

## Isarna Announces Orphan Drug Designation in the European Union for ISTH0036 to Treat Advanced-Stage Glaucoma

**Munich, Germany, May 21, 2015** – Isarna Therapeutics, the leader in transforming growth factor beta (TGF- $\beta$ ) isoform targeted antisense therapeutics, today announced that the European Medicines Agency (EMA) has granted orphan drug designation for ISTH0036, a locked nucleic acid-modified antisense oligonucleotide, for the prevention of scarring post filtration surgery in glaucoma. With EMA Orphan Drug Designation, Isarna is eligible for development fee reductions and incentives including 10-year market exclusivity for ISTH0036.

“Orphan designation for ISTH0036 in the European Union (EU) is a substantial accomplishment and corporate milestone for Isarna,” said Dr. Philippe Calais, President and Chief Executive Officer of Isarna Therapeutics. “Currently, patients with advanced-stage glaucoma have limited long-term treatment options. The EMA’s recognition of the potential of ISTH0036 to help protect glaucoma patients’ vision in this stage of their disease with orphan drug status is a significant step forward for the ongoing development of this novel therapy.”

Glaucoma is a progressive optic neuropathy frequently associated with elevated intraocular pressure (IOP), ocular vascular changes and extracellular matrix remodeling, namely of the trabecular meshwork, that can lead to progressive visual field loss and, ultimately, blindness. TGF- $\beta$ 2 is substantially elevated in the eyes of glaucoma patients and has specifically been identified as having a critical role in the pathophysiology of glaucoma. It affects (1) changes in the ocular outflow region (trabecular meshwork) that can lead to open-angle glaucoma, has a (2) direct pathophysiologic effect on the optic nerve head, and leads to (3) so-called “bleb closure” post glaucoma filtration surgery (GFS) by driving the fibrosis/scarring process.

GFS is often the last line of treatment for patients with advanced-stage glaucoma. Scarring post GFS leads to closure of the surgically opened drainage canal, resulting in GFS failure and re-rise of IOP. ISTH0036 is currently the sole compound in clinical development worldwide that directly targets TGF- $\beta$ 2, which is seen as a core driver of glaucoma pathophysiology and the scarring process post GFS. In addition to glaucoma, several other diseases in ophthalmology have been linked to the modulation of TGF- $\beta$ , including proliferative vitreoretinopathy, diabetic retinopathy and corneal diseases.

In April 2015 Isarna initiated a Phase 1 trial with ISTH0036 in patients with advanced-stage glaucoma post GFS.

### About Glaucoma

Glaucoma is the leading cause for irreversible blindness worldwide. The disease has been linked to elevated intraocular pressure, due to decreased fluid outflow (aqueous humor) from the eye, based upon alteration of the trabecular meshwork. Recent scientific data indicate that glaucoma progression is associated with elevated levels of TGF- $\beta$ 2 resulting in alteration of the trabecular meshwork (Prendes et al. 2013; Br J Ophthalmol.) and a potential direct pathophysiologic effect on the optic nerve (Fuchshofer 2011; Exp Eye Res.). Approximately 10% of glaucoma patients lose vision despite optimum treatment. More information on glaucoma can be found at [www.glaucoma.org](http://www.glaucoma.org), a website of the Glaucoma Research Foundation.

### About ISTH0036

ISTH0036 is a locked nucleic acid-modified antisense oligonucleotide selectively targeting the messenger ribonucleic acid (mRNA) of TGF- $\beta$ 2. TGF- $\beta$  (transforming growth factor beta) plays an important role in key pathways such as cell proliferation, cell differentiation, immune response and tissue modeling. Because TGF- $\beta$  is chronically elevated in many diseases, including ophthalmic and fibrotic diseases and cancer, and involved in their pathophysiology, it is an extremely versatile drug target throughout the body. Preclinical studies have demonstrated that ISTH0036 is highly potent and



shows selective target engagement (TGF- $\beta$ 2 mRNA and protein downregulation) and long-lasting tissue uptake and pharmacodynamic effects.

### **About Isarna Therapeutics**

Isarna Therapeutics has an unmatched commitment to developing selective TGF- $\beta$  inhibitors to effectively treat ophthalmic and fibrotic diseases and fight cancer. We are advancing a unique pipeline of novel oligonucleotides and combination modalities to transcend clinical response and improve patient outcomes. Isarna is established in the Netherlands, Germany, and the United States.

[www.isarna-therapeutics.com](http://www.isarna-therapeutics.com).

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