

Zeltia announces that subsidiary Sylentis has attained the primary endpoint of the Phase IIa clinical trial with its compound SYL040012.

- *SYL040012 is a novel compound arising from Sylentis's research in ophthalmological disorders.*
- *It is indicated for treating ocular hypertension associated with glaucoma.*
- *SYL040012 is a chemical entity under the heading of interference RNA (RNAi).*
- *Sylentis is one of only five companies in the world with RNAi-based products undergoing clinical trials.*

Madrid, 7 June 2013: Sylentis, a biopharmaceutical subsidiary of Grupo Zeltia (MC: ZEL) and a pioneer in the research and development of new drugs based on gene silencing (interference RNA, RNAi), has attained the primary endpoint of its Phase IIa clinical trial with SYL040012.

This trial evaluated the safety of SYL040012 on the eye surface and its effect on intraocular pressure following a daily dose for 14 days in patients with ocular hypertension or open-angle glaucoma. The three doses analysed in the trial were well-tolerated both locally (cornea and conjunctiva) and systemically, and they reduced intraocular pressure. The 300 microgram dose of SYL040012 was found to produce a statistically significant reduction in intraocular pressure with respect to the placebo.

The next clinical trial will be planned once all of the trial's variables have been analysed.

The Phase IIa multicentre, randomised, parallel-group, placebo-controlled, masked trial was performed in Spain, Estonia and Germany. The preceding Phase I trial on this molecule's tolerance and safety showed that it was safe when administered under the trial conditions. The results of that trial were presented at the 7th Conference of the Spanish Society for Glaucoma.

The endpoint of the Phase IIa trial was to evaluate tolerance and the effect of a range of doses of the drug on 80 patients with ocular hypertension or glaucoma in the three countries. This is Sylentis's fourth clinical trial using RNAi-based products, evidencing the



company's commitment to developing innovative compounds to treat eye diseases. Sylentis is the first company in Spain and one of only five companies in the world with RNAi-based products in clinical trials.

The company has another compound, SYL1001, which has completed a Phase I clinical trial in eye discomfort associated with dry eye syndrome.

About SYL040012

In preclinical trials with SYL040012, the siRNAs administered topically to treat ocular hypertension associated with open-angle glaucoma have proven effective in vivo. These trials concluded that the model of transient hypertension induced by fluid overload is valid for evaluating the efficacy of different drugs on glaucoma since it does not produce alterations in the various ocular structures. These trials showed that pretreatment with SYL040012 prevents the induced increase in intraocular pressure in this ocular hypertension model. The prophylactic effect of this compound is greater than the one described previously in this model with the drugs currently used for treating glaucoma, such as timolol or Xalatan.

About Sylentis

Founded in 2006 as a spin-off from Grupo Zeltia subsidiary Genómica, S.A.U., Sylentis is a subsidiary of Grupo Zeltia and a key player in the search for new therapies based on interference RNA (RNAi). Its strategy focuses on the efficient design of siRNAs using proprietary technology: SIRFINDER®, which finds small fragments of RNAi (short interfering RNAs, siRNAs) with pharmaceutical potential by searching the appropriate sequences using bioinformatics; once the disease's target gene has been identified, SYLENTIS develops a quick and economical solution for siRNAs to silence that gene.

About interference RNA (RNAi)

Interference RNA (RNAi) has arisen in recent years as a promising technology with therapeutic applications. Discovered in plants in the 1990s, RNAi consists of highly efficient selective and specific inhibition of gene expression (Fire et al., 1998). Interference RNA is mediated by small fragments of double-stranded RNA, consisting of 19-23 nucleotides, which promote degradation of mRNA, thus inhibiting synthesis of the proteins for which they code. As this mechanism is used naturally by cells to regulate gene expression in a way that is both non-toxic and highly effective, RNAi has great therapeutic potential.

About open-angle glaucoma

Primary open-angle glaucoma (POAG) is the most prevalent form of glaucoma, accounting for approximately two-thirds of all diagnosed cases of glaucoma. It is defined as a multifactorial optic neuropathy consisting of a loss of retinal ganglion cells and characteristic atrophy of the optical nerve leading to progressive, irreversible blindness. The risk factors of POAG include high intraocular pressure (IOP), a family history of the disease, and old age (Marquis and Wilson, 2005). Although the physiopathological mechanisms by which high pressure leads to neuron damage are not known, most current therapies include drugs or surgery which seek to reduce IOP to a level that safely prevents progressive loss of vision.



About eye discomfort associated with dry eye syndrome

Eye pain can be described as a burning, throbbing or stabbing sensation in the eye or around it, or the feeling that there is a foreign body in the eye. Chronic eye pain is generally associated with eye pathologies such as dry eye syndrome. Easing this symptom is essential for improving patients' quality of life. There are currently no drugs approved specifically for reducing chronic eye pain.

About Zeltia

Zeltia S.A. is a world-leading biopharmaceutical company specialised in the development of marine-based drugs for use in oncology. Grupo Zeltia consists mainly of the following companies: PharmaMar, the world-leading biotechnology company in advancing cancer care through the discovery and development of innovative marine-derived medicines; Genómica, Spain's leading molecular diagnostics company; Sylentis, dedicated to researching therapeutic applications of gene silencing (RNAi).

Important note

PharmaMar, which is headquartered in Madrid (Spain), is a subsidiary of Zeltia, S.A. (Spanish stock exchange: ZEL), which has been listed on the Spanish Stock Exchange since 1963 and on Spain's Electronic Market since 1998. This document is a press release, not a prospectus. This document does not constitute or form part of an offering or invitation to sell or a solicitation to purchase, offer or subscribe shares of the company. Moreover, no reliance should be placed upon this document for any investment decision or contract and it does not constitute a recommendation of any type with regard to the shares of the company.

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(*) This note is also available on the Sylentis website: www.sylentis.com and on the Zeltia website: www.zeltia.com