ZELTIA NEWS:

PharmaMar to present new studies with Yondelis® at ASCO

- Two studies that will be presented are especially noteworthy, as Yondelis® was administered as first-line treatment in patients with different types of soft tissue sarcoma.

- The ASCO Annual Meeting is one of the world’s leading events in cancer research.

Madrid, 16 May 2013: At the 2013 Annual Meeting of the American Society of Clinical Oncology (ASCO), to be held in Chicago from 31 May to 4 June, communications on marine-based anti-tumour drug Yondelis® (trabectedin) will be presented. Yondelis® is the first marine-based antitumour drug commercialized by PharmaMar, a biopharmaceutical company owned by Grupo Zeltia (ZEL.MC).

The ASCO Annual Meeting, one of the world’s main events in cancer research, brings together over 30,000 oncology professionals to discuss the latest developments in this therapeutic area.

Two communications that will be presented were especially noteworthy because Yondelis® was administered as first-line treatment in patients with different types of soft tissue sarcoma (STS).

The first, “A Phase II single-arm multicenter study of doxorubicin in combination with trabectedin as a first-line treatment of inoperable or metastatic uterine leiomyosarcoma (U-LMS) and soft tissue LMS (ST-LMS): First results of LMS-02 trial in patients with U-LMS”, will be presented orally during the event. Based in preliminary observations of Yondelis® activity in recurrent leiomyosarcoma, the French Sarcoma Group conducted a clinical trial with trabectedin in combination with doxorubicin as first-line treatment in U-LMS. The primary endpoint was to determine the disease control rate, and the data presented from the uterine cohort
suggested that the combination of Yondelis® with Doxorubicin was an effective first-line treatment in patients with U-LMS, since it provides significant clinical benefits and has an acceptable and manageable safety profile.

The second trial "Results of the randomized phase III trial of trabectedin versus doxorubicin-based chemotherapy as first-line therapy in patients with translocation-related sarcoma", refers to a prospective III trial involving 121 patients with different subtypes of translocation-related sarcomas. The primary endpoint was to evaluate the efficacy of both treatments by comparing progression free survival (PFS), while secondary endpoints included comparing overall survival (OS). The conclusions of this prospective trial suggests that the PFS and OS results with Yondelis® as first-line treatment are comparable to standard treatment based on doxorubicin in first-line treatment. These results will be presented at a poster discussion session.

The other communications to be presented at the general poster session or as e-abstracts are:

- “A large retrospective analysis of trabectedin in patients with advanced soft tissue sarcoma (ASTS)” refers to a retrospective analysis of data from 885 sarcoma patients treated with trabectedin in real life in 26 French centers during a period of four years. The results show that patients who responded or stabilised following six cycles of treatment with Yondelis® and continued treatment beyond six cycles had an improvement in overall survival compared to those who stopped after cycle 6.

- “Safety of trabectedin in elderly patients with advanced soft tissue sarcoma (STS)”: a retrospective analysis which confirmed that Yondelis® is well-tolerated in elderly patients (median age of participants was 69).

- “Efficacy of trabectedin for advanced soft tissue sarcoma (ASTS): a retrospective single center analysis” reports on a retrospective analysis of patients with ASTS treated with Yondelis® from November 2006 through April 2012 at the Hospital Miguel Servet in Spain. Results confirm previous findings from clinical trials which show that Yondelis® is active in the treatment of ASTS.

- “A retrospective tumor response assessment in locally unresectable or metastatic sarcoma soft tissue sarcoma (aSTS) patients (pts): A three-year
Regina Elena Cancer Institute experience with trabectedin therapy": STS patients treated with Yondelis® as second-line or further treatment and patients with ASTS who received more lines of treatment were analysed retrospectively. Tumour response was evaluated using three measurement criteria: RECIST, mChoi and MASS. The findings with mChoi and MASS are similar to those using RECIST. A prospective trial is required to confirm this conclusion.

- In advanced ovarian cancer, 4 studies will be presented, showing the activity of trabectedin as single agent, as well as exploring nibrin as a potential marker in AOC

- “Efficacy and safety outcomes in heavily pretreated patients (PTS) with recurrent ovarian cancer (ROC) after single agent trabectedin treatment": Phase II multicenter trial that evaluated the efficacy and safety of single agent in the palliative treatment of heavily pretreated patients with recurrent ovarian cancer. Yondelis® exhibited notable clinical benefit and acceptable safety profile.

- “Prolonging the platinum-free interval (PFI) with trabectedin allows retreatment with platinum-based chemotherapy in patients with platinum-refractory and resistant recurrent ovarian cancer (PROC)”: Retrospective analysis of patients with recurrent ovarian cancer treated with trabectedin as single agent in a single institution. Results suggest that Yondelis® can extend the PFI and re-sensitise patients with PROC and PPS ROC to new platinum-based therapies, leading to significant benefits.

- “Phase II study of trabectedin in pretreated patients with recurrent epithelial ovarian cancer (REOC)”: Results of this trial performed in Italy confirmed the antitumor activity of trabectedin monotherapy in this heavily pretreated population, with good tolerability

- “Exploratory analysis of nibrin in advanced ovarian cancer (AOC) patients treated in the pivotal Phase III OVA-301 trial": nibrin is a protein that plays an essential role in repairing double-strand DNA breaks. This analysis used immunohistochemical techniques to investigate nibrin's as a potential biomarker in patients with AOC. The results suggest that nibrin expression may play an important role in predicting the outcome of patients with AOC.
Prospective clinical trials are necessary to evaluate the usefulness of this marker in patients with another standard treatment.

Other trials are:

- “A phase II trial of trabectedin (T) in patients with hormone receptor positive, HER2 negative advanced breast cancer, according to xeroderma pigmentosum gene (XPG) expression”: Yondelis® exhibited antitumour activity in other trials in patients with breast cancer and a poor prognosis. It was also observed that breast cancer patients with XPG overexpression responded better to Yondelis®. Therefore, this trial included patients with hormone-receptor-positive, HER2-negative advanced breast cancer that had previously been treated with anthracyclines and/or taxanes, stratified according to their XPG expression levels. The conclusion was that Yondelis® exhibited moderate efficacy and an acceptable safety profile in this subgroup of patients, regardless of XPG expression, with the result that XPG does not appear to predict breast cancer patients' response to treatment with Yondelis®.

- “Phase 1/2a, randomized, open-label, drug-drug interaction study of trabectedin and rifampin in patients with advanced cancer ("ET743-OVC-1002")”: In the body, Yondelis® is first metabolised by cytochrome P450 3A4 (CYP3A4), with the result that potent inducers or inhibitors of this enzyme can alter plasmatic concentrations of Yondelis®. This trial evaluated the effects of rifampin, a strong CYP34A inducer, on the pharmacokinetics and safety of Yondelis®. The conclusion is that coadministration of potent CYP34A inducers with Yondelis® can increase metabolism and excretion of Yondelis® from the body.

- “Heat-shock (H-S) and trabectedin efficacy in human soft-tissue sarcoma (STS) cells in vitro”: the rationale behind combining Yondelis® with in vitro heat shock is that exposure to heat increases tumour cells' sensitivity by inhibiting the system that repairs double-strand DNA breaks. The conclusion obtained in this in vitro trial is that combining Yondelis® with heat shock increases cytotoxicity.
About PharmaMar

PharmaMar is a biopharmaceutical subsidiary of Grupo Zeltia; it is a world leader in discovering, developing and selling marine-based drugs to treat cancer. Yondelis® is the first marine-based antitumour drug. PharmaMar has four other compounds in clinical development: Aplidin®, Zalypsis®, PM01183 and PM060184. PharmaMar also has a rich pipeline of pre-clinical candidates and a major R&D programme.

About Zeltia

Zeltia S.A. is a world-leading biopharmaceutical company specialised in the development of marine-based drugs for use in oncology. Grupo Zeltia consists mainly of the following companies: PharmaMar, the world-leading biotechnology company in advancing cancer care through the discovery and development of innovative marine-derived medicines; Genómica, Spain's leading molecular diagnostics company; Sylentis, dedicated to researching therapeutic applications of gene silencing (RNAi).

Important note

PharmaMar, which is headquartered in Madrid (Spain), is a subsidiary of Zeltia, S.A. (Spanish stock exchange: ZEL), which has been listed on the Spanish Stock Exchange since 1963 and on Spain's Electronic Market since 1998. This document is a press release, not a prospectus. This document does not constitute or form part of an offering or invitation to sell or a solicitation to purchase, offer or subscribe shares of the company. Moreover, no reliance should be placed upon this document for any investment decision or contract and it does not constitute a recommendation of any type with regard to the shares of the company.

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