PharmaMar's investigational drug PM1183 plus doxorubicin shows remarkable activity in small cell lung cancer

Chicago, June 1st 2015: PharmaMar today announced data from a Phase 1b study of the transcriptional inhibitor PM1183 in combination with doxorubicin in second line therapy in patients with small cell lung cancer (SCLC) showing that the treatment induced objective responses in 67% of the patients, including 10% of them where all signs of cancer disappeared (complete responses). Every patient with SCLC denominated primary chemotherapy-sensitive (their chemotherapy-free interval (CTFI) is more than 90 days) responded to treatment, including 18% of complete responses. In primary chemotherapy-resistant patients, where cancer was progressing within 90 days or less of previous chemotherapy, a remarkable 30% achieved a response. Notably, the treatment resulted in durable responses, with an overall progression-free survival (PFS) of 4.6 months, which was 3.6 months in resistant patients. The most common adverse drug reaction was reversible myelosuppresion but no cardiotoxicity or drug-related deaths were observed.

"The rate, depth and length of responses that we have observed with this treatment in the second-line setting are remarkable, even in those patients that are usually considered harder to treat", said Dr. Martin Forster, University College Hospital, London, UK. "Small cell lung cancer is an unmet clinical need with very few recent advances and the scientific community is committed to help new develop effective therapies."

The lead author Dr. Martin Forster, University College Hospital, London, UK. will present the full data today at the 51th Annual Meeting of the American Society of Clinical Oncology (ASCO) (Abstract#7509, Monday, June 1 from 8:00 AM to 11:30 AM at S Hall A Poster Board 256). This study will be further discussed later today at a Poster Discussion Session on Targeted Therapies In Unselected Patients from 1:15 PM - 2:30 PM at E Hall D2

"No therapies have been approved in the last 17 years for small cell lung cancer, so we are very excited about the results obtained with PM1183 in these patients. The

novel mechanism of action and lack of platinum cross-resistance of PM1183 are an advantage for treating these tumors." pointed out Arturo Soto, Director of Clinical Development at PharmaMar.

About the Phase 1b study with PM1183 and doxorubicin

- PM1183 is an inhibitor of transcription by specifically targeting the enzyme RNA polymerase II (in its active state) for degradation[i], thereby blocking the expression of certain genes important for tumor progression. This targeting of the transcriptional machinery is also coupled to a DNA repair pathway called nucleotide excision repair (NER), which is important to repair DNA breaks. A recent preclinical study has shown that SCLC may be particularly sensitive to transcription inhibitors[ii], and PM1183 plus doxorubicin demonstrated a synergistic and robust anticancer effect in SCLC mouse models[iii].
- This Phase 1b study is an expansion cohort of approximately 20 evaluable SCLC patients that have failed after one chemotherapy-containing prior line to assess in second line treatment the remarkable activity of the combination treatment (71% of objective partial responses[iv]) previously observed during the escalation phase.
- After 12 months of follow up, the overall response rate as measured by RECIST criteria was 67% and a complete response was achieved by 10% of the patients. Durable responses were observed with an overall PFS of 4.6 months (4.8 months in sensitive patients and 3.6 months in resistant patients).
- CTFI was the only variable with statistically significant (p=0.001) correlation with response – all sensitive patients responded (95%CI: 71-100%) and a remarkable 30% of resistant patients also showed a response.
- The response rate observed with the combination of PM1183 and DOX in second line is comparable to those observed with first line chemotherapy treatments in this same population.
- Reversible myelosuppression was the most frequent adverse drug reaction observed. There were no unexpected or drug-related deaths. DOX dose may be adapted, with or without CSF prophylaxis, to reduce associated myelosuppression.

About small cell lung cancer

SCLC is a very aggressive cancer that usually presents with distant metastases and has already spread at the time of diagnosis, thus limiting the role of traditional approaches and posing a worse prognosis compared to other lung cancer types. The 5-year survival rate is about 5%[v]. About 18% of all the lung cancer cases diagnosed are SCLC, and only in the US more than 34,000 new cases are recorded every year. This tumor is strongly associated with tobacco smoking, posing an important public health problem[vi]. After failure to treatment with a platinum-based therapy in first line, there are almost no therapeutic alternatives, and the approval of the last drug for this disease took place a few decades ago.

About PM1183 (lurbinectedin)

PM1183 is an investigational drug from the class of inhibitors of the enzyme RNA polymerase II, which is crucially involved in transcription. By targeting transcription, the drug inhibits the expression of factors important for tumor progression, and impairs the DNA repair system called NER, thereby enhancing tumor cell killing. PM1183 (lurbinectedin) is currently being investigated in different tumor types, including a Phase 3 study for platinum-resistant ovarian cancer, a Phase 2 study for BRCA1/2-associated metastatic breast cancer and a Phase 1b study for SCLC.

About PharmaMar

Headquartered in Madrid, PharmaMar is the world-leading biopharmaceutical company in advancing cancer care through the discovery and development of innovative marine-derived anticancer drugs. The company has a rich pipeline of drug candidates and a robust R&D oncology program. YONDELIS® is the first anticancer drug of marine origin and is commercially available in 81 countries for the treatment of advanced soft tissue sarcomas as a single-agent, and for relapsed platinum-sensitive ovarian cancer in combination with DOXIL®/CAELYX®. PharmaMar develops and commercializes YONDELIS® in Europe and has three clinical-stage programs under development for several types of solid and hematological cancers, PM1183, plitidepsin, and PM60184. PharmaMar is a global biopharmaceutical company with subsidiaries in Germany, Italy, France, Switzerland and the United States. To learn more about PharmaMar, please visit us at www.pharmamar.com.

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[i] http://www.pharmamar.com/en/press/pharmamar-results-antitumoral-compounds-and-their-mechanism-action-eortcnciaacr-emphasize

[ii] http://www.cell.com/cancer-cell/abstract/S1535-6108%2814%2900516-9

[iii] http://www.pharmamar.com/en/press/pharmamar-present-data-anticancer-candidates-pm1183-and-plitidepsin-aacr-annual-meeting-2015-0

[iv] http://www.pharmamar.com/en/press/pharmamar-will-start-phase-iii-study-pm1183-combination-doxorubicin-relapsed-sclc-38352

[v] http://www.cancer.gov/types/lung/hp/small-cell-lung-treatment-pdq

[vi] http://www.jnccn.org/content/11/1/78.full.pdf