



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

Colmenar Viejo (Madrid), January 3, 2018

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

“In relation to the Significant Fact n. 259611 dated December 15th, 2017, Pharma Mar, S.A. informs that it has requested the initiation of the process of re-examination from the European Medicines Agency (EMA) for Aplidin® (plitidepsin) for the indication of relapsed and refractory multiple myeloma. It is worth noting that the re-examination procedure is handled by the EMA’s CHMP (Committee for Medicinal Products for Human Use) and usually lasts around 4 months. It concludes with either the confirmation of the previous negative Opinion or with the issuing of a new positive Opinion by the CHMP. After finalizing this process of re-examination, the European Commission will be in charge of emitting the final verdict on the Marketing Authorization Application for Aplidin® (plitidepsin), which could arrive around June or July, 2018.

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



PharmaMar has requested the process of re-examination for Aplidin® from the EMA

Madrid, January, 3rd, 2018. PharmaMar (MSE:PHM) has announced the initiation of the re-examination process by the European Medicines Agency (EMA) for Aplidin® (plitidepsin) for the indication of relapsed and refractory multiple myeloma.

PharmaMar believes this novel molecule that could become part of the therapeutic arsenal available for the treatment of multiple myeloma in Europe.

It is worth noting that the re-examination procedure is handled by the EMA's CHMP and usually lasts around 4 months. It concludes with either the confirmation of the negative opinion or with the issuing of a new positive opinion by the CHMP.

After finalizing this process of re-examination, the European Commission will be in charge of emitting the final verdict on the Marketing Authorization Application (MAA) for Aplidin® (plitidepsin), which could arrive around June or July, 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 multiplyⁱ. 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 infectionsⁱⁱ. 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 diseaseⁱⁱⁱ. In Europe, the incidence is 4.5–6.0 out of 100 000 diagnosed per year^{iv}.

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.

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

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

ⁱⁱⁱ <http://seer.cancer.gov/statfacts/html/mulmy.html>

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