Amarna Therapeutics BV
www.amarnatherapeutics.com

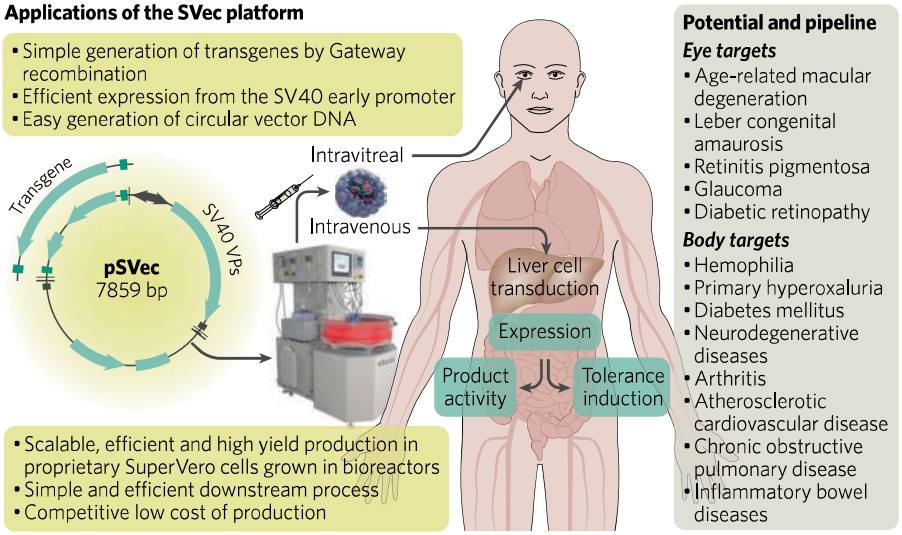
Dual approach SVec targets genetic and autoimmune disorders

Amarna Therapeutics has developed SVec, a non-immunogenic viral vector platform for the development of candidates to treat genetic and autoimmune disorders, overcoming immune barriers to gene therapy delivery and unlocking autoimmunity by inducing tolerance.

The gene therapy sector has advanced in recent years, with the first products coming to market and investors providing the capital for a pipeline of prospects. Yet, the limitations of existing delivery vectors is holding the field back and depriving patients with genetic diseases of durable, one-time treatments. Amarna Therapeutics is developing non-immunogenic viral vectors to overcome those limitations and simultaneously unlock an immune tolerance induction approach to treat autoimmune diseases.

Adeno-associated virus (AAV) vectors are widely used in gene therapy, but suffer from major shortcomings. Notably, infection with wild-type AAVs is common in the human population, and so pre-existing immunity to AAVs limits the use of AAV vector-based gene therapies and reduces their efficacy and safety in patients with an immune memory for AAVs who are eligible for AAV vector-based gene therapy. Finally, the AAV vector-triggered immune responses compromise the option for re-administration that may be needed in some indications to optimize efficacy.

When combined with other limitations of AAV vector-based therapies, such as the high vector doses needed to treat disease, the immunity shortcomings create substantial barriers to the realization of the full potential of gene therapy. Researchers have tried to eliminate the barriers for AAV vectors using IgG-cleaving enzymes and steroids, but these have encountered safety concerns and failed to consistently address the immunity problems.



Creating a better vector

Amarna has developed its SVec technology to overcome immune barriers to gene therapy delivery. SVec, a replication-defective, non-immunogenic vector, is derived from the macaque polyomavirus SV40. This polyomavirus strictly replicates in macaques where it causes chronic symptomless infections. SV40 is not found in humans, which means that everyone is immunologically naïve to this virus. As SV40-based vectors are fully replication-defective, we now know that SVec particles will be considered harmless and induce immune tolerance to itself and the transgene protein when expressed in the liver after intravenous administration. In the context of gene replacement therapies, this means SVec achieves long-term transgene expression and can be repeatedly administered to improve therapeutic efficacy or to treat other genetic disorders in the same patient.

The unique capacity of SVec to induce immune tolerance opens opportunities to use the technology in the treatment of autoimmune diseases. Applied to diseases such as type 1 diabetes mellitus and multiple sclerosis, the vector could enable the long-term expression of self-antigens in the liver and thereby restore immune tolerance to the self-proteins at the root of the autoimmune conditions.

In mice, Amarna has shown intraocular delivery of SVec-based gene therapies causes sustainable, long-term expression of the desired transgene. In addition, these studies demonstrated that intravenous administration of the vector drives efficient in vivo expression in the liver.

Amarna has developed a flexible, generic production platform to support all the applications open to SVec. The platform features a novel Vero-based packaging cell line called SuperVero. Using SuperVero, Amarna can produce fully replication-defective vectors. Vector particle yield is comparable to existing packaging cell lines, and contamination with wild-type SV40 particles is prevented.

Moving into the clinic

Amarna is currently running proof-of-principle experiments in advanced animal models to validate the potential of the platform in type 1 diabetes mellitus and multiple sclerosis. In parallel, the company is preparing to move its lead gene replacement candidate into clinical development in a genetic liver disease, such as primary hyperoxaluria or hemophilia.

The clinical trial—scheduled to start in 2022—aims at generating phase 1/2a proof-of-concept data, and hopes to further validate that SVec is non-immunogenic in humans and induces long-term transgene expression. In doing so, Amarna could obtain a general validation of the platform for gene replacement therapy and show its vector induces the immune tolerance key to its use in the treatment of autoimmune diseases.

Given the number of autoimmune indications, the market size and the resources needed to target them, Amarna is seeking partners to support the development of SVec-based therapies. Partner companies will gain access to a pioneering approach with the potential to permanently change the field of autoimmune diseases by introducing causal rather than symptomatic treatments.

The dual applications of SVec enable Amarna to address two major, distinct sets of medical needs. Through its gene replacement therapies, Amarna stands to overcome some of the shortcomings of AAV vectors that have limited use of a potentially powerful modality so far. At the same time, the immune tolerance feature of SVec sets Amarna up to improve the lives of people with autoimmune diseases.

CONTACT
Steen S. Klysner, CEO
Amarna Therapeutics BV
Leiden, the Netherlands
Tel: +31 71 332 2197
Email: steen.klysner@amarnatherapeutics.com