



CNMV  
Markets Directorate General  
C/ Edison núm. 4  
28006 Madrid

Madrid, December 3, 2020

In accordance with Article 226 of the recast Spanish Securities Market Act (*Ley del Mercado de Valores*), is hereby reported the following:

### **INSIDE INFORMATION**

Further to relevant event published on July 30, 2018 (registered number 268655) Pharma Mar announces results from the ATLANTIS Phase III multicenter, randomized, controlled study evaluating Zepzelca™ (lurbinectedin) in combination with doxorubicin versus physician's choice of topotecan or cyclophosphamide/doxorubicin/vincristine (CAV) for adult patients with small cell lung cancer (SCLC) whose disease progressed following one prior platinum-containing line. Patients received lurbinectedin at 2.0mg/m<sup>2</sup> in the experimental arm, which is lower than the FDA approved dose of lurbinectedin at 3.2mg/m<sup>2</sup>.

The study did not meet the pre-specified criteria of significance for the primary endpoint of overall survival (OS) in the intent-to-treat (ITT) population, comparing lurbinectedin in combination with doxorubicin to the control arm, though there was no adverse effect on OS with the experimental arm. Based on the study design, no additional hypotheses were formally tested. Importantly, key secondary and subgroup analyses favored the lurbinectedin combination arm. Lurbinectedin monotherapy was not tested in ATLANTIS.

The safety data in this study was consistent with the known safety profile of lurbinectedin monotherapy with no new safety signals observed. The experimental arm showed a favorable safety and tolerability with regard to Grade-3 or greater related adverse events (AEs), deaths due to AEs, hematologic toxicity, dose reductions and treatment discontinuations due to AEs, compared to the control arm.

Results will be discussed with the appropriate regulatory authorities and will be presented at a future medical meeting.

Pharma Mar management will host a conference call and webcast for investors and analysts today December 3<sup>rd</sup>, 2020, at 14:00 CET (08:00 AM, New York time) as follows. The numbers to connect to the teleconference are 1 646 664 1960 (from USA or Canada), +34 91 901 16 44 (from Spain) and +44 20 3936 2999 (other countries). Participants access code: 752381 Interested parties can also follow the conference call live via the following link: [www.incommuk.com/customers/online](http://www.incommuk.com/customers/online)

The recording of the teleconference will be available for thirty days and it can be accessed on Pharma Mar's website by visiting the [Events Calendar](#) section of the Company's website [www.pharmamar.com](http://www.pharmamar.com).

Please find attached press release that will be distributed to the media today.

Pharma Mar S.A.  
Avda. de los Reyes, 1  
P.I. La Mina  
28770 Colmenar Viejo  
(Madrid) Spain  
[www.pharmamar.com](http://www.pharmamar.com)



## PharmaMar and Jazz Pharmaceuticals announce results of the ATLANTIS phase III study with lurbinectedin

Madrid, December 3<sup>rd</sup>, 2020. – PharmaMar (MSE:PHM), along with its partner Jazz Pharmaceuticals plc (Nasdaq: JAZZ), have announced today results from the ATLANTIS Phase III multicenter, randomized, controlled study evaluating Zepzelca™ (lurbinectedin) in combination with doxorubicin versus physician's choice of topotecan or cyclophosphamide/doxorubicin/vincristine (CAV) for adult patients with small cell lung cancer (SCLC) whose disease progressed following one prior platinum-containing line. Patients received lurbinectedin at 2.0mg/m<sup>2</sup> in the experimental arm, which is lower than the FDA approved dose of lurbinectedin at 3.2mg/m<sup>2</sup>.

The study did not meet the pre-specified criteria of significance for the primary endpoint of overall survival (OS) in the intent-to-treat (ITT) population, comparing lurbinectedin in combination with doxorubicin to the control arm, though there was no adverse effect on OS with the experimental arm. Based on the study design, no additional hypotheses were formally tested. Importantly, key secondary and subgroup analyses favored the lurbinectedin combination arm. Lurbinectedin monotherapy was not tested in ATLANTIS.

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*"Bringing Zepzelca to the U.S. market earlier this year alongside our partner, PharmaMar, was an important advance for adults with metastatic SCLC, an aggressive disease with a historically poor prognosis," said **Robert Iannone M.D., M.S.C.E.**, executive vice president, research and development of Jazz Pharmaceuticals. "While lurbinectedin when used in combination did not meet the OS primary endpoint, the overall results support the activity and tolerability of lurbinectedin in this line of therapy. We look forward to the further development of lurbinectedin in SCLC and other tumors, both as monotherapy and in combination."*



*"We remain committed to improving outcomes for patients with metastatic small cell lung cancer where there is a high unmet medical need; we continue to evaluate the safety and efficacy of lurbinectedin in SCLC and other tumors. The drug's activity in this disease and setting has been reinforced in this trial",* said **Luis Mora**, General Manager of PharmaMar's Oncology Business Unit. *"We extend our gratitude to the patients, physicians and their staff as well as caregivers who participated in this clinical study."*

*"Patients with relapsed SCLC historically have had very limited options for treatment. As a physician treating patients with SCLC, I'm confident in lurbinectedin as an effective new monotherapy option in this often-challenging therapeutic area,"* **Alberto Chiappori, MD**, senior member of oncology and medicine for the Thoracic Oncology Program at the H. Lee Moffitt Cancer Center and Research Institute and ATLANTIS Phase III study investigator.

Results will be discussed with the appropriate regulatory authorities and will be presented at a future medical meeting.

The U.S. Food and Drug Administration (FDA) approved Zepzelca™ (lurbinectedin) under accelerated approval in June 2020 for the treatment of adult patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy. The approval is based on objective response rate (ORR) and duration of response (DoR) demonstrated in an open-label, monotherapy clinical study. The companies will provide the ATLANTIS data to FDA and look forward to working with the agency to determine the confirmatory data that is needed for full approval.

### **ATLANTIS Phase III Study Design**

The ATLANTIS Phase III study enrolled 613 patients at 154 sites primarily in the U.S., Canada, Latin America and Western Europe from September 2016 through July 2018. Patients enrolled were  $\geq 18$  years with histologically or cytologically confirmed diagnosis of limited or extensive stage SCLC, had failed one prior platinum-containing regimen, and had a chemotherapy-free interval (CTFI, time from the last dose of first-line chemotherapy to the occurrence of progressive disease)  $\geq 30$  days. Patient inclusion criteria included small-cell carcinoma of unknown primary site with or without neuroendocrine features confirmed in histology test(s) performed on metastatic lesion(s) are eligible, if Ki-67/MIB-1 is expressed in  $>50$  percent of tumor cells.



In the trial, patients were randomized in a 1:1 ratio to receive lurbinectedin in combination with doxorubicin or physician's choice of topotecan OR cyclophosphamide/doxorubicin/vincristine (CAV). The primary endpoint was overall survival. The secondary endpoints were 1) the difference in OS for patients in the lurbinectedin/doxorubicin arm compared to patients treated with CAV; 2) OS and progression free survival (PFS) in patients with or without CNS involvement; 3) PFS by independent review committee (IRC); 4) antitumor activity defined by objective response rate (ORR) per IRC; 5) duration of response per IRC.

The study sample was stratified by the following factors: CTFI (chemotherapy free interval); ECOG performance status (0 vs. 1-2); CNS involvement vs. no involvement; prior immunotherapy against either programmed cell death protein-1 (PD-1) or programmed death ligand-1 (PD-L1) and investigator preference of topotecan and CAV.

### **PharmaMar Conference Call for Investors and Analysts**

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### **Legal warning**

This press release does not constitute an offer to sell or the solicitation of an offer to buy securities, and shall not constitute an offer, solicitation or sale in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of that jurisdiction.

### **About PharmaMar**

Headquartered in Madrid, PharmaMar is a biopharmaceutical company, focused on oncology and committed to research and development which takes its inspiration from the sea to discover molecules with antitumor activity. It is a company that seeks innovative products to provide healthcare professionals with new tools to treat cancer. Its commitment to patients and to research has made it one of the world leaders in the discovery of antitumor drugs of marine origin.

PharmaMar has a pipeline of drug candidates and a robust R&D oncology program. It develops and commercializes Yondelis® in Europe and has other clinical-stage programs under development for several types of solid cancers: Zepzelca™ (lurbinectedin, PM1183), PM184 and PM14. With subsidiaries in

Germany, Italy, France, Switzerland, Belgium, Austria and the United States. PharmaMar wholly owns other companies: GENOMICA, a molecular diagnostics company; Sylentis, dedicated to researching therapeutic applications of gene silencing (RNAi). To learn more about PharmaMar, please visit us at [www.pharmamar.com](http://www.pharmamar.com).

#### **About Jazz Pharmaceuticals**

Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a global biopharmaceutical company dedicated to developing and commercializing life-changing medicines that transform the lives of patients with serious diseases - often with limited or no options. We have a diverse portfolio of marketed medicines and novel product candidates, from early- to late-stage development, in key therapeutic areas. Our focus is in neuroscience, including sleep and movement disorders, and in oncology, including hematologic malignancies and solid tumors. We actively explore new options for patients including novel compounds, small molecule advancements, biologics and innovative delivery technologies. Jazz is headquartered in Dublin, Ireland and has employees around the globe, serving patients in more than 90 countries. For more information, please visit [www.jazzpharmaceuticals.com](http://www.jazzpharmaceuticals.com) and follow @JazzPharma on Twitter.

#### **About lurbinectedin**

Lurbinectedin (Zepzelca™), also known as PM1183, is an analog of the marine compound ET-736 isolated from the sea squirt *Ecteinacidia turbinata* in which a hydrogen atom has been replaced by a methoxy group. It is a selective inhibitor of the oncogenic transcription programs on which many tumors are particularly dependent. Together with its effect on cancer cells, lurbinectedin inhibits oncogenic transcription in tumor-associated macrophages, downregulating the production of cytokines that are essential for the growth of the tumor. Transcriptional addiction is an acknowledged target in those diseases, many of them lacking other actionable targets.

#### **Media Contact:**

Alfonso Ortín – Communications Director [aortin@pharmamar.com](mailto:aortin@pharmamar.com) Mobile: +34 609493127  
Miguel Martínez-Cava – Communication Manager [mmartinez-cava@pharmamar.com](mailto:mmartinez-cava@pharmamar.com) Mobile: +34 606597464  
Álvaro Mateo - Communication Manager [amateo@pharmamar.com](mailto:amateo@pharmamar.com) Mobile: +34 650726009

Phone: +34 918466000

#### **Capital Markets & Investor Relations:**

José Luis Moreno– Capital Markets & Investor Relations Director  
María Marín de la Plaza – Capital Markets & Investor Relations  
[investorrelations@pharmamar.com](mailto:investorrelations@pharmamar.com)  
Phone: +34 914444500



Or please visit our website at [www.pharmamar.com](http://www.pharmamar.com)