Pursuant to Article 17 of Regulation (EU) nº 596/2014 on market abuse and Article 228 of the consolidated text of the Spanish Securities Market Act, approved by Royal Legislative Decree 4/2015, of 23 October, we hereby make the following REGULATORY ANNOUNCEMENT:

"Find attached press release that Pharma Mar, S.A. will distribute to the media where Pharma Mar announces that the Phase III trial HELIX, which is conducted by Sylentis, S.A.U. (Pharma Mar’s subsidiary) for the treatment of the signs and symptoms of dry eye disease, has reached the number of 300 patients recruited."

In Madrid, on 19 October 2018
Sylentis, PharmaMar Group, announces the end of patient recruitment for its HELIX trial

- Sylentis has reached the target of recruiting patients for its Phase III trial "HELIX" for the treatment of the signs and symptoms of dry eye disease.
- We estimate that the results of the trial will be available in the first four months of 2019.

Madrid, October 19th, 2018.- Sylentis, PharmaMar Group (MSE:PHM), has announced today that it has reached its target of recruiting 300 patients for the Phase III trial "HELIX" for the treatment of the signs and symptoms of dry eye disease.

We estimate that the results of the trial will be available in the first four months of 2019.

The primary endpoint of this study is to evaluate the effect of tivanisiran, administrated in ophthalmic drops, on the signs and symptoms of patients with this pathology, for which therapeutic options are currently limited. The HELIX trial enrolled 329 patients which have been recruited in 39 centers in 6 European countries: Spain, Germany, Estonia, Portugal, Slovakia and Italy.

"Completing recruitment for the HELIX trial is an important milestone in the development of tivanisiran for the treatment of dry eye disease. We have confidence in our technology, which is new in its field, and we hope that tivanisiran can become an alternative for treating the millions of people who suffer from dry eye in the world", says Ana Isabel Jiménez, COO of Sylentis.

Sylentis presented results from previous phase II study of tivanisiran during the Annual Congress of the Association for Research in Vision and Ophthalmology (ARVO), which was held from April 29 to May 3 in Honolulu, Hawaii. The poster presented, "Tivanisiran, a new treatment for Dry Eye Disease, that improved signs and symptoms in clinical trials", showed the drug's impact on inflammatory eye parameters, tear quality, and saw a reduction in eye pain associated with dry eye.

The mechanism of action of tivanisiran is based on RNA interference technology (RNAi), thus acting by blocking the synthesis of the transient receptor potential cation channel (TRPV1), involved in dry eye disease.
Tivanisiran, administered in the form of ophthalmic drops, is directed to the treatment of signs and symptoms of this pathology and its novel mechanism of action positions it as a potential treatment of dry eye disease.

**About dry eye syndrome**

This disease occurs when the eye does not produce tears correctly or when the tears do not have the necessary consistency and evaporate very quickly\(^2\). It especially affects populations in developed countries, where factors such as pollution, air conditioning, the use of contact lenses, refractive surgery operations or the continued use of computers are the main causes. The most noticeable symptoms of the pathology are burning, incessant itching, eye fatigue, dryness, blurred vision, sensation of a foreign body or pain\(^3\), among others.

In our country, 1 out of 5 visits to the ophthalmologist are motivated by this problem. In fact, more than 5 million people in Spain suffer from this condition, which represents between 10% and 20% of the population. The most common profile are mostly women over the age of 40\(^4\) and practically 100% of the elderly. Globally, the number of people affected by dry eye is 344 million.

**Learn more about the clinical trial:**

**Explanatory videos:**
What is RNA interference?  [https://youtu.be/T21N_dPM0_k](https://youtu.be/T21N_dPM0_k)
Dry Eye Syndrome:  [https://youtu.be/R-h_4_Yyq2g](https://youtu.be/R-h_4_Yyq2g)

**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**
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\(^\circledR\) in Europe and has other clinical-stage programs under development for several types of solid cancers: 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); and a chemical enterprise, Zelnova Zeltia. To learn more about PharmaMar, please visit us at www.pharmamar.com.

About Sylentis
Sylentis is a pharmaceutical company that develops innovative therapies using gene silencing or RNAi technologies. This technology allows 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 solid program in ophthalmology with a candidate in a Phase III clinical trial: tivanisirán, for the treatment of dry eye; and another in Phase II: bamosiran, for the treatment of glaucoma. Sylentis also researches and develops other new products for the treatment of different ocular diseases such as ocular allergies and retinal diseases. For more information visit www.sylentis.com.

About tivanisirán (SYL1001)
SYL1001 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. SYL1001 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.

SYL1001 is a product undergoing development for the signs and symptoms related to dry eye syndrome, and has 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 animal 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.

Media Contact:
Alfonso Ortín – Communications Director aortin@pharmamar.com Mobile: +34 609493127
Miguel Martínez-Cava – Digital Communication Manager mmartinez-cava@pharmamar.com Mobile: +34 606597464
Phone: +34 918466000

Investor Relations:
Phone: +34 914444500 / +34 902 10 19 00
Email: investorrelations@pharmamar.com


