

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

Madrid, September 17, 2020

In accordance with article 227 of the recast Spanish Securities Market Act (*texto refundido de la Ley del Mercado de Valores*), is hereby reported the following:

OTHER RELEVANT INFORMATION

At the European Society of Medical Oncology (ESMO) Congress, Pharma Mar presented new data on lurbinectedin in platinum-sensitive, second-line, Small-Cell Lung Cancer (SCLC) patients, who have received prior platinum-based chemotherapy and relapsed within a period equal to, or greater than 90 or 180 days after its completion and who, according to the *ESMO Clinical Practice Guidelines* and the *National Comprehensive Cancer Network (NCCN) Guidelines*, are candidates for platinum “re-challenge”.

The poster, titled “*Activity of Lurbinectedin in Second-line SCLC Patients Candidates for Platinum Re-challenge*”, presents the evaluation of platinum sensitive patients with a CTFI (*Chemotherapy-Free Interval*) ≥ 90 days, i.e., those who have suffered a relapse in a period equal to or greater than 90 days, from the phase II basket trial, carried out both in the USA and in Europe.

In the subgroup of 60 patients with a CTFI ≥ 90 days, the median Overall Survival (OS) was 11.9 months, with an Overall Response Rate (ORR) of 45%, according to the investigator's evaluations, and 11.9 months, with an ORR of 43% by the Independent Review Committee (IRC).

Of these 60 platinum-sensitive patients with CTFI ≥ 90 days, in the subgroup of 20 patients with CTFI ≥ 180 days, an OS of 16.2 months and an ORR of 60% was observed, as assessed by the investigator, and an OS of 16.2 months and an ORR of 50%, by the IRC.

These results show that patients with a CTFI ≥ 180 days, who according to NCCN guidelines, are candidates for platinum “re-challenge”, have got benefit compared with previous studies using this strategy, where data showed an ORR of 43-46% and an OS of 14.3-15.7 months. Therefore, these results suggest that lurbinectedin could be a therapeutic alternative for this type of patients.

In addition, lurbinectedin has a safety and tolerability profile, that is encouraging compared to alternatives, and particularly with regard to hemotoxicity that is lower than in historical platinum treatments.



The Phase II trial of lurbinectedin was a single-arm, open-label study, that has enrolled a total of 105 patients with both platinum-sensitive and platinum-resistant SCLC, who had disease progression after previous platinum-based chemotherapy. This study was carried out in 26 hospitals in six European countries, in addition to the United States.

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

PharmaMar has presented new results for Zepzelca™ (lurbinectedin) in sensitive patients with Small-Cell Lung Cancer, candidates for “re-challenge”

- **New data have been released on lurbinectedin in second-line Small-Cell Lung Cancer patients who had received previous platinum-based chemotherapy and relapsed after 90 or 180 days.**
- **The efficacy results show that in patients with a Chemotherapy-Free Interval equal to or greater than 90 days (CTFI \geq 90), the median Overall Survival (OS) was 11.9 months, and Overall Response Rate (ORR) of 45%.**
- **In the subgroup of patients with a CTFI \geq 180 days, who are candidates for platinum re-challenge, an OS of 16.2 months and an ORR of 60% were observed.**
- **The results show that lurbinectedin has a favourable safety profile, compared to platinum.**

Madrid, 17th September, 2020. At the European Society of Medical Oncology (ESMO) Congress, PharmaMar (MSE:PHM) presented new data on lurbinectedin in platinum-sensitive, second-line, Small-Cell Lung Cancer (SCLC) patients, who have received prior platinum-based chemotherapy and relapsed within a period equal to, or greater than 90 or 180 days after its completion and who, according to the *ESMO Clinical Practice Guidelines* and the *National Comprehensive Cancer Network (NCCN) Guidelines*, are candidates for platinum “re-challenge”.

The poster, titled “*Activity of Lurbinectedin in Second-line SCLC Patients Candidates for Platinum Re-challenge*”, presents the evaluation of platinum sensitive patients with a CTFI (*Chemotherapy-Free Interval*) \geq 90 days, i.e., those who have suffered a relapse in a period equal to or greater than 90 days, from the phase II basket trial, carried out both in the USA and in Europe.

In the subgroup of 60 patients with a CTFI \geq 90 days, the median Overall Survival (OS) was 11.9 months, with an Overall Response Rate (ORR) of 45%, according to the investigator's evaluations, and 11.9 months, with an ORR of 43% by the Independent Review Committee (IRC).

Of these 60 platinum-sensitive patients with CTFI \geq 90 days, in the subgroup of 20 patients with CTFI \geq 180 days, an OS of 16.2 months and an ORR of 60% was observed, as assessed by the investigator, and an OS of 16.2 months and an ORR of 50%, by the IRC.

These results show that patients with a CTFI \geq 180 days, who according to NCCN guidelines, are candidates for platinum “re-challenge”, have got benefit compared with previous studies using this strategy, where data showed an ORR of 43-46% and an OS of 14.3-15.7 months. Therefore, these results suggest that lurbinectedin could be a therapeutic alternative for this type of patients.

In addition, lurbinectedin has a safety and tolerability profile, that is encouraging compared to alternatives, and particularly with regard to hemotoxicity that is lower than in historical platinum treatments^{i,ii,iii,iv}.

The Phase II trial of lurbinectedin was a single-arm, open-label study, that has enrolled a total of 105 patients with both platinum-sensitive and platinum-resistant SCLC, who had disease progression after previous platinum-based chemotherapy. This study was carried out in 26 hospitals in six European countries, in addition to the United States^v.

According to **Dr. Ali Zeaiter**, M.D., Director of Clinical Development at PharmaMar, *“these results are compelling compared with available data of alternative options in similar populations, and we are pleased to offer treating physicians, patients and caregivers a new therapeutic option for this aggressive and currently hard to treat disease.”*

Dr Zeaiter also pointed that *“with the recent accelerated approval of lurbinectedin by the FDA for relapsed Small-cell Lung Cancer, this group of sensitive patients, with a chemotherapy free interval greater than 90 days may be seen to particularly derive benefit, with a notable improvement in overall survival.”*

In June 2020, the Food and Drug Administration (FDA) granted the accelerated approval of lurbinectedin for adult patients with metastatic SCLC with disease progression, after platinum-based chemotherapy. This approval allowed Jazz Pharmaceuticals to make lurbinectedin commercially available in the U.S. in early July this year.

SCLC comprises approximately 13-15% of all lung cancer cases at the time of diagnosis, and its treatment and survival have not changed substantially over the past two decades^{vi}.

E-Posters will be available for delegates to view on demand on the Congress platform starting from 09:00 CET (03:00 ET) on Thursday, 17th September 2020 until 20:00 CET (14:00 ET) on Monday, 21st September 2020.

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 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.

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.

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- ⁱ Inoue A, Sugawara S, Maemondo M, et al. Randomized phase II trial comparing amrubicin with rechallenge of platinum doublet in patients with sensitive-relapsed small-cell lung cancer: North Japan Lung Cancer Study Group trial 0702. *Lung Cancer* 2015; 89:61-65.
- ⁱⁱ Wakuda K, Kenmotsu H, Naito T, et al. Efficacy of rechallenge chemotherapy in patients with sensitive relapsed small cell lung cancer. *Am J Clin Oncol* 2015; 38:28-32.
- ⁱⁱⁱ Genestreti G, Tiseo M, Kenmotsu H, et al. Outcomes of Platinum-Sensitive Small-Cell Lung Cancer Patients Treated With Platinum/Etoposide Rechallenge: A Multi-Institutional Retrospective Analysis. *Clin Lung Cancer* 2015; 16:e223-228.
- ^{iv} Monnet I, Baize N, Greillier L, et al. OA15.02 Carboplatin-Etoposide Versus Topotecan as Second-Line Treatment for Sensitive Relapsed Small-Cell Lung Cancer: Phase 3 Trial. *J Thorac Oncol* 2019;14:S246
- ^v Trigo J, Subbiah V, Besse B, et al. Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial. *Lancet Oncol.* 2020 May;21(5):645-654.
- ^{vi} Früh M, De Ruysscher D, Popat S, Crinò L, Peters S, Felip E. Cáncer de pulmón microcítico (CPCP): Guía de práctica clínica de la ESMO para su diagnóstico, tratamiento y seguimiento. *Ann Oncol.* 2013; 24 : 99-105. [https://www.annalsofncology.org/article/S0923-7534\(19\)31548-0/fulltext](https://www.annalsofncology.org/article/S0923-7534(19)31548-0/fulltext)