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PRESS RELEASE

Results of a Meta-Analysis Show Neovascularization Increases Risk for Corneal Transplant Rejection and Failure

Gene Signal's Aganirsen (GS-101) Being Developed in Phase III to Treat corneal Neovascularization

Lausanne, Switzerland, July 1, 2010 – Gene Signal, a company focused on developing innovative drugs to manage angiogenesis based conditions, today announced that a meta-analysis performed on 19 studies involving nearly 25,000 corneal transplants showed an increased risk of rejection and failure was associated with corneal neovascularization (abnormal new blood vessel growth). Graft failure can be caused by multiple factors. However, graft rejection refers to a specific immunologic process between the individual and the donor tissue, which in some cases will progress to graft failure. The publication, entitled "Corneal neovascularization as a risk factor for graft failure and rejection following keratoplasty: An evidence-based meta-analysis", appears in the July issue of the journal Ophthalmology.

"To our knowledge, this is the first extensive, systematic review and meta-analysis published to quantify corneal neovascularization as a risk factor for graft rejection and failure following keratoplasty, the transplantation procedure," noted Dr. Claus Cursiefen of the Department of Ophthalmology, Friedrich-Alexander University Erlangen-Nürnberg, Germany, an author of the paper. "We believe these data support the use of topical antiangiogenic therapies such as aganirsen to precondition the cornea and reduce the neovascularization prior to the grafting procedure."

"This extensive meta-analysis demonstrates the role of neovascularization as a risk factor in cornea graft rejection. In clinical studies, aganirsen has demonstrated the ability to inhibit and regress neovascularization, so we believe it could help reduce the risk of corneal graft rejection," stated Eric Viaud, CEO of Gene Signal.

Meta-Analysis Details

Using predetermined inclusion criteria, electronic databases and corneal registries were searched for publications involving keratoplasty. Relevant data, including summaries of study/patient characteristics and numeric association findings, were extracted and checked by a second reviewer. Meta-analyses were used to pool the association between

corneal neovascularization and corneal graft failure and rejection across studies. A total of 19 studies involving 24,944 grafts undergoing keratoplasty were included. Most studies were single site and three were used based on large national corneal graft registries. The risk of rejection was reported in seven studies, with all seven reporting increased risk in the presence of neovascularization. The pooled risk ratio in four applicable studies was 2.07 (95% CI:0.98 to 3.15). Fourteen studies reported an association between neovascularization and an increased risk of failure. The overall risk ratio in nine studies with data applicable for pooling was 1.32 (95% CI:1.15 to 1.49).

“A key strength of this analysis was the comprehensiveness of source data. We recognize that there were some study limitations and emphasize longer follow up studies are needed, however the overall outcome of linking neovascularization to an increased risk of graft rejection and failure has been well established,” commented Prof. Rod Taylor, Peninsula Medical School of Medicine & Dentistry, Universities of Exeter and Plymouth, UK.

“Given the limited availability of donor grafts, it is therefore desirable to treat recipient neovascularisation before proceeding to keratoplasty,” added Dr. Cursiefen.

About Corneal Grafts and Aganirsen
Every year, approximately 64,000 corneal grafts are performed in Western Europe and USA each year to cure or prevent blindness making this procedure the most frequently performed transplant surgery. However, the 5 year failure rate for corneal grafts is currently around 35%. As with many other graft procedures, donor grafts are always in limited supply, with waiting times for the procedure ranging from 6 months to 2 years. One of the main reasons for graft failure is the natural immune response of the body.

Normally, the cornea is avascular, or deprived of blood and lymphatic vessels, protecting the donor cornea from being rejected. However, under certain circumstances, abnormal new blood vessel creation or neovascularisation occurs, inducing an immune response against the donor graft that can lead to immunological corneal graft rejection.

As currently there is no therapy available, Gene Signal is working on new ways to prevent this syndrome. With aganirsen, its antisense oligonucleotide approach, which benefits from orphan designation in Europe, the company aims to block the inflammatory pathways (keratitis) leading to the formation of blood vessels in the cornea. This approach uses short DNA fragments that specifically target and block the production of IRS-1, a protein required for the formation and growth of new blood vessels.

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, an antisense oligonucleotide currently in phase III trials for treating keratitis (inflammation) associated with the neovascularization threat linked to corneal graft rejection as well as clinical trials for additional angiogenesis based ophthalmology and dermal indications. Gene Signal's diverse pipeline also includes four molecules at the discovery stage addressing indications in the field of vascular disease and oncology.

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 license out its therapeutic portfolio of candidate drugs for co-development and commercialisation. 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, Switzerland, with its research programs based in France and product development in Canada.

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