Isarna Presents First Interim Phase I Data for ISTH0036 in Advanced Glaucoma at ARVO 2016 Annual Conference

-- Preliminary Data Shows That ISTH0036 was Safe and Well Tolerated at Therapeutic Dose Levels --

Munich, Germany, May 03, 2016 – Isarna Therapeutics, the leader in transforming growth factor beta (TGF-β) isoform targeted antisense therapeutics, today announced the presentation of the first clinical interim data for its lead candidate ISTH0036, a locked nucleic acid-modified antisense oligonucleotide, currently in phase I development for the treatment of advanced-stage glaucoma.

The purpose of this first-in-human Phase I trial, conducted at the ophthalmology departments of the University Hospitals of Mainz, Tuebingen and Magdeburg, Germany, is to evaluate safety and tolerability and preliminary clinical efficacy of intravitreal injections of ISTH0036 in patients with advanced primary open angle glaucoma undergoing filtration surgery (trabeculectomy) with Mitomycin C due to uncontrollable elevated intraocular pressure.

Glaucoma patients scheduled for filtration surgery receive a single intravitreal injection of ISTH0036 at the end of trabeculectomy in escalating total doses of 6.75 µg, 22.5 µg, 67.5 µg or 225 µg, respectively, resulting in calculated intraocular ISTH0036 concentrations in the vitreous humor of 0.3 µM, 1 µM, 3 µM or 10 µM after injection. Outcomes assessed include: type and frequency of adverse events, intraocular pressure, number of interventions post trabeculectomy, bleb survival, visual acuity and visual field, slit lamp biomicroscopy and optic disc status.

The first three dose levels have been completed meanwhile and enrollment for the trial is planned to be completed in Q2/2016. Safety analyses of the 9 patients treated so far at the first 3 dose levels up to 67.5 µg revealed excellent tolerability for ISTH0036. No treatment associated adverse events, serious adverse events or dose limiting toxicities were observed. The preliminary results suggest that intravitreal injection of ISTH0036, a potent and selective antisense oligonucleotide targeting transforming growth factor beta 2 (TGF-β2), is safe and well tolerable at therapeutic dose levels.

“We are very glad to see that ISTH0036 demonstrates excellent safety and tolerability when administered via an intravitreal injection to patients at doses considered to be therapeutic. This provides an encouraging basis for a continued development in glaucoma but potentially also other TGF-β2 associated diseases such as Diabetic Retinopathy, AMD and Proliferative Vitreoretinopathy,” commented Prof. Eugen Leo, Head of Clinical Development at Isarna.

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 positive interim data of our first Phase I trial in advanced glaucoma represent a significant step forward for our company. We look forward to advancing this program further and to expanding our Ophthalmology program to other eye diseases by 2017.”

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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