PharmaMar presented 13 new studies at ASCO on four marine-derived antitumour compounds

Zeltia Group presented promising data on efficacy about YONDELIS® (trabectedin), Aplidin® (plitidepsin), Irvalec® (PM02734), and Zalypsis® (PM00104) at the 2009 ASCO Annual Meeting

Madrid, June 2nd, 2009: PharmaMar, a biopharmaceutical company of Zeltia Group (ZEL.MC), presented the results of 13 new studies on Yondelis® (trabectedin), Aplidin® (plitidepsin), Irvalec® (PM02734) and Zalypsis® at the American Society of Clinical Oncology (ASCO) Annual Meeting held in Orlando (Florida), May 29 – June 2.

Nine trials provide new data about Yondelis®, a novel anti-tumor agent of marine origin discovered in the Caribbean tunicate Ecteinascidia turbinate and now manufactured synthetically. In September 2007, it received marketing authorisation from the European Commission for the treatment of advanced or metastatic soft tissue sarcoma. In 2008, registration dossiers were submitted to the European Medicines Agency (EMEA) and Food and Drug Administration (FDA) for Yondelis® administered in combination with DOXIL®/Caelyx™ (pegylated liposomal doxorubicin, PLD) for the treatment of women with relapsed ovarian cancer.

According to analysis of data from phase III trial OVA-301, the combination of Yondelis® with PLD results in superior efficacy in patients with relapsed ovarian cancer with no added decrement to overall health status.

A prospective, international, randomized study evaluated two Yondelis® dosing regimens in adult patients with unresectable and/or metastatic liposarcoma or leiomyosarcoma following failure of prior anthracycline and ifosfamide chemotherapy. Final survival data identified the best Yondelis regimen associated with improved outcomes while maintaining an acceptable safety profile in this patient population.

New trials describe the role of Yondelis® as part of the management of advanced uterine leiomyosarcoma in patients with advanced sarcomas failing doxorubicin, in the rechallenge with trabectedin in patients of myxoid liposarcoma, and as neoadjuvant therapy in patients with advanced myxoid/round cell liposarcoma.
Two new studies will help identify what kind of patients at highest chance for response to Yondelis® treatment. According to a new Phase II trial presented at ASCO, Yondelis® shows a manageable safety profile in three groups of metastatic breast cancer patients with promising efficacy in certain DNA-repair machinery sub-categories defined molecularly.

PharmaMar also presented new data on Irvalec®, a new synthetic depsipeptide resulting from PharmaMar's internal investigation for obtaining derivatives of marine natural compounds. Preliminary in vitro studies identified Irvalec® as a new antiproliferative drug demonstrating activity against a broad spectrum of tumour types: breast, colon, pancreas, lung, and prostate, among others. Patients with metastatic or advanced solid tumors were enrolled in a phase I, open-label, dose-escalating study to assess safety, tolerability, pharmacokinetics as well as to identify the dose limiting toxicity and recommended dose. Irvalec® appears to be safe, well tolerated and shows evidence of activity in patients with advanced solid tumors. Irvalec® is currently in Phase II studies.

Separately, another phase I study has confirmed the Zalypsis® safety profile and its anti-tumor activity in patients with advanced malignancies. Zalypsis®, currently in Phase II studies, is a novel chemical entity related to the natural marine compound Jorumycine.

A multicenter phase IB study has shown promising results of Aplidin® alone or in combination with dacarbazine as a first-line treatment for advanced unresectable melanoma. A randomised phase II study of Aplidin® alone or with dacarbazine is currently in progress.

Data from the following studies were selected for oral presentation and posters:

**Preliminary safety and activity results of trabectedin in a phase II trial dedicated to triple-negative (ER-, PR-, HER2-), HER2+++, or BRCA1/2 germ-line-mutated metastatic breast cancer (MBC) patients (pts).**

**Author Block:** S. Delaloge, K. L. Tedesco, J. Blum, A. Gonçalves, J. Lubinski, N. Efrat, C. Osborne, C. Lebedinsky, J. C. Tercero, F. A. Holmes; Institut Gustave Roussy, Villejuif, France; US Oncology, New York Oncology Hematology, Albany, NY; Baylor Sammons Cancer Center, Texas Oncology, US Oncology, Dallas, TX; Institut Paoli-Calmettes, Marseille, France; International Hereditary Cancer Center, Szczecin, Poland; Kaplan Medical Center, Rehovot, Israel; PharmaMar, Colmenar Viejo, Madrid, Spain; US Oncology Research, Houston, TX.
Rechallenge with trabectedin in patients with responding myxoid liposarcoma.

**Author Block:** R. Sanfilippo, F. Grosso, E. Virdis, C. Morosi, J. C. Tercero, A. Gronchi, S. Pilotti, M. D'Incalci, P. G. Casali; Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; PharmaMar, Madrid, Spain; Istituto Mario Negri, Milan, Italy.

Trabectedin for advanced sarcomas failing doxorubicin: Analysis of 189 unreported patients in a compassionate use program.

**Author Block:** J. Blay, N. Penel, A. Italiano, F. Duffaud, M. Rios, O. Collard, F. Bertucci, N. Isambert, L. Chaigneau, P. Zintl; Centre Léon Bérard, Lyon, France; Centre Oscar Lambret, Lille, France; Institut Bergonié, Bordeaux, France; Hopital de la Timone, Marseille, France; Centre Alexis Vautrin, Nancy, France; Institut de Cancérologie de la Loire, Saint Etienne, France; Institut Paoli-Calmettes, Marseille, France; Centre Georges-François Leclerc, Dijon, France; CHU Besançon, Besançon, France; PharmaMar, Madrid, Spain

A phase II clinical trial of neoadjuvant trabectedin in patients with nonmetastatic advanced myxoid/round cell liposarcoma (MRCL).

**Author Block:** A. Gronchi, A. Le Cesne, N. B. Bui, E. Palmerini, G. Demetri, P. Hohenberger, R. J. Hohl, S. Pilotti, I. Perez, P. Lardelli; Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Institut Gustave Roussy, Paris, France; Institute Orthopedici Rizzoli, Bologna, Italy; Dana-Farber Cancer Institute, Boston, MA; Division of Surgical Oncology and Thoracic Surgery, Mann, Mannheim, Germany; University of Iowa, Iowa City, IA; PharmaMar, Madrid, Spain

Long-term results of a randomized phase II study of trabectedin by two different dose and schedule regimens in patients with advanced liposarcoma or leiomyosarcoma after failure of prior anthracyclines and ifosfamide

**Author Block:** G. D. Demetri, S. Schuetze, J. Blay, S. Chawla, M. von Mehren, P. Casali, D. Morris, E. Bayever, V. Alfaro, A. LeCesne; Dana-Farber Cancer Institute, Boston, MA; University of Michigan, Ann Arbor, MI; Centre Léon Bérard, Lyon, France; Sarcoma Oncology Center of Santa Monica, Santa Monica, CA; Fox Chase Cancer Center, Philadelphia, PA; Istituto Nazionale Tumori, Milan, Italy; Tom Baker Cancer Centre, Calgary, AB, Canada; Johnson & Johnson, New Brunswick, NJ; PharmaMar, Madrid, Spain; Institut Gustave Roussy, Paris, France

Role of trabectedin (T) in the management of advanced uterine leiomyosarcoma (U-LM).

**Author Block:** F. Grosso, R. Sanfilippo, R. L. Jones, P. Collini, C. Morosi, F. Raspagliesi, J. C. Tercero, M. D'Incalci, I. R. Judson, P. G. Casali; Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Royal Marsden Hospital, London, United Kingdom; PharmaMar, Madrid, Spain; Mario Negri Institute for Pharmacological Research, Milan, Italy
Plitidepsin alone or with dacarbazine (DTIC) as first-line treatment for advanced unresectable melanoma (AUM).

Author Block: R. Plummer, L. Hayward, P. Lorigan, V. Soriano, V. Moiseyenko, S. Szyldergemajn, R. Prados, J. Smyth, H. Calvert; Newcastle General Hospital, Northern Center for Cancer Treatment, Newcastle upon Tyne, United Kingdom; Western General Hospital, Edinburgh, United Kingdom; The Christie NHS Foundation Trust, Manchester, United Kingdom; Instituto Valenciano de Oncología, Valencia, Spain; Research Institute of Oncology named after Petrov, Saint Petersburg, Romania; PharmaMar, Madrid, Spain; Western General Hospital, Edinburgh, United Kingdom

Circulating tumor cells (CTC) in a study of relapsed/recurrent advanced ovarian cancer: An exploratory analysis in the ova-301 phase III study of pegylated liposomal doxorubicin (PLD) compared with trabectedin and PLD.

Author Block: A. Poveda, S. B. Kaye, R. T. McCormack, S. Wang, D. Ricci, E. Broderick, T. Parekh, C. Lebedinsky, J. C. Tecero, B. J. Monk; Instituto Valenciano de Oncología, Valencia, Spain; The Royal Marsden Hospital, Sutton, United Kingdom; Ortho Clinical Diagnostics, Raritan, NJ; Ortho Biotech Oncology Research & Development, Raritan, NJ; PharmaMar, Madrid, Spain; University of California Irvine Medical Center, Orange, CA

Correlation of CA-125 and RECIST evaluation in recurrent ovarian cancer (ROC): Results from a randomized phase III study of trabectedin (T) with pegylated liposomal doxorubicin (PLD) versus PLD alone.

Author Block: T. J. Herzog, J. B. Vermorken, E. Pujade-Lauraine, J. Li, E. Bayever, J. Gomez, A. Yovine, B. J. Monk; Columbia University Medical Center, New York, NY; University Hospital Antwerp, Antwerp, Belgium; Hôtel-Dieu, Paris, France; Johnson & Johnson PRD, USA, Raritan, NJ; PharmaMar, Colmenar Viejo, Madrid, Spain; University of California Irvine Medical Center, Orange, CA

Health-related quality of life/patient-reported outcomes in relapsed ovarian cancer: Results from a randomized phase III study of trabectedin with pegylated liposomal doxorubicin (PLD) versus PLD alone.

Author Block: C. N. Krasner, A. Poveda, T. Herzog, J. Vermorken, B. Monk, P. Zintl, J. Li, Y. Su, R. Dhawan, S. Kaye; Massachusetts General Hospital, Boston, MA; Fundación Instituto Valenciano de Oncología, Valencia, Spain; Columbia University Medical Center, New York, NY; Universitair Ziekenhuis Antwerpen, Edegem, Belgium; Chao Family Comprehensive Cancer Center UC, Orange, CA; PharmaMar, S.A., Madrid, Spain; Johnson & Johnson, Raritan, NJ; Royal Marsden Hospital, Sutton, United Kingdom
Phase I study of the novel anticancer drug PM00104 as a 24-hour IV infusion every 3 weeks (q3w) in patients (pts) with advanced solid tumors or lymphoma.

**Author Block:** J. Capdevila, S. Clive, J. Taberner, P. Lardelli, A. Soto-Matos, J. Baselga, A. Piera, I. Pardos, R. Rye, J. F. Smyth; Vall d'Hebron University Hospital, Barcelona, Spain; Western General Hospital Edinburgh, Edinburgh, United Kingdom; PharmaMar, Colmenar Viejo, Madrid, Spain

Phase I dose-escalating study of PM02734 in a 24-hour infusion schedule every 21 days in advanced solid tumors.

**Author Block:** T. R. Evans, A. Oaknin, R. J. Jones, A. Vandermeeren, C. Coronado, A. Soto-Matos, J. R. Germa, D. Crawford, P. Frontelo, R. Salazar; University of Glasgow, Glasgow, United Kingdom; Catalan Institute of Oncology, L'Hospitalet de Llobregat, Spain; PharmaMar, Colmenar Viejo, Madrid, Spain

Trabectedin phase II clinical trials: Pooled analysis of safety in patients with solid tumors.

**Author Block:** A. Cioffi, A. LeCesne, J. Blay, S. Delaloge, A. Yovine, R. Maki, A. Nieto, J. J. Jiao, G. D. Demetri; Institute of Cancerology Gustave Roussy, Villejuif, France; Centre Léon Bérard, Lyon, France; PharmaMar, Madrid, Spain; Memorial Hospital, New York, NY; Johnson & Johnson, Cambridge, MA; Dana-Farber Cancer Institute, Boston, MA

**PharmaMar**

PharmaMar is a biopharmaceutical company of the Spanish Zeltia Group committed to advancing the treatment of cancer through the discovery and development of new marine-derived drugs. PharmaMar has four new compounds in clinical development. Yondelis® has received marketing approval in the European Union for the treatment of advanced soft tissue sarcoma. Aplidin®, Zalypsis® and Irvalec® are new marine-derived agents in clinical development. PharmaMar also has two additional molecules in advanced preclinical development and an extensive portfolio of products in research and a robust R & D.

**For more information:**
**Media Relations (tel. +34 91 846 60 00)**
Fernando Mugarza

**Capital Markets (tel. + 34 91 444 45 00)**
Alfonso Hurtado de Mendoza - Florencia Radizza