



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

Colmenar Viejo (Madrid), December 15, 2017

Pursuant to article 228 of the consolidated text of the Spanish Securities Market Act, we hereby inform you of the following **SIGNIFICANT EVENT**:

“As expected in the announcement made by PharmaMar on November 8th (Significant Fact nº 258359), the Committee for Medicinal Products for Human Use (CHMP) has finally emitted its Opinion against the approval of the Marketing Authorization Application (MAA) of Aplidin® (plitidepsin), for the treatment of patients with relapsed multiple myeloma, in combination with dexamethasone. After the Opinion of the CHMP, the European Commission will be in charge of emitting the final verdict, which could arrive around March or April, 2018.

In this regards please find attached press release that Pharma Mar, S.A. will distribute to the media today”.

The CHMP confirms its earlier trend towards a negative vote for the commercialization of plitidepsin in Europe

- As expected after the Company announcement of the 8th of November, the Committee for Medicinal Products for Human Use (CHMP), belonging to the EMA, has emitted an opinion against the approval of Aplidin[®] for the treatment of multiple myeloma.

Madrid, December, 15, 2017. As expected in the announcement made by PharmaMar on November 8th, the Committee for Medicinal Products for Human Use (CHMP) has finally emitted its opinion against the approval of the Marketing Authorization Application (MAA) of Aplidin[®] (plitidepsin), for the treatment of patients with relapsed multiple myeloma, in combination with dexamethasoneⁱ.

After the opinion of the CHMP, the European Commission will be in charge of emitting the final verdict, which could arrive around March or April, 2018.

About APLIDIN[®] (plitidepsin)

Plitidepsin is an investigational anticancer agent of marine origin, originally obtained from the ascidian *Aplidium albicans*. It specifically binds to the eEF1A2 and targets the non-canonical role of this protein, resulting in tumor cell death via apoptosis (programed death). Plitidepsin is currently in clinical development for hematological cancers, including a Phase Ib trial in relapsed or refractory multiple myeloma as a triple combination of plitidepsin and bortezomib, and a Phase II in patients with multiple myeloma refractory to lenalidomida and bortezomib. Furthermore, a Phase II study in relapsed or refractory angioimmunoblastic T-cell lymphoma. A Phase III trial in multiple myeloma relapsed or refractory has been completed. Plitidepsin has received orphan drug designation in the European Union and the United States of America.

About multiple myeloma

Multiple myeloma is a relatively uncommon type of blood cancer, which accounts for 10% of all hematological malignancies, this being caused by malignant plasma cells that very rapidly multiplyⁱⁱ. Normal plasma cells are white blood cells, which form part of the immune system, found in the bone marrow that produce the antibodies necessary for fighting infectionsⁱⁱⁱ. Abnormal cells produce a type of antibody that does not benefit the body and accumulate, thus preventing normal cells from functioning properly. In 2015, 26,850 new cases were diagnosed in the US, and about 11,200 people died from this disease^{iv}. In Europe, the incidence is 4.5–6.0 out of 100 000 diagnosed per year^v.

About PharmaMar

Headquartered in Madrid, PharmaMar is a world-leading biopharmaceutical company in the discovery and development of innovative marine-derived anticancer drugs. The company has a pipeline of drug candidates and a robust R&D oncology program. PharmaMar develops and commercializes YONDELIS[®] in Europe and has other clinical-stage programs under development for several types of solid and

hematological cancers, Zepsyre™ (PM1183), plitidepsin, PM184 and PM14. PharmaMar is a global biopharmaceutical company with subsidiaries in Germany, Italy, France, Switzerland, United Kingdom, Belgium, Austria and the United States. PharmaMar fully owns other companies: GENOMICA, a leading molecular diagnostics company; Sylentis, dedicated to researching therapeutic applications of gene silencing (RNAi); and two other chemical enterprises, Zelnova Zeltia and Xylazel. To learn more about PharmaMar, please visit us at www.pharmamar.com.

Disclaimer

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.

Media Contact:

Alfonso Ortín – Communications Director aortin@pharmamar.com Mobile: + 34609493127
Paula Fernández – Media Relations Manager pfalarcon@pharmamar.com Mobile: +34 638796215
Phone: +34 918466000



Investor Relations:

Phone: +34 914444500

Or please visit our website at www.pharmamar.com

ⁱ <https://www.pharmamar.com/wp-content/uploads/2017/11/HR-ENG-8-NOV-2017.pdf>

ⁱⁱ <http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-what-is-it>

ⁱⁱⁱ <http://www.myeloma.org.uk/information/what-is-myeloma/>

^{iv} <http://seer.cancer.gov/statfacts/html/mulmy.html>

^v <http://www.esmo.org/Guidelines/Haematological-Malignancies/Multiple-Myeloma>