Gene signal GS-101 data shows safe and effective inhibition of ophthalmic blood vessel growth

September 1 2009

Gene Signal, a company focused on developing innovative drugs to manage angiogenesis based conditions, today announced the publication of interim results from a phase II study suggesting that the antisense oligonucleotide GS-101 (eye drops) is safe and effective at inhibiting and regressing corneal neovascularisation (abnormal new blood vessel growth). Neovascularisation in this part of the eye is a major risk factor in corneal graft rejection, the most common transplantation procedure that saves the sight of approximately 46,000 people worldwide each year.

The data were published in the September 2009 issue of *Ophthalmology* by researchers led by Claus Cursiefen, MD, from the Department of Ophthalmology at the Friedrich-Alexander University Erlangen-Nürnberg, in Erlangen, Germany. Gene Signal is now conducting an international phase III trial with GS-101 for the prevention of pathologic corneal neovascularisation and thereby corneal graft rejection. GS-101 has been granted Orphan Drug status for this indication in Europe.

"Compared to the placebo group in which 100% of patients suffered from progression of corneal neovascularisation, the optimal GS-101 treatment group showed regression in 86% of patients. We are very encouraged by these results as they represent real progress in the development of GS-101 as a new treatment to combat corneal graft rejection," explained Dr. Claus Cursiefen of the Department of

Ophthalmology, Friedrich-Alexander University Erlangen-Nürnberg. "We urgently need new options for the thousands of graft recipients, whose current treatment options for threatened rejection such as immunosuppressants are not ideal due to side effects. GS-101 is the first specific angiogenesis inhibitor that has demonstrated activity at the anterior part of the eye, where numerous diseases associated with pathologic angiogenesis endanger vision."

"The publication of these positive phase II results for GS-101 is a major milestone for Gene Signal. As a novel approach to the management of ophthalmic angiogenesis, we are keen to provide rigorous scientific backup to support our ongoing clinical development program. We also recently published data in the Journal of Pharmacology and Experimental Therapeutics confirming that GS-101 prevents in vivo expression of IRS-1, a protein associated with new blood vessel formation (angiogenesis), and we intend to present additional data on GS-101 at various scientific forums in the near future," noted Eric Viaud, CEO of Gene Signal.

Study Data

The aim of this randomised, double-blind, multicenter phase II clinical study was to test the efficacy and tolerability of GS-101 (eye drops), an antisense oligonucleotide against insulin receptor substrate-1 (IRS-1), versus placebo, against progressive corneal neovascularisation (excessive or harmful angiogenesis). Forty patients non-responsive to conventional therapy participated in the study. Four groups of 10 patients were treated for three months comparing three doses of GS-101 (eye drops: 2x/day; 43, 86 and 172 ?g/day total) to placebo (10 patients per group). The primary endpoint was measured by the reduction in area covered by pathologic corneal blood vessels measured morphometrically on digitised slit-lamp pictures using image analysis techniques.

Treatment with GS-101 was generally well tolerated, with no associated serious side effects. At 86 micro g/day GS-101 eye drops produced a significant inhibition and regression of corneal neovascularisation (-2.04 ±1.57% of total corneal area; p=0.0047). The low dose tended to stabilise growth (0.07±2.94; p=0.2088) compared to placebo (0.89±2.15), where corneal neovascularisation progressed in all patients in the 3 month period. The high dose of GS-101 was found to have no additional benefit.

About Corneal Grafts and GS101

Every year, approximately 46,000 corneal grafts are performed worldwide 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 from6 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 GS-101, its antisense oligonucleotide approach, which benefits from orphan designation in Europe, the company aims to block the pathways 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.

Source: Halsin Partners