td>
<td>Solid Tumors</td>
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<td>Ongoing</td>
</tr>
</tbody>
</table>

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

* *Subject to finalization 1H’18
Zepsyre®: Platinum Resistant Ovarian Cancer

Market overview: Orphan Indication US/EU¹

- ~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

<table>
<thead>
<tr>
<th>Time to recurrence (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 months</td>
</tr>
<tr>
<td>6 months</td>
</tr>
<tr>
<td>12 months</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>End of frontline therapy</th>
<th>Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>30% Refractory</td>
<td></td>
</tr>
<tr>
<td>70% Resistant</td>
<td></td>
</tr>
<tr>
<td>30% Sensitive</td>
<td></td>
</tr>
</tbody>
</table>

Approved Drugs:

- Nothing
- *Hycamptin*³ 1996
- *Doxil*³ 1999
- *Avastin* (combo) 2014
- Olaparib
- Niraparib (US)
- *Platinum*³/Taxane
- *Yondelis*³/PLD³ (EU)

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1. Source: Estimated ovarian cancer incidence and mortality, all ages. GLOBOCAN 2012 and PharmaMar market research studies
2. Investigational Drug. Not approved in any jurisdiction
3. DNA Damaging agent
Zepsyre®: Phase II Platinum Resistant Ovarian Cancer

Trial results

PFS

HR: 0.30 (95% CI 0.12-0.72)

p = 0.005*

Superior PFS

OS

HR: 0.40 (95% CI 0.16-0.99)

p = 0.039* (log-rank test)

Superior OS

Source: ASCO 2014 Poveda et al.
Zepsyre®: Phase III Platinum Resistant Ovarian Cancer
CORAIL Trial Design

Phase III
443 Patients

Randomization 1:1
Stratified by:
- ECOG PS (0 vs. ≥1)
- PFI (1-3 vs. >3mths)
- Prior CT (1-2 vs. 3 lines)

Arm A:
Zepsyre
(D1 q3wk i.v.)
3.2mg/m²

Arm B:
PLD
(D1 q4wk i.v.)
or
Topotecan
(D1-D5 q3wk i.v.)

No Crossover

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 January 18
Zepsyre®: Small Cell Lung Cancer (SCLC)
Market overview. Orphan Indication US/EU

In the US per annum¹:
- ~ 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 annum¹:
- ~ 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 American Cancer Society, Decision Resources, Inc.
2 Triptych Health Partners held a Thoracic Oncology Strategic Advisory Board, June 2017
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)

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

CR 10%
SD 14%
PR 57%
PD 19%

M. Forster et al. ASCO 2015

Kaplan-Meier global PFS and according to CTFI (n=21)
PFS: 4.6 months (95%CI: 3.3-8.0 months)

Other examples ORR in SCLC:
- CAV 19%
- Topotecan 24%
- Paclitaxel 29%
- Gemcitabine 12%
- Vinorelbine 12%

PFS reported in registration Topotecan trial study:
- CAV : 2.8 months
- Topotecan : 3 months


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

<table>
<thead>
<tr>
<th>Response Evaluable patients</th>
<th>Lurbinectedin+DOX (q3wk)</th>
<th>Lurbinectedin +TAX (q3wk)</th>
<th>Lurbinectedin single-agent (q3wk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort A</td>
<td>Cohort B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L 3-5 mg FD D1 + DOX 50 mg/m² D1 (n=21)</td>
<td>L 2 mg/m² D1 + DOX 40 mg/m² D1 (n=27)</td>
<td>L 2.2 mg/m² D1 + TAX 80 mg/m² D1 &amp; D8 (n=7)</td>
<td>L 3.2 mg/m² D1 (n=36)</td>
</tr>
<tr>
<td>CR</td>
<td>2 (10%)</td>
<td>1 (4%)</td>
<td>1 (14%)</td>
</tr>
<tr>
<td>PR</td>
<td>12 (57%)</td>
<td>9 (33%)</td>
<td>4 (57%)</td>
</tr>
<tr>
<td>ORR</td>
<td>14 (67%)</td>
<td>10 (37%)</td>
<td>5 (71%)</td>
</tr>
<tr>
<td>SD</td>
<td>3 (14%)</td>
<td>9 (33%)</td>
<td>-</td>
</tr>
<tr>
<td>PD</td>
<td>4 (19%)</td>
<td>8 (30%)</td>
<td>2 (29%)</td>
</tr>
<tr>
<td>DCR</td>
<td>17 (81%)</td>
<td>19 (70%)</td>
<td>5 (71%)</td>
</tr>
<tr>
<td>DOR (mo)</td>
<td>4.5</td>
<td>5.2</td>
<td>2.3</td>
</tr>
<tr>
<td>PFS (mo)</td>
<td>4.7</td>
<td>5.3</td>
<td>3.9</td>
</tr>
<tr>
<td>CTFI &gt;30d*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PFS (mo) Platinum-sensitive</td>
<td>5.8</td>
<td>6.2</td>
<td>3.9</td>
</tr>
</tbody>
</table>

Phase III dose at primary endpoint
Zepsyre®: Phase III 2nd line Small Cell Lung Cancer
ATLANTIS Trial Design SCLC (Trial initiated August 2016); Anticipate data 2019

- Primary endpoint: median PFS
  - HR≤ 0.7 in PFS with 90% power;
  - Futility analysis planned at n~150 after 2 cycles*
- Key secondary endpoints:
  - OS
- Registration Strategy
  - Trial supported by ongoing monotherapy trial (Target n=100; n=36 at ESMO 2017)
  - Factorial synergy supported by CAV control arm (includes Anthracycline ~ Doxo)

Eligible SCLC pts 1 prior platinum n~600

R (1:1)

Arm A:
Zepsyre (2mg/m²) & Doxo (40mg/m²)
(up to 10 cycles)

No Crossover

Arm B:
Topotecan or CAV

Zepsyre mono (following doxo maximum cumulative dose) at 3.2 mg/m² q3w until PD

* Futility analysis passed @ n~150, 15 November 2017
# Zepsyre® – Phase IIb in BRCA 1/2- Breast Cancer

Best ORR in specific subpopulations

<table>
<thead>
<tr>
<th>Prior Platinum</th>
<th>BRCA</th>
<th>Hormone Status</th>
<th>Prior advanced CT lines</th>
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<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>No (n: 27)</td>
<td>1 (n: 31)</td>
<td>2 (n: 23)</td>
<td>1/2 (n: 54)</td>
</tr>
<tr>
<td></td>
<td>56% (35.3-55.6)</td>
<td>26% (11.9-25.8)</td>
<td>61% (38.5-60.9)</td>
</tr>
<tr>
<td></td>
<td>10.2 m (3.0-13.5)</td>
<td>5.9 m (2.8-12.8)</td>
<td>6.6 m (2.8-12.8)</td>
</tr>
<tr>
<td></td>
<td>25 (93%)</td>
<td>19 (70%)</td>
<td>23 (74%)</td>
</tr>
<tr>
<td></td>
<td>19 (70%)</td>
<td>14 (52%)</td>
<td>14 (45%)</td>
</tr>
</tbody>
</table>

* Includes 2 pts also HER-2 +

**Source:** ESMO 2016
Zepsyre®: Planned Registrational trial² BRCA2 Breast
Orphan Indication US/EU

In the US per annum¹:
- ~ 7,500 new cases of HR+, HER2-, BRCA2 mutated Breast cancer

In the EU-28 per annum¹:
- ~ 11,000 new cases of HR+, HER2-, BRCA2 mutated Breast cancer

HR+, HER2-, BRCA2 mutated mBC pts n~116

Zepsyre single arm (3.5mg/m² iv d1 q3wk)

- Primary endpoint: ORR
- Secondary endpoints: DOR, PFS

2 prior hormone Tx
1 CDK4/6 if available
1 or 2 prior chemo
no prior PARP

2. Subject to finalization and changes
Zepsyre®: Endometrial Cancer
Market overview\(^2\): Orphan Indication US/EU

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 gynecologic cancer in developed countries, beginning in the uterus, mainly afflicting those >50

- SOC first line: Type 1 (80%): Hormone therapy, Type 2: Doxorubicin, paclitaxel, cisplatin (TAP). ORR 57%, OS 15.3m

- The majority of endometrial cancer (72%) is diagnosed in early stages, however 15% to 20% of these carcinomas will recur\(^1\).

- There have not been any drug approvals for endometrial cancer over decades

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\(^2\) Source: Globocan 2012
Zepsyre®: Phase Ib in 2L Endometrial Cancer
ASCO 2017 Abstract 5586

**Phase 3 regimen**

<table>
<thead>
<tr>
<th></th>
<th>L+DOX (q3wk)</th>
<th>L+TAX (q3wk)</th>
<th>L alone (q3wk)</th>
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<tbody>
<tr>
<td><strong>Response</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>(evaluable patients)</td>
<td>L 3-5 mg FD D1 + DOX</td>
<td>L 2 mg/m² D1 + DOX</td>
<td>L 3.2 mg/m² D1</td>
</tr>
<tr>
<td>CR</td>
<td>2 (14%)</td>
<td>-</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>PR</td>
<td>2 (14%)</td>
<td>8 (44%)</td>
<td>3 (27%)</td>
</tr>
<tr>
<td>ORR</td>
<td>4 (28%)</td>
<td>8 (44%)</td>
<td>3 (27%)</td>
</tr>
<tr>
<td>SD</td>
<td>8 (57%)</td>
<td>7 (39%)</td>
<td>2 (18%)</td>
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<tr>
<td>PD</td>
<td>2 (14%)</td>
<td>3 (16%)</td>
<td>6 (55%)</td>
</tr>
<tr>
<td>DCR</td>
<td>9 (85%)</td>
<td>15 (83%)</td>
<td>5 (45%)</td>
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<tr>
<td>DOR (mo)</td>
<td>19.5</td>
<td>6.8</td>
<td>6.1</td>
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<tr>
<td>PFS (mo)</td>
<td>7.8</td>
<td>7.7</td>
<td>1.9</td>
</tr>
</tbody>
</table>

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.
Zepsyre®: Planned Phase III Advanced Endometrial Cancer
Subject to finalization and changes. Planning to start in 1H 2018

Phase III
500 Patients

Randomization 1:1
Stratified by:
- Histology (endometrioid vs. other)
- ECOG PS (0 vs. 1)
- TFI (> 6 vs. ≤ 6 months)

Arm A:
Zepsyre + Doxo*
(2.0 mg/m² D1 q3wk i.v
+40 mg/m² D1 +

Arm B:
Doxo
60 mg/m² D1
q3wk i.v.

No Crossover

Interim safety analysis (100 patients) IDMC

Primary endpoint: OS

* With prophylactic G-CSF
# Pipeline - Aplidin®
First in class drug with a novel mechanism of action

<table>
<thead>
<tr>
<th>Aplidium albicans</th>
<th>PLITIDEPSIN</th>
<th>MECHANISM OF ACTION</th>
</tr>
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<tbody>
<tr>
<td><img src="image1.png" alt="Aplidium albicans" /></td>
<td><img src="image2.png" alt="PLITIDEPSIN" /></td>
<td>- Targets eEF1A2</td>
</tr>
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</table>

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

Losada A et al: Plitidepsin inhibits autophagy, the main mechanism of acquired resistance to bortezomib. NCI-AACR-EORTC Abstract# B027, 2017
Aplidin® - ADMYRE TRIAL
Phase III in Relapsed / Refractory Multiple Myeloma

Phase III MM
250 Patients
After 3, but no more than 6 lines of chemotherapy

Randomization 2:1

Arm A: Aplidin® + Dexamethasone (n=167)

Arm B: Dexamethasone only (n=83)

Crossover

Median PFS (confirmation PD by Investigator): 3.8 months m vs 1.9 months
HR=0.611; p= 0.0048
Median PFS (IRC): 2.6 months vs 1.7 months (HR=0.650 p= 0.0062)

OS (ex-cross over): 11.6m vs estimated 6.7m  (HR= 0.667; p=0.0069)
OS (crossover): 11.6m vs 8.9m (HR=0.797; p=0.1273)

CHMP recommendation expected December 17

Data to be presented at ASH 2017