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FOR IMMEDIATE RELEASE

Gene Signal announces completion of private funding round

Company set to embark on aggressive three-year clinical and commercialisation plan for angiogenesis therapies

Lausanne, Switzerland, 23 January, 2013

Gene Signal, a Swiss-based biotechnology company pioneering the development of innovative therapies for angiogenesis-based diseases, today announced the completion of its latest funding round. This was raised principally through the same group of private investors who have backed the company since its formation in 2000. The proceeds will be used to complete a number of Phase II trials in back of the eye angiogenic diseases and to take through to commercialisation its lead product Aganirsen for the Orphan Drug indication neovascular-associated corneal graft rejection (NV-CGR), a rare eye disease. Phase III results in NV-CGR are due to be announced in mid-2013.

The company has built one of the industry's leading angiogenesis-focused pipelines, with six candidates in development for eleven indications in ophthalmology, dermatology, vascular disorders and cancer. The lead product Aganirsen (GS-101) is well-positioned to bring significant benefits to patients and physicians thanks to its novel mechanism of action, its excellent local tolerability and its application in the form of eye-drops or emulsion compared to current therapies such as lasers or injections.

Eric Viaud, CEO and co-founder of Gene Signal, commented: "We are delighted that our existing and new shareholders have reaffirmed their confidence in our team and our science. Together we have built a pipeline of great promise to address the significant unmet needs of angiogenesis-based diseases. The funds will enable Gene Signal to implement its clear strategy of developing and commercialising assets for orphan drug indications ourselves, while keeping all options open for development and commercialisation in major global indications such as age related macular degeneration and diabetic retinopathy."

The company has reached this impressive stage of maturity through three forms of financing: private investor funding; support of government health departments in Switzerland, France and Canada for various R & D activities; and revenues in Switzerland, France and Spain from compassionate use (named patient sales) for patients receiving Aganirsen for treating the orphan indication NV-CGR.

In the coming three years 2013 -15, Gene Signal plans to achieve significant milestones, including:

- Phase III results, filing and commercialisation of Aganirsen in Europe for the Orphan Drug indication neovascular-associated corneal graft rejection (NV-CGR)



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- Start of a Phase II trial of Aganirsen for the Orphan Drug indication neovascular glaucoma
- Start of Phase II trials for Aganirsen in non-orphan eye diseases such as age-related macular degeneration and diabetic retinopathy
- Results of a pilot study and start of a Phase II trial of Aganirsen for psoriasis
- Development to Phase I of other product candidates – proteins, small peptides and monoclonal antibodies – in various oncology and wound-healing indications.

About angiogenesis-based diseases

Angiogenesis is the growth of new capillary blood vessels. This natural process is controlled by a precise balance of growth and inhibitory agents produced in the body by healthy tissue for healing and reproduction. Abnormal blood vessel growth leads to many diseases including various ischemic and inflammatory diseases as well as cancer. According to the Angiogenesis Foundation, more than one billion people worldwide are believed to be affected by angiogenesis related conditions. In recent years, a concentrated research effort has been made to discover the specific pro- and anti-angiogenic molecules involved in the complex interactions of the angiogenesis process. According to Global Industry Analysts, the global market for Angiogenesis inhibitors and stimulators is expected to reach US\$ 53.5 Billion by 2015.

About Aganirsen Antisense Oligonucleotide

Gene Signals' compound, Aganirsen, is a novel compound which is applied topically, i.e. in eye-drop formulation and has the ability to inhibit unwanted angiogenesis.

Early signs are that Aganirsen, an antisense DNA oligonucleotideⁱ, is topically effective. Formulated as a small complementary DNA fragment, Aganirsen emulsion has demonstrated its ability to effectively inhibit neovascularisation in the cornea and to reach and to act on the retinaⁱⁱ, when other drugs have to be injected.

Aganirsen inhibits the insulin receptor substrate 1 (IRS-1) which is over-expressed in pathological angiogenesisⁱⁱⁱ, and it has been demonstrated to target pathological vessels without inhibiting normal vessel turnover^{iv}. Thanks to its entirely novel mechanism of action, Aganirsen is expected to be the topical and safe alternative to existing anti-VEGF intra-vitreal injections depending on the indication.

Additionally, 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.



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Gene Signal is a Swiss-based biotechnology company pioneering the development of innovative therapies for angiogenesis-based diseases. Its product candidates are a new class of oligonucleotides, proteins and monoclonal antibodies which are derived from genes that are exclusively involved in the angiogenesis process. Six candidates are in development for eleven indications in ophthalmology, dermatology, vascular disorders and cancer.

The company's lead compound, Aganirsen (GS-101), an antisense DNA oligonucleotide, will complete in 2013 a European Phase III trial for the treatment of neovascular-associated corneal graft rejection. The compound is currently also being prepared for Phase II trials in neovascular glaucoma, age-related macular degeneration, diabetic retinopathy and psoriasis.

Gene Signal's discovery program leverages a patented discovery platform, GENE-MAAP, which streamlines the identification process of genes exclusively involved in the regulation of angiogenesis, resulting in the identification and patenting of more than 94 such genes.

The company was founded in 2000, is privately owned, and is led by a team of highly qualified scientific and commercial talents. Its headquarters are in Lausanne (EPFL Swiss Federal Institute of Technology), Switzerland, with research programs based in France (Bioparc Genopole, Evry) and product development in Canada (Montreal).

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ⁱAn antisense Oligonucleotide is a short strand of DNA designed to prevent translation of messenger RNA into an unwanted protein

ⁱⁱCloutier F, Lawrence M. et al "Anti-angiogenic activity of Aganirsen in non-human primate and rodent models of retinal neovascular disease following topical administration" Invest. Ophthalmol. Vis. Sci. (IOVS) February 9, 2012 iovs.11-9064

ⁱⁱⁱ Al Mahmood S et al "Potent in vivo antiangiogenic effects of GS-101 (5'-TATCCGGAGGGCTCGCCATGCTGCT-3'), an antisense oligonucleotide preventing the expression of insulin receptor substrate-1", J. Pharmacol Exp Ther. (JPET) 2009 May;329(2):496-504. Epub 2009 Feb 10

^{iv} Cloutier F. IOVS 2012