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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 reports that the publication titled "***Plitidepsin has potent preclinical efficacy against SARS-CoV-2 by targeting the host protein eEF1A***" has been published in Science. This publication has been the result of a collaboration between Pharma Mar and the laboratories of Kris White, Adolfo García-Sastre and Thomas Zwaka, at the Departments of Microbiology and of Cell, Regenerative and Developmental Biology, in the Icahn School of Medicine; of Kevan Shokat and Nevan Krogan, at the Quantitative Biosciences Institute of the University of California San Francisco, and of Marco Vignuzzi at the Institute Pasteur of Paris.

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

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The Peer Review journal *Science* confirms the potent activity of PharmaMar's plitidepsin against SARS-CoV-2

- **The trial demonstrated a reduction of viral replication, resulting in a 99% reduction of viral load.**
- **Antiviral efficacy and toxicity profile are encouraging in both *in vitro* and *in vivo* experiments.**
- **Authors conclude that plitidepsin is the most potent compound, and should be tested in expanded clinical trials for the treatment of COVID-19.**

Madrid, January 26th, 2021. – PharmaMar (MSE:PHM) has announced today that the publication titled "***Plitidepsin has potent preclinical efficacy against SARS-CoV-2 by targeting the host protein eEF1A***" has been published in Science. This publication has been the result of a collaboration between PharmaMar and the laboratories of Kris White, Adolfo García-Sastre and Thomas Zwaka, at the Departments of Microbiology and of Cell, Regenerative and Developmental Biology, in the Icahn School of Medicine; of Kevan Shokat and Nevan Krogan, at the Quantitative Biosciences Institute of the University of California San Francisco, and of Marco Vignuzzi at the Institute Pasteur of Paris.

The paper comments that "the antiviral activity of plitidepsin against SARS-CoV-2 is mediated through inhibition of the known target eEF1A" and notes that *in vitro* plitidepsin showed strong anti-viral potency, compared to other anti-virals against SARS-CoV-2, with limited toxicity. Here, in two different animal models of SARS-CoV-2 infection,

the trial demonstrated reduction of viral replication, resulting in a 99% reduction of viral loads in the lung of plitidepsin-treated animals.

The manuscript also states that while toxicity is a concern with any host-targeted antiviral, the safety profile of plitidepsin is well established in humans, and that the well tolerated doses of plitidepsin used in the COVID-19 clinical trial are significantly lower than those used in these experiments.

The publication concludes that "this study establishes plitidepsin as a host-targeted anti-SARS-CoV-2 agent with *in vivo* efficacy. We believe that our data and the initial positive results from PharmaMar's clinical trial suggests that plitidepsin should be strongly considered for expanded clinical trials for the treatment of COVID-19."

As COVID-19 is continuing to spread around the world and growing desperation for treatments, UCSF's QBI (Quantitative Biosciences Institute) Director **Nevan Krogan, Ph.D.**, in 2020 joined forces with researchers at UCSF, Gladstone Institute, Icahn School of Medicine at Mount Sinai, Institut Pasteur, and Howard Hughes Medical Institute to apply their expertise to aid in finding a treatment for the growing pandemic. Together, this group of researchers now known as QBI Coronavirus Research Group (QCRG), were the first to extensively map out the genome of COVID-19 and discover that the virus interacts with 332 human host proteins. These researchers form the nexus of the experiments cited in the paper.

Adolfo García-Sastre, Ph.D., is Professor in the Department of Microbiology and Director of the Global Health Emerging Pathogens Institute, Icahn School of Medicine at Mount Sinai, New York, USA. He is also the Principal Investigator of one of the NIH funded Centers of Excellence for Influenza Research and Surveillance, and a member of

the Royal Academy of Pharmacy in Spain, and of the National Academy of Sciences in USA. Since the discovery of the causative agent of COVID-19, his lab has been at the forefront of studies on the molecular biology, pathogenesis, treatment and prophylaxis of SARS-CoV-2 infections.

Kris M. White, Ph.D., is an Assistant Professor in the Department of Microbiology, Icahn School of Medicine at Mount Sinai, New York, USA. Throughout the pandemic, his lab has been focused on repurposing of clinically-approved drugs from other indications to treat COVID-19. This has allowed for COVID-19 clinical trials to begin within months, rather than years. His work has also given important mechanistic insights into how these novel antivirals exert their inhibitory effects and should benefit the scientific community in the development of future SARS-CoV-2 antiviral agents.

Nevan J. Krogan, **Ph.D.**, is a professor in the Department of Cellular and Molecular Pharmacology at the University of California San Francisco, commented "*Our work studying the host response to SARS-CoV-2 infection over the past ten months has led us to a number of drugs and compounds that we feel are great candidates for COVID-19. By far the most potent has been plitidepsin in multiple systems and it has been a great pleasure to work with PharmaMar over this time to try and get this drug into humans for the treatment of COVID-19.*"

Adolfo García-Sastre, Ph.D., Professor in the Department of Microbiology at the Icahn School of Medicine at Mount Sinai commented "*Of all the SARS-CoV-2 inhibitors that we have been characterizing in tissue culture and animal models since we started our studies with SARS-CoV-2, plitidepsin has been the most potent one, underscoring its potential as a therapeutic for the treatment of COVID-19.*"

Kris M. White, Ph.D., Assistant Professor in the Department of Microbiology, Icahn School of Medicine at Mount Sinai commented "*Plitidepsin is an extremely potent inhibitor of SARS-CoV-2, but its most important strength is that it targets a host protein rather than a viral protein. This means that if plitidepsin is successful in the treatment of COVID-19, the SARS-CoV-2 virus will be unable to gain resistance against it through mutation, which is a major concern with spread of the new UK and South African variants.*"

PharmaMar is discussing with different regulatory agencies the start of the anticipated Phase III trials.

Science has been a journal of AAAS (American Association for the Advancement of Science) since 1880, publishing the very best in research across the sciences, with articles that consistently rank among the most cited in the world. *Science* is striving to provide the best and timeliest research, analysis, and news coverage of COVID-19 and the coronavirus that causes it. All related content is free to access.

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™ (lurbinectedin, PM1183), PM184 and PM14. 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 www.pharmamar.com.

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