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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*), is hereby reported the following:

OTHER RELEVANT INFORMATION

Sylentis, S.A.U., a wholly owned subsidiairy of Pharma Mar, has announced today the initiation and enrollment of the first patient in the United States in a new Phase III trial to evaluate the long-term safety of tivanisiran for the treatment of the signs and symptoms of dry eye disease.

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

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Sylentis, a wholly owned subsidiary of PharmaMar, initiates a new Phase III trial in the United States to evaluate the safety of tivanisiran in patients with dry eye disease

- **This Phase III study, called FYDES, will involve 26 hospitals in the United States.**
- **It will evaluate the long-term safety of tivanisiran ophthalmic solution in patients with mild to severe dry eye disease.**
- **The study has been authorized by the FDA and will be part of the New Drug Application.**

Madrid, April 1st, 2022. – Sylentis, a wholly owned subsidiairy of PharmaMar (MSE:PHM), has announced today the initiation and enrollment of the first patient in the United States in a new Phase III trial to evaluate the long-term safety of tivanisiran for the treatment of the signs and symptoms of dry eye disease.

This is a multicenter, randomized study in which approximately 300 patients in around 26 centers with mild to severe dry eye disease will be enrolled to either tivanisiran or placebo. The primary endpoint of the trial is to evaluate the safety of tivanisiran administered in both eyes, once daily for 1 year in the form of eye drops. In addition, efficacy parameters (signs and symptoms) of these patients will be evaluated.

The long-term safety study design has been cleared by the FDA and will be part of the New Drug Application (NDA), which consists of three trials: a Phase III initial efficacy trial, which started in2021; the ongoing long-term safety trial and, finally, a third confirmatory efficacy trial.

Tivanisiran represents a novel approach whose mechanism of action is based on gene silencing RNA interference (RNAi). It is a compound administered in drops for the control of the characteristic signs and symptoms of dry eye disease.

Dry eye disease is a pathology that affects more than 300 million people worldwide and for which the available therapeutic options are currently very limited. This disease is one of the most frequent causes of consultation to the ophthalmologist and occurs when the eye does not produce tears correctly, or when they do not have the necessary consistency and evaporate very quickly. It especially affects people in developed countries, where pollution, air conditioning, the use of contact lenses, refractive surgery or the continuous use of computers are major risk factors. Some of the most notorious symptoms of the pathology are pain, burning, incessant itching, eye fatigue, dryness, blurred vision, sensitivity to light or the sensation of having a foreign body within the eye.

Explanatory videos:

What is RNA interference?

Legal warning

This press release does not constitute an offer to sell or the solicitation of an offer to buy securities, and shall not constitute an offer, solicitation or sale in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of that jurisdiction.

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 and ecubectedin. Headquartered in Madrid (Spain), PharmaMar has subsidiaries in Germany, France, Italy, Belgium, Austria, Switzerland 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.

About Sylentis

Sylentis is a biotechnology company fully owned that develops innovative therapies harnessing the technology of post-transcriptional gene silencing or RNA interference (RNAi). Sylentis has developed an approach to efficiently design RNAi-based therapeutics that can be used to silence numerous disease-causing genes. We currently have a robust therapeutic program in ophthalmology with two candidates under development in Phase II and III studies for glaucoma (bamosiran) and ocular pain (SYL1001), respectively. Sylentis is also developing new products for the treatment of several eye diseases such as ocular allergies and retina diseases. To know more about us, please visit us at www.sylentis.com.

About tivanisiran (SYL1001)

Tivanisiran is a drug based on RNAi that is administered as preservative-free eye drops; it selectively inhibits production of the transient receptor potential cation channel (TRPV1). These receptors are ion channels that mediate the transmission of ocular pain. Tivanisiran is a small synthetic double-stranded RNA oligonucleotide (siRNA) with a novel and highly selective mechanism of action. Non-clinical studies conducted by Sylentis with SYL1001 have demonstrated it has high ability to inhibit this specific target and block the perception of ocular pain in animals.

Tivanisiran is a product under development for the treatment of signs and symptoms related to dry eye syndrome and has the potential to be developed for other pathologies that cause ocular pain (corneal lesions, refractive surgery, etc.).

About RNA interference (RNAi)

RNA interference (RNAi) is a natural cellular process that regulates the expression of certain genes, providing a role in innate defense and development in animals and plants. This process is used to specifically silence genetic transcripts that encode protein-causing diseases. The therapeutic application of targeted siRNAs is booming given the specificity of gene silencing for a particular protein in a given tissue and the lack of side effects. This new approach to drug discovery is a promising technology that is rapidly moving in the translational research space.

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