PRESS RELEASE

Gene Signal and Collaborators Demonstrate Successful Activity of Topical Aganirsen in Models of Retinal Neovascular disease

Data Published in IOVS Journal Shows Efficacy of Topical Aganirsen Equivalent to Lucentis in Models of AMD and Ischemic Retinopathy

Lausanne, Switzerland, February 14, 2012 – Gene Signal, a company focused on developing innovative drugs to manage angiogenesis based conditions, today announced the publication of data demonstrating the significant activity of aganirsen (GS-101, eye drops) in two important models of retinal neovascular disease, wet age-related macular degeneration (AMD) and ischemic retinopathy. Gene Signal's aganirsen is an antisense oligonucleotide that is expected to complete a phase III trial for the treatment of progressive neovascularisation in the cornea in 2012. These data, published online in Investigative Ophthalmology & Visual Science (doi:10.1167/iovs.11-9064), demonstrate the ability of aganirsen to reach and exert activity on the retina.

"Age-related macular degeneration and ischemic retinopathies are major causes of blindness that are associated with neovascularisation. This can lead to sub-retinal and intravitreal hemorrhage, and tragically retinal detachment, which causes blindness," explained lead author Dr. Sylvain Chemtob, Université de Montréal, Montreal, Canada.

"For the first time in this study, we have demonstrated that IRS-1, an angiogenic protein, is expressed in the retina and that aganirsen is able to effectively attenuate neovascularization by inhibiting IRS-1 expression, without affecting normal vascularisation, " noted co-lead author Dr. Matthew Lawrence from RxGen Inc., Hamden, CT, USA.

Aganirsen blocks pathological neovascularization by inhibiting IRS-1. Clinical studies to date have shown that aganirsen is able to safely and effectively inhibit the development of progressive corneal neovascularization secondary to infectious keratitis or chemical burns both of which could lead to corneal graft replacement.

"The only effective drugs approved to target neovascularization in AMD and ischemic retinopathies are intraocular injections of anti-VEGF compounds, such as Lucentis. The studies reported in Investigative Ophthalmology & Visual Science, if confirmed in clinical trials, show unprecedented evidence that topical aganirsen is an innovative compound that may offer advantages over currently available drugs due to its topical delivery and different mode of action as well as an excellent efficacy and safety profile. A topical agent for retinal neovascular disease would revolutionize treatment," noted Eric Viaud, CEO of Gene Signal.

Study Details
Aganirsen (topical emulsion) was applied daily in non-human primates following laser induced choroidal neovascularisation (CNV), a model of wet age-related macular degeneration [AMD]), and in newborn rats following oxygen-induced retinopathy (OIR), a model of ischemic retinopathy. Retinal aganirsen concentrations were assessed in monkeys following topical delivery (21.5, 43 or 86 mg). Clinical significance was further evaluated by determination of IRS-1 expression in monkey and human retinal biopsies.

Topical application of aganirsen inhibited neovascular lesion development dose-dependently in African green monkeys, with incidence of high-grade CNV lesions (grade IV) decreasing from 20.5% in vehicle-treated animals to 1.7% ($p<0.05$) at the 86 mg dose. Topical aganirsen inhibited retinal neovascularization following OIR in rats ($p<0.05$); furthermore, a single intravitreal injection of aganirsen reduced OIR as effectively as ranibizumab (Lucentis), and the effects of both compounds were additive. Topical applications of aganirsen did not interfere with physiological retinal vessel development in newborn animals.

About Gene Signal
Gene Signal (www.genesignal.com) is developing a robust pipeline of novel antisense oligonucleotides, proteins and monoclonal antibodies to treat a range of conditions based on its innovative angiogenesis modulating technology. The company's most advanced therapeutic product is aganirsen (GS-101), an antisense oligonucleotide that has nearly completed phase III for the prevention of corneal graft rejection. Aganirsen is also entering phase II clinical trials for additional angiogenesis based diseases, such as wet age-related macular degeneration (AMD), neovascular glaucoma, and dermal indications. Antisense oligonucleotides confer distinctive advantages versus other biologics: they can be readily transported across cell membranes, are associated with low immunogenicity, and can be produced by simple chemical synthesis, unlike larger proteins and monoclonal antibodies that require cell culture and complex purification steps.

Through world leading expertise in discovering genes involved in the regulation of angiogenesis, Gene Signal has built a significant intellectual property portfolio that has relevance in multiple disease areas. Gene Signal plans to seek partnership with the pharmaceutical industry for the next steps of development and marketing. The company was founded in 2000 and has assembled an outstanding leadership team that includes scientific, medical, regulatory and business professionals with successful track records in developing and commercialising state of the art drugs. Gene Signal's headquarters are in Lausanne (PSE, EPFL), Switzerland, with its research programs based in France (Bioparc Genopole, Evry) and product development in Canada (Montréal).

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