



Life Science Alliance journal publishes results of plitidepsin in patients with COVID-19, which includes additional data on its antiviral activity against Delta and Omicron variants

- The final results of the APLICOV-PC study (Phase I-II), which were initially released last May and which the Company shared with the scientific community, demonstrate the safety of plitidepsin's use in patients with COVID-19 and postulate a positive therapeutic impact on the evolution of the disease.
- PharmaMar confirms *in vitro* activity of plitidepsin against several variants, including Delta and Omicron.
- The Life Science Alliance journal is co-founded by the Rockefeller University, the European Molecular Biology Organization (EMBO) and Cold Spring Harbor Laboratory.

Madrid, January 11th, 2022. - PharmaMar (MSE:PHM) has announced today the publication of an article in the Life Science Alliance journal, entitled "**Pre-clinical and randomized phase I studies of plitidepsin in adults hospitalized with COVID-19,**" which includes a study on the *in vitro* activity of plitidepsin against the main SARS-CoV-2 variants, including the current Omicron variant.

According to the final data published in this article, plitidepsin has been shown to have a potent antiviral activity in all variants at very low (nanomolar) concentrations, with a positive *in vitro* therapeutic index. These studies were led by Dr. Adolfo Garcia-Sastre, Professor in the Department of Microbiology at the Icahn School of Medicine at Mount Sinai, New York, N.Y., USA.

Laboratory *in vivo* studies have also demonstrated a preferential distribution of plitidepsin to lung tissue, which is the organ primarily affected in patients with COVID-19. These studies showed a reduction in viral replication, resulting in a 99% decrease in viral loads in the lung of plitidepsin-treated animals.



The article also reviews data from the APLICOV-PC clinical trial, which demonstrated the safety of plitidepsin in patients with COVID-19 requiring hospital admission. The trial met the primary safety endpoint and showed clinical efficacy; in addition the study gathered consistent evidence of a plitidepsin mediated impact on viral load, on inflammatory pathways and on lymphopenia normalization.

In this Phase I-II study, 45 patients were enrolled, of whom 86.7% had moderate or severe disease. 41 patients (91%) had pneumonia, 32 (71% of the global sample) of them with bilateral pneumonia. Of note were the data observed in 23 patients with moderate disease, 74% of whom were discharged from hospital within the first week of treatment.

These results are the basis for the Phase III NEPTUNO clinical trial that is currently recruiting patients in 17 hospitals in Spain and 9 other countries mainly in Europe and Latin America.

José F. Varona, M.D., Ph.D., at the Department of Internal Medicine, Hospital Universitario HM Montepíncipe in Madrid has highlighted “our clinical impression with plitidepsin in the APLICOV-PC trial has been met, since in addition to satisfactorily meeting the safety objectives, we have observed in some cases an improvement in symptoms and objective data (microbiological parameters, oximetry parameters and radiological parameters) after administration of the drug.”

Adolfo García-Sastre, Ph.D., professor at the Department of Microbiology at the Icahn School of Medicine at Mount Sinai, New York, commented, “It is noteworthy that the clinical data are consistent with the preclinical data, suggesting a benefit of plitidepsin administration to patients with COVID-19, and that, in pre-clinical models, plitidepsin has potent antiviral activity, not only for SARS-CoV-2 and its variants, including Delta and Omicron, but also against other coronaviruses.”

José María Fernández Sousa-Faro, Ph.D., PharmaMar's Chairman stated “all the data we have seen so far with plitidepsin corroborate our initial hypothesis about its antiviral activity. In studies conducted both by PharmaMar and leading researchers from around the world, plitidepsin has demonstrated previously unseen potency against SARS-CoV-2. We hope that patient recruitment for the NEPTUNO trial will



continue to progress, so that we can bring this treatment to all patients affected by the coronavirus and requiring hospitalization, as soon as possible. ”

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About Life Science Alliance

Life Science Alliance is a global, open-access, editorially independent, and peer-reviewed journal founded by an alliance of EMBO Press, Rockefeller University Press, and Cold Spring Harbor Laboratory Press. Life Science Alliance is committed to rapid, fair, and transparent publication of valuable research from across all areas in the life sciences. Papers published in Life Science Alliance meet high scientific and editorial standards established by the alliance partners. Life Science Alliance welcomes new results, community resources such as datasets, screens, and new methods as well as important confirmatory, negative, and refuting data.

About PharmaMar

Headquartered in Madrid, PharmaMar is a biopharmaceutical company, focused on oncology and committed to research and development which takes its inspiration from the sea to discover molecules with antitumor activity. It is a company that seeks innovative products to provide healthcare professionals with new tools to treat cancer. Its commitment to patients and to research has made it one of the world leaders in the discovery of antitumor drugs of marine origin.

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

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