

ZELTIA NEWS:

Sylentis receives authorisation to commence Phase IIb clinical trial with bamosiran (SYL040012) for treating ocular hypertension associated with glaucoma

- *The main endpoint of the trial is to establish the most effective dose of bamosiran for reducing intraocular pressure after 28 days' treatment.*
- *The Phase IIb trial with bamosiran will be conducted at 21 centres in Spain, Germany, Estonia and the United States, enrolling 180 patients.*

Madrid, 17 July 2014: Grupo Zeltia (MC:ZEL) has announced today that Sylentis, a pioneer in the research and development of new drugs based on gene silencing through RNA interference (RNAi), has been authorised by the Estonian authorities to commence a Phase IIb trial with bamosiran (SYL040012) for the treatment of glaucoma and ocular hypertension. This is the first authorisation in the list of countries where the trial is to be conducted, and it enables patient enrolment to commence.

The trial, named SYLTAG, is a dose-finding parallel randomized, investigator-masked trial involving 4 groups receiving bamosiran and a fifth group receiving an active control (timolol). It will be conducted at 21 centres in Spain, Estonia, Germany and the United States and will recruit 180 patients.

The primary endpoint of this Phase IIb trial is to establish the most effective dose of bamosiran, administered once per day in the form of eye drops, in terms of its effect on intraocular pressure after 28 days of treatment.

Secondary endpoints include:

- Secondary efficacy-related endpoints: Assessment of the effect of treatment in comparison with the control (timolol), and changes in the quality of life in patients treated with the two drugs.
- Secondary safety-related endpoints: evaluation of local tolerability (eye discomfort), visual acuity, biomicroscopy, pachymetry, ophthalmoscopy, systemic tolerability, and adverse side effects.

This trial is part of the development of bamosiran as a topical drug for the treatment of ocular hypertension and glaucoma. It will make it possible to ascertain the optimal dose with a view to progressing to Phase III trials.

About bamosiran (SYL040012)

In preclinical trials with bamosiran, the siRNAs administered topically to treat ocular hypertension associated with open-angle glaucoma have proven effective in vivo. Three clinical trials have been conducted with bamosiran to date: Phase I (tolerability and effect on healthy volunteers), Phase Ib (tolerability and effect on patients), and Phase IIa (dose-finding and comparison with placebo). The positive results obtained in previous trials led to the design of this trial, in which Sylentis plans to find the most effective dose and assess its effect and tolerability in comparison with one of the benchmark drugs on the market for the treatment of intraocular pressure.

About Sylentis

Sylentis, a biopharmaceutical company in Grupo Zeltia (MC: ZEL), is a pioneer in the research and development of new drugs based on gene silencing (RNA interference—RNAi). 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 is based on the efficient design of small fragments of RNAi (short interfering RNAs, siRNAs) with pharmaceutical potential by searching the most appropriate sequences using bioinformatics; once a 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). RNAi 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 Whitson, 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.



For more information, contact Grupo Zeltia's Corporate Communications department on +34 91 444 4500.

This note is also available on the websites of Sylentis: www.sylentis.com and Zeltia: www.zeltia.com