PRESS RELEASE

Isarna Presents Positive Clinical Data for ISTH0036 in Advanced Glaucoma and Preclinical Data Supportive of AMD/DME Potential at ARVO 2017 Annual Conference

Oral presentation of clinical data and poster presentation of preclinical results support further exploration of ISTH0036 in several major ophthalmic indications

Munich, Germany, May 15, 2017 – Isarna Therapeutics, the leader in transforming growth factor beta (TGF-β) isoform targeted antisense therapeutics, today announced the presentation of the Phase I safety and efficacy data for its lead candidate ISTH0036, a locked nucleic acid-modified antisense oligonucleotide, in advanced-stage glaucoma patients. Overall, the treatment was safe and well tolerated at all dose levels and the post-operative intraocular pressure course provided preliminary evidence for a beneficial effect of ISTH0036 at the two highest dose levels. Separately, Isarna provided positive preclinical results in a poster presentation demonstrating ISTH0036's potential as novel therapeutic intervention in a murine model of Choroidal Neovascularization (CNV), supporting clinical exploration in indications such as wet Age-related Macular Degeneration (AMD) and Diabetic Macular Edema (DME). Both results were presented at The Annual Meeting of the Association for Research in Vision and Ophthalmology (ARVO), held from May 7 to 11 in Baltimore, Maryland.

"The Phase I clinical study demonstrates not only that ISTH0036 can be administered safely to patients, but also gives preliminary evidence for clinical efficacy. Seeing such preliminary signs of a dose-response effect and improved postoperative intraocular pressure control in patients within this limited-size Phase I study is quite impressive," commented Prof. Alon Harris, Director of Clinical Research, Department of Ophthalmology at Indiana University/USA, and Chair of the Glaucoma Scientific Advisory Board for Isarna Therapeutics.

The purpose of the first-in-human Phase I trial, conducted at the ophthalmology departments of the University Hospitals of Mainz, Tuebingen and Magdeburg, Germany, was 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 received 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. Administration of all dose levels was completed safely and none of the reported treatment emergent adverse events was considered related to ISTH0036 or the intravitreal injection.

Although this Phase I trial was not dimensioned and designed to provide statistically significant efficacy data, regarding the important endpoint postoperative control of intraocular pressure (IOP), signs for a dose-response trend and an encouraging potentially improved postoperative IOP control (no patient exceeding with his IOP the 10 mmHg threshold after three months) was observed for patients treated at dose level 3 and 4.

Prof. Eugen Leo, Head of Clinical Development at Isarna commented: "These results are very encouraging for a Phase I study and exceed our expectations significantly. We are now moving towards Phase II development in advanced glaucoma but also other TGF-β2 associated diseases such as wet wet Age-related Macular Degeneration (AMD) and other TGFβ2-associated diseases

such as Diabetic Macular Edema (DME), well supported by the recent preclinical data we could gather for these diseases."

In a separate poster presentation of preclinical results for ISTH0036 in a mouse model of CNV, single intravitreal administration of ISTH0036 demonstrated inhibition of neovascularization and vascular leakage, but also decreased the extent of collagen I deposition (fibrosis) in the choroidal lesion areas in a dose-dependent manner.

The purpose of the preclinical studies, conducted at both the Vision Core Leuven (KU Leuven, Belgium) and Experimentica Ltd. (Kuopio, Finland), was to evaluate the efficacy of intravitreal injection of ISTH0036 in mouse CNV experimental model compared with anti-VEGF agents (DC101 or Eylea/aflibercept) as benchmark study control. In these studies, laser-induced burns of the Bruch's membrane were performed around the optic disk of anesthetized mice, after which 1.5-μL intravitreal injections of either saline, 6.2-μg DC101, 80-μg aflibercept, or 0.1- to 1-μg ISTH0036 were performed. Neovascularization was evaluated by OCT, choroidal FA and analysis of retinal images, and vascular leakage was assessed by HRA-FA over the following 4 weeks. Collagen I deposition was assessed at the end of the study.

Dr. Michel Janicot, Head of Preclinical Development at Isarna Therapeutics commented: "Generated in the experimental 'gold standard' model to support development of drug candidates in neovascular ocular indications, the preclinical data are very encouraging and consistent with the proposed key role of TGF-β2 in the onset and development of these pathologies. We are convinced of ISTH0036's potential to have broad application in treating diseases of the eye."

TGF-β plays an important role in key pathways such as cell proliferation, cell differentiation, epithelial-to-mesenchymal transition, fibrosis and the immune response. Significantly elevated levels of TGF-β have been identified in glaucomatous eyes in the anterior chamber, the vitreous, and optic nerve head. TGF-β also appears to play a distinct role in the ocular pathology for diseases such as age-related macular degeneration, diabetic retinopathy and proliferative vitreoretinopathy, among others.

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 Munich, Germany. www.isarna-therapeutics.com.

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