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

Colmenar Viejo (Madrid), June 1, 2019

Pursuant to Article 17 of Regulation (EU) nº 596/2014 on market abuse and Article 226 of the consolidated text of the Spanish Securities Market Act, approved by Royal Legislative Decree 4/2015, of 23 October, we hereby make the following **REGULATORY ANNOUNCEMENT**:

"In relation to Significants Facts nº 276.396, 276.625 and 278.282 dated March 25, 2019, April 1, 2019 and May 16, 2019, respectively, Pharma Mar, S.A. announces that the results of Phase II study with lurbinectedin as a single agent for the treatment of relapsed small cell lung cancer, which achieved its primary endpoint, were presented today to the American Society of Clinical Oncology (ASCO) conference by Dr. Luis Paz-Ares, Head of the Oncology Department at the Hospital Universitario 12 de Octubre in Madrid and lead author of the study. In his presentation entitled "Efficacy and safety profile of lurbinectedin in second-line SCLC patients: Results from a phase II single-agent trial", Dr..Paz-Ares updated the data from the lurbinectedin study, where an ORR of 35.2% in the total population, 45% in patients with sensitive disease (CTFI≥90 days, i.e., those who have suffered a relapse of the disease in a period greater than or equal to 90 days) and 22.2% in patients with resistant disease (CTFI<90 days, i.e., those patients who have suffered a relapse of the disease in a period less than 90 days) has been seen. As additional study results, the Disease Control Rate (DCR) was 68.6% in the overall population, 81.7% in sensitive patients and 51.1% in resistant patients. The median Duration of Response (DOR) was 5.3 months in the overall population, 6.2 months in sensitive patients and 4.7 months in resistant patients. The median Progression Free Survival (PFS) was 3.9 months in the overall population, 4.6 months in sensitive patients, and 2.6 months in resistant patients. The median OS was 9.3 months in the overall population, 11.9 months in sensitive patients, and 5.0 months in resistant patients. The most common treatment-related adverse effects have been neutropenia, nausea or vomiting, and fatigue. Grade 3-4 neutropenia occurred in 22.9% of cases, grade 3-4 febrile neutropenia in 4.8%, grade 3-4 anemia in 6.7%, and grade 3-4 thrombocytopenia in 4.8%. Please find attached press release that will be distribute to the media in this regard".

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Positive results of lurbinectedin Phase II trial (PharmaMar) for the treatment of relapsed small cell lung cancer are presented at ASCO

- **Lurbinectedin (PharmaMar) achieved the primary endpoint of Overall Response Rate (ORR) in the Phase II trial and has been shown to be active as a single agent in the second line treatment of small cell lung cancer.**
- **The ORR was 35.2% and the median Overall Survival (OS) was 9.3 months.**
- **Lurbinectedin's activity is encouraging in sensitive patients (CTFI≥90) with an ORR of 45% and a median OS of 11.9 months.**
- **Also noteworthy is the activity demonstrated by lurbinectedin in resistant patients (CTFI<90), for whom there is no approved product on the market, with an ORR of 22.2% and a median OS of 5 months.**
- **Lurbinectedin has been seen to have a favorable and manageable safety.**

Madrid, June 1st, 2019.- The results of PharmaMar's (MSE:PHM) Phase II study with lurbinectedin as a single agent for the treatment of relapsed small cell lung cancer were presented today to the American Society of Clinical Oncology (ASCO) conference, which is currently being held in Chicago. The results of this trial, which achieved its primary endpoint, have been presented orally by Dr. Luis Paz-Ares, Head of the Oncology Department at the Hospital Universitario 12 de Octubre in Madrid and lead author of the study,

In his presentation entitled "*Efficacy and safety profile of lurbinectedin in second-line SCLC patients: Results from a phase II single-agent trial",* Dr.Paz-Ares updated the data from the lurbinectedin study, where an ORR of 35.2% in the total population, 45% in patients with sensitive disease (CTFI≥90 days, i.e., those who have suffered a relapse of the disease in a period greater than or equal to 90 days) and 22.2% in patients with resistant disease (CTFI<90 days, i.e., those patients who have suffered a relapse of the disease in a period less than 90 days) has been seen.

"Lurbinectedin is showing to be a new potential treatment alternative for second-line small cell lung cancer, where, until now, no progress has been made for more than two decades," says **Dr. Luis Paz-Ares**.

Additional Study Results

- The Disease Control Rate (DCR) was 68.6% in the overall population, 81.7% in sensitive patients and 51.1% in resistant patients.
- The median Duration of Response (DOR) was 5.3 months in the overall population, 6.2 months in sensitive patients and 4.7 months in resistant patients.
- The median Progression Free Survival (PFS) was 3.9 months in the overall population, 4.6 months in sensitive patients, and 2.6 months in resistant patients.
- The median OS was 9.3 months in the overall population, 11.9 months in sensitive patients, and 5.0 months in resistant patients.

"Having been chosen to present positive results at ASCO is an honor for any pharmaceutical company. These results demonstrate that lurbinectedin is a strong candidate to become a therapeutic alternative for patients with small cell lung cancer, a large unmet medical need" explains **José María Fernández**, President of PharmaMar.

In terms of product safety, lurbinectedin has shown a favorable and manageable safety profile. The most common treatment-related adverse effects have been neutropenia, nausea or vomiting, and fatigue.

Grade 3-4 neutropenia occurred in 22.9% of cases, grade 3-4 febrile neutropenia in only 4.8%, grade 3-4 anemia in 6.7%, and grade 3-4 thrombocytopenia in 4.8%.

By way of reference, the data provided for lurbinectedin compares favorably (non head-to-head) to the data included in the topotecan FDA label[1], the last molecule approved for second-line treatment, in 1996. The topotecan arm saw an ORR of 24%, [median] PFS of 3.9 months and median OS of 5.8 months was seen. In terms of safety, topotecan showed grade 4 neutropenia in 70% of the patients, grade 3-4 febrile neutropenia in 28% and grade 3-4 anemia in 42%. The difference between the results of both these molecules, although not having comparable face-to-face studies, speaks of the potential of lurbinectedin as a potential new alternative treatment for second-line small cell lung cancer.

[1] https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/022453s002lbl.pdf

The single-agent lurbinectedin study is a single-arm, Phase II, multicenter trial, involving 105 patients recruited from 39 centers in 9 countries in Western Europe along with the USA, studying the safety and efficacy of lurbinectedin in second line treatment of small cell lung cancer.

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: 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); and a chemical enterprise, Zelnova Zeltia. To learn more about PharmaMar, please visit us at www.pharmamar.com.

About lurbinectedin

Lurbinectedin (PM1183) is a synthetic compound currently under clinical investigation. 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.

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