CNMV
Markets Directorate General
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In accordance with article 227 of the recast Spanish Securities Market Act (*texto refundido de la Ley del Mercado de Valores*), approved by Royal Legislative Decree 4/2015, of 23 October, and related provisions, is hereby reported the following:

OTHER RELEVANT INFORMATION

The Company announces that it has obtained the authorization from the Spanish Agency for Medicines and Health Products (AEMPS) to initiate the Phase III NEPTUNO clinical trial, which will determine the efficacy of plitidepsin for the treatment of hospitalized patients with moderate COVID-19 infection.

Please find attached press release that will be distributed to the media today.

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PharmaMar receives authorization to initiate the Phase III NEPTUNO clinical trial with plitidepsin for the treatment of COVID-19

- **The Spanish Agency for Medicines and Health Products (AEMPS) has led the Voluntary Harmonization Procedure (VHP), in which several European countries will participate.**
- **The rest of the countries participating in the VHP procedure will adhere to the authorization as soon as their regulatory agencies ratify it.**
- **The efficacy of plitidepsin will be evaluated in comparison with the standard of care authorized in each country.**

Madrid, April 29th, 2021. – PharmaMar (MSE:PHM) has announced today that it has obtained the authorization from the Spanish Agency for Medicines and Health Products (AEMPS) to initiate the Phase III NEPTUNO clinical trial, which will determine the efficacy of plitidepsin for the treatment of hospitalized patients with moderate COVID-19 infection.

This authorization has been obtained through the European Union's Voluntary Harmonization Procedure (VHP) for clinical trials. This allows the simultaneous evaluation of the clinical study by the respective national authorities. The rest of the countries participating in this procedure (France, Portugal and Sweden) will adhere to the authorization as soon as their regulatory agencies ratify it.

This is in addition to the authorization already received from the British Medicines and Healthcare products Regulatory Agency (MHRA).

Both the protocol design of this trial and its authorization by the regulatory authorities are based on the scientific evidence of safety and efficacy obtained in the Phase I-II APLICOV-PC trial with plitidepsin for the treatment of patients with COVID-19, along with all the data from the 1,300 patients already treated with plitidepsin in other indications.

The primary objective of the study is to compare plitidepsin versus the standard of care authorized in each country (dexamethasone or dexamethasone plus remdesivir). The primary endpoint will be the percentage of patients who achieve complete recovery by day 8 (±1), and who are not re-admitted for COVID-19 infection after 31 days.

This is a Phase III, multicenter, randomized, controlled, clinical trial, to determine the efficacy and safety of two dose levels of plitidepsin compared to the standard of care in adult patients requiring hospitalization for the medical treatment of moderate COVID-19 infection. This trial expects to enroll more than 600 patients. In addition to Europe, the trial will be opened in several countries around the world, as the corresponding regulatory authorizations are obtained.

In January, the journal Science published a research article entitled "***Plitidepsin has potent preclinical efficacy against SARS-CoV-2 by targeting the host protein eEF1A***". The paper states that "the antiviral activity of plitidepsin against SARS-CoV-2 is mediated through inhibition of the known target eEF1A" and mentions that *in vitro*, plitidepsin showed strong anti-viral potency compared to other anti-virals against SARS-CoV-2, with a good therapeutic window. In two different animal models of SARS-CoV-2 infection, the trial demonstrated a reduction of viral replication, resulting in a 99% reduction of viral loads in the lungs of plitidepsin-treated animals.

Plitidepsin acts by blocking the eEF1A protein, which is present in human cells and is used by SARS-CoV-2 to replicate and infect other cells. This blockade prevents the virus from reproducing inside the cell, making it unviable, and preventing it from spreading to other cells.

About PharmaMar

PharmaMar is a biopharmaceutical company focused on the research and development of new oncology treatments, whose mission is to improve the healthcare outcomes of patients afflicted by serious diseases with our innovative medicines. The Company is inspired by the sea, driven by science, and motivated by patients with serious diseases to improve their lives by delivering novel medicines to them. PharmaMar intends to continue to be the world leader in marine medicinal discovery, development and innovation.

PharmaMar has developed and now commercializes Yondelis® in Europe by itself, as well as Zepzelca® (lurbinectedin), in the US; and Aplidin® (plitidepsin), in Australia, with different partners. In addition, it

has a pipeline of drug candidates and a robust R&D oncology program. PharmaMar has other clinical-stage programs under development for several types of solid cancers: lurbinectedin, PM184 and PM14. Headquartered in Madrid (Spain), PharmaMar has subsidiaries in Germany, Italy, France, Switzerland, Belgium, Austria and the United States. PharmaMar also wholly owns other companies: GENOMICA, a molecular diagnostics company; and Sylentis, dedicated to researching therapeutic applications of gene silencing (RNAi). To learn more about PharmaMar, please visit us at www.pharmamar.com.

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