CNMV
Markets Directorate General
C/ Edison núm. 4
28006 Madrid

Madrid, December 18, 2023

In accordance with the provisions of article 227 of the Spanish Securities Markets and Investment Services Act (*Ley de los Mercados de Valores y de los Servicios de Inversión*), approved by Law 6/2023, of 17 March, and concordant provisions, is hereby reported the following:

OTHER RELEVANT INFORMATION

Sylentis, S.A.U., a wholly owned subsidiairy of Pharma Mar, announces that the FYDES study to evaluate the safety of tivanisiran in patients with dry eye disease has met its primary endpoint. This clinical trial was conducted at 26 centers in the United States and involved 301 patients.

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

Pharma Mar S.A.
Avda. de los Reyes, 1
P.I. La Mina
28770 Colmenar Viejo
(Madrid) Spain
www.pharmamar.com

Sylentis, a PharmaMar Group company, announces the FYDES study to evaluate the safety of tivanisiran in patients with dry eye disease has met its primary endpoint

- **FYDES achieved the primary endpoint of the study by demonstrating the long-term safety of tivanisiran ophthalmic solution administration.**
- **301 patients with dry eye disease recruited from 26 centers in the United States participated.**

Madrid, December 18th, 2023. – Sylentis, a wholly owned subsidiary of PharmaMar (MSE:PHM), has obtained the results of the FYDES clinical trial to evaluate the long-term safety of tivanisiran as eye drops for the treatment of adults with dry eye disease. This clinical trial was conducted at 26 centers in the United States and involved 301 patients.

FYDES is a Phase III, randomized, placebo controlled, multicenter study, in which the safety of tivanisiran sodium ophthalmic solution was evaluated after being administered to patients with dry eye disease, once daily for approximately 360 days.

The FYDES safety study is part of the tivanisiran development plan along with the SYL1001_V efficacy study in patients with dry eye disease associated with Sjögren's Syndrome and whose results will be available in the first quarter of 2024.

Of the 301 patients randomized, 203 were assigned to the tivanisiran group and 98 to the control arm (2:1 ratio).

Analysis of the primary endpoint showed that the overall frequency and percentage of patients experiencing at least one adverse event (ocular or non-ocular, related or unrelated) was similar in both treatment groups: 40.4% in the tivanisiran group and 39.8% in the control arm.

The only adverse events related to tivanisiran were conjunctival hyperemia (1%), eye pruritus (1%), papillary conjunctivitis (0.5%) and blurred vision (0.5%).

After one year of treatment, no clinically significant changes in other ocular safety parameters, laboratory values or body temperature have been observed. At upcoming medical meetings additional data and analyses will be submitted for presentation.

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 air 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 foreign body sensation.

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 and with different partners. Zepzelca® (lurbinectedin) in the US and Aplidin® (plitidepsin) in Australia under different partner agreements. 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, ecubectedin, PM534 and PM54. It also has a preclinical and clinical program in virology. Headquartered in Madrid (Spain), PharmaMar has subsidiaries in Germany, France, Italy, Belgium, Austria, Switzerland and The United States. PharmaMar also wholly owns Sylentis, a company 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 pharmaceutical company that develops innovative therapies based on gene silencing technologies or RNAi. This technology enables the design of molecules capable of selectively inhibiting the synthesis of disease-causing proteins. Sylentis has developed numerous therapies based on this novel technology and currently has a strong program in ophthalmology with one candidate in Phase III clinical trials: tivanisiran, for the treatment of dry eye. Sylentis is also researching and developing other new products for the treatment of various eye diseases such as ocular allergies and retinal diseases. For more information, visit 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 tivanisiran have demonstrated it has a 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 is a technology that seeks to reduce abnormal protein production by silencing messenger RNA. RNAi represents a breakthrough as a new mechanism of action to address numerous pathologies. Some pathologies, such as age-related macular degeneration, are caused by an alteration of certain proteins. This technology can act by reducing or controlling in a very specific way the production of the proteins involved in each pathology. Compounds based on RNAi technology tend to have a longer effect than traditional drugs and few side effects, due to their high specificity.

Media Contact:

Lara Vadillo – Communication Director lvadillo@pharmamar.com
Miriam Collados Gordo – Corporate Communication Manager mcollados@pharmamar.com
Phone: +34 918466000

Capital Markets & Investor Relations:

José Luis Moreno– VP, Capital Markets & Investor Relations Director
Natalia Amo – Capital Markets & Investor Relations
investorrelations@pharmamar.com
Phone: +34 914444500

Or please visit our website at www.pharmamar.com