Isarna Initiates First-in-Human Phase I Trial for ISTH0036 to Treat Advanced Glaucoma

Munich, Germany, April 16, 2015 – Isarna Therapeutics, the leader in transforming growth factor beta (TGF-β) targeted antisense therapeutics, announced today the initiation of a Phase I clinical trial with ISTH0036, an antisense oligonucleotide selectively targeting TGF-β2 to treat advanced glaucoma.

This first-in-human Phase I trial, conducted at the University Hospitals of Mainz and Tuebingen, Germany, is designed to evaluate the safety and long-term tolerability of ISTH0036 in patients with advanced glaucoma undergoing filtration surgery (trabeculectomy) due to uncontrollable elevated intraocular pressure (IOP). The trial will enroll approximately 24 - 30 patients, who will be treated with escalating doses of ISTH0036. In addition to safety, patients will be monitored for intraocular pressure and visual field preservation.

“Glaucoma is the leading cause of irreversible blindness in the world, and ISTH0036 with its expected three-directional activity, which includes blocking TGF-β2-mediated trabecular meshwork alteration, and inhibiting both direct optic nerve toxicity and scarring post trabeculectomy, has the potential to substantially alter the course of this disease and protect the patient’s vision,” commented Prof. Eugen Leo, Isarna’s Head of Clinical Development. He added: “Notably, ISTH0036 is currently the sole compound in clinical development worldwide that directly targets the core driver of the pathophysiology of glaucoma: TGF-β2.”

Prof. Sir Peng Khaw, Professor of Glaucoma and Ocular Healing, University College London/Moorfields Eye Hospital and clinical advisor to Isarna stated: “This novel oligonucleotide selectively targeting TGF-β2, an important driver of glaucoma, seems to possess impressive PK-PD properties that could make it a valuable treatment for different aspects of glaucoma. I am very much looking forward to the clinical exploration of this compound.”

TGF-β plays an important role in key pathways such as cell proliferation, cell differentiation, immune response and tissue modeling. Significantly elevated levels of TGF-β have been identified in glaucomatous eyes in the anterior chamber, the vitreous, and optic nerve head. TGF-β has been shown to directly cause increased intraocular pressure, a critical risk factor in the progression of glaucoma through complex interaction with the trabecular meshwork, leading to decreased aqueous humor outflow and has been linked to direct optic nerve toxicity.

Dr. Philippe Calais, CEO of Isarna Therapeutics, concluded: “The start of our first Phase I trial in advanced glaucoma is a major corporate milestone, one that we have achieved two years after starting this program thanks to an outstanding and expedited preclinical program. We are excited to move this and other compounds forward to successfully treat glaucoma and other major ophthalmic diseases.”

About Glaucoma
Glaucoma is the leading cause for irreversible blindness worldwide. Recent scientific data indicate that glaucoma progression is associated with elevated levels of TGF-β2 resulting in alteration of the trabecular meshwork (Prendes et al. 2013; Br J Ophthalmol.) and a potential direct toxic 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, 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-β2. TGF-β (transforming growth factor beta) plays an

important role in key pathways such as cell proliferation, cell differentiation, immune response and tissue modeling. Because TGF-β 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-β2 mRNA and protein downregulation) consistent with long-lasting tissue uptake and pharmacodynamic effects.

About Isarna Therapeutics
Isarna Therapeutics has an unmatched commitment to developing selective TGF-β inhibitors to fight cancer and to effectively treat ophthalmic and fibrotic diseases. We are advancing a unique pipeline of novel oligonucleotides and combination modalities to transcend clinical response and improve patient outcomes. Isarna is headquartered in Germany, and registered as a Dutch BV as well as a U.S. Corporation. www.isarna-therapeutics.com.

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