ZELTIA NEWS:

Preliminary results for twelve trials with PharmaMar compounds to be presented at the European Cancer Congress 2013 (ECCO-ESMO-ESTRO)

Madrid, 12th 2013: Twelve trials with three marine-based compounds from PharmaMar, GrupoZeltia’s (MC:ZEL) biotechnology subsidiary, will be presented at the 17th Congress of the European Cancer Organization (ECCO), the 38th Congress of the European Society of Medical Oncology (ESMO), and the 32nd Congress of the European Society for Therapeutic Radiology and Oncology (ESTRO), to be held in Amsterdam from 27 September to 1 October.

A very important abstract to be presented by the French Sarcoma group during the congress is “Trabectedin in patients with advanced soft tissue sarcoma (ASTS): Importance of maintenance therapy in responding patients after 6 cycles of trabectedin”. It is one of the largest retrospective analyses of the real life experience in patients with ASTS treated with Yondelis® between January 2008 and December 2011. Most patients had leiomyosarcoma (36%), liposarcoma (18%) or synovial STS (11%). The trial included 885 patients with an average age of 54 years. After six cycles of treatment, 75% of patients with non-progressive disease received trabectedin (Yondelis®) as maintenance therapy and obtained higher rates of progression free survival (PFS) and overall survival (OS) than those who stopped Yondelis® after 6 cycles.

Another very important trial to be presented is "LMS-02: A Phase II single-arm multicenter study to determine the efficacy of doxorubicin in combination with trabectedin as a 1st line treatment of metastatic and/or locally advanced leiomyosarcoma of uterine (U-LMS) or soft tissue (ST-LMS) origin: results of the soft tissue group”, which evaluates the combination of Yondelis® with doxorubicin. Leiomyosarcomas are rare tumours and have poor prognoses. The combination of Yondelis® with doxorubicin in patients with U-LMS yielded very promising results and results presented are focused on patients with LMS located in soft tissues.
Overall, 61 patients with an average age of 60 years were enrolled in the trial up to January 2013. For 36 patients with at least one evaluation, a disease control rate was of 94%, while median PFS at 12 weeks is currently 95% (95%IC: 84-99). Common grade 3/4 toxicities (≥10%) were neutropenia (40.7%) and thrombopenia (19.7%). Therefore, despite expected toxicity, trabectedin in combination with doxorubicin seems to be an effective first line treatment in ST-LMS.

“GEIS-20-randomized, open, multicenter, prospective, phase II clinical trial of doxorubicin vs. trabectedin plus doxorubicin in the first line treatment of patients with advanced non operable and/or metastatic soft tissue sarcoma”: The combination in first line of Yondelis® with doxorubicin was not found to be superior to treatment with doxorubicin as monotherapy in patients with STS.

The differences in study design and populations limit direct comparisons between LMS02 and GEIS 20 and are likely the main reason for discrepancy in results.

The other trials to be presented with Yondelis® are:

- “Safety of trabectedin versus doxorubicin-based chemotherapy (DXCT) as first-line therapy in patients with translocation-related sarcoma (TRS)”: Both treatments were generally well tolerated with manageable adverse events and limited incidence of severe side effects. No new safety signals have emerged from this trial.

- “Phase I and Pharmacokinetic Study of Trabectedin in Japanese Patients with Soft Tissue Sarcoma”: This dose escalation trial was designed to define the recommended dose (RD) of Yondelis® for the Phase II trial and the pharmacokinetic profile of Japanese patients with STS, which was determined to be 1.2 mg/m² and 1.5mg/m² was the maximum tolerated dose.

- “Hyperthermia combined with Trabectedin prolongs cell cycle arrest and reduces cellular survival in human tumour cells”: Previous trials showed that hyperthermia combined with chemotherapy improves response and survival rates in patients with high-risk STS, since exposure to heat inhibits repair of chemotherapy-induced cell damage by degrading the BRCA2 protein, which is crucial for cell repair. This trial combined Yondelis® with hyperthermia and analysed the effect of the combination on four human tumour cell lines. The
conclusion was that concomitant hyperthermia increases the activity of Yondelis®.

- “A retrospective analysis of trabectedin infusion in an outpatient setting by Peripherally Inserted Central venous Catheters (PICC): A multicentric Italian experience”: Results of this trial suggest that Yondelis® infusion via PICC in an outpatient setting is safe and well accepted. PICC showed a preferable cost efficient ratio than PORT-chamber catheters in patients requiring a short standing of the device.

- “Efficacy of trabectedin for advanced soft tissue sarcoma: A retrospective single center analysis”, in which outcomes from patients with ASTS treated with Yondelis® from November 2006 to April 2012 in a Spanish center (Hospital Miguel Servet, Zaragoza) were retrospectively analysed. The results of this real-life retrospective analysis confirmed the findings of previous trials showing that trabectedin is an active drug in the treatment of ASTS.

Two other important abstracts to be presented during the congress refers to PM01183, one of PharmaMar's most promising compounds:

- “Lurbinectedin (PM01183) activity in platinum-resistant/refractory ovarian cancer patients: updated results of a randomized study”: this phase II trial demonstrated that PM01183 is superior in terms of overall response rate and progression free survival to topotecan in patients with platinum-resistant/refractory ovarian cancer. The compound's toxicity is predictable and manageable.

- “Lurbinectedin (PM01183) in combination with doxorubicin (DOXO): preliminary results of a phase Ib study”: this trial included patients in successive cohorts with the objective of defining PM01183's RD when combined with doxorubicin with or without prophylaxis using colony-stimulating factors (CSF). The RD is 4mg of PM01183 + 50mg/m² of doxorubicin. This combination is leading to impressive response rates, including 4 complete responses in patients with ovarian, breast and endometrial cancer and synovial sarcoma. The global activity has been remarkable in patients with second line small cell lung cancer (5 out of 8 patients with partial response, ORR=63%) and in patients with advanced endometrial cancer after one prior line for metastatic disease (one complete
response and one partial response, both still on-going, and one stabilization of 10 months out of the 3 patients included). The combination's toxicity is manageable and predictable.

Two trials with PharmaMar's newest compound, PM060184, will also be presented:

- "First-in-Man Phase I, Open-label, Dose-escalating Clinical and Pharmacokinetic Study of the Novel microtubule inhibitor PM060184 Administered over 10 Minutes on Days 1, 8, and 15 Every Four Weeks to Patients with Advanced Malignant Solid Tumors": the conclusion of this trial is that the compound is well tolerated and has a manageable safety profile at the recommended dose, defined as 12 mg/m². There was also evidence of activity in several tumor types, including 2 partial responses in cervix cancer and NSCLC.

- "Phase I, Open-label, Dose-escalating Clinical and Pharmacokinetic Study of the Novel microtubule inhibitor PM060184 Administered over 10 Minutes on Day 1 and 8 Every Three Weeks to Patients with Advanced Malignant Solid Tumors": the conclusion of this trial is that the compound is well tolerated and has a manageable safety profile at the recommended dose, defined as 9.3 mg/m². There has been evidence of activity in terms of tumour shrinkage and prolonged disease stabilizations in heavily pre-treated patients.

The European Society for Medical Oncology (ESMO) is the leading European professional organization, committed to advancing the specialty of medical oncology and promoting a multidisciplinary approach to cancer treatment and care. ESMO's mission is to advance cancer care through fostering and disseminating best scientific practices which lead to better clinical practice and medicine by evaluating the most relevant innovations arising each year in the field of oncology.

The 17th ECCO - 38th ESMO - 32nd European Cancer Congress ESTRO is organised in cooperation with ESSO 33, EACR, EONS and SIOPE. The European Cancer Congresses (ECC) are unique in Europe, offering an excellent multidisciplinary and multiprofessional educational opportunity in oncology and encouraging participation by all cancer specialties.
The ECC 2013 Scientific Programme will present cutting-edge advances and expertise in scientific and clinical research, patient management, and practices through scientific and educational symposiums, special sessions, instructional conferences, workshops, discussions, etc.

About PharmaMar

PharmaMar is a biopharmaceutical subsidiary of GrupoZeltia; 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. GrupoZeltia 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 company in molecular diagnostics based on DNA analysis; and 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.

For more information +34 91 444 4500

This note is also available on the PharmaMar website: www.pharmamar.com and at Zeltia's website: www.zeltia.com