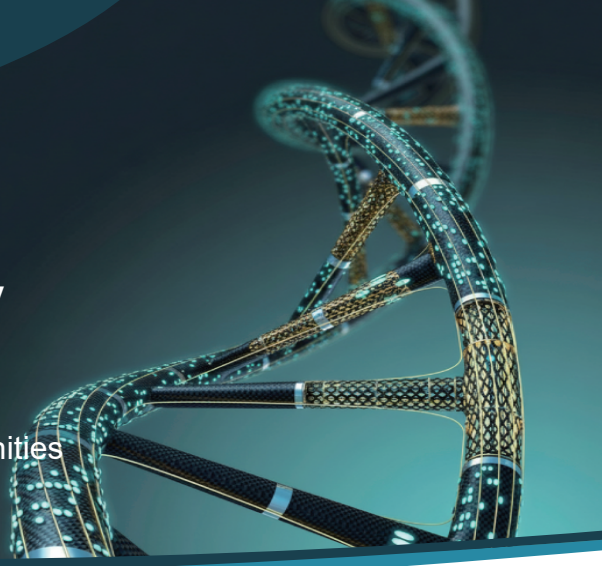
Protheragen



Gene Therapies Based on Revolutionary AAV Vector Technologies

Seeking Out-licensing, Co-development, and Financing Opportunities

Potential and Challenges of AAV-Based Therapies

Gene therapy demonstrates unique and irreplaceable advantages in treating hereditary and degenerative diseases that are difficult to address with traditional treatment. In gene therapy, exogenous genetic material must enter the nucleus to be expressed within human cells; therefore, the selection of an ideal vector is the critical factor for success. Common viral vectors include Adeno-associated virus (AAV), Lentivirus (LV), and Adenovirus (ADV). Among these, AAV is the most widely utilized due to its characteristics of low immunogenicity, high safety profile, non-integration of exogenous genes, and long-term expression. However, challenges in AAV vector drug development include:

• Hepatotoxicity and immune responses triggered by high-dose administration;
• The complexity of manufacturing processes required to achieve high purity and high titers;
• Prohibitively high commercial pricing resulting from exorbitant production costs.

Core Technology Platforms for Addressing Challenges

Based on the concept of "process revolution + technological innovation", G* Biotech has established multiple core technology platforms to overcome the technical difficulties and industrialization challenges of AAV drugs.

• Two-Plasmid Technology

Compared with the three-plasmid system, the two-plasmid system features a simplified production process, better batch-to-batch stability, significantly reduced costs, and higher-purity AAV drugs.

• Expression Cassette Optimization Technology

Through the engineering modification of tissue-specific promoters, the optimization of target gene codons, and the design of cis-regulatory elements such as introns, the safety of the vector is further improved, and more efficient tissue-specific expression can be achieved.

• Capsid Screening Technology

AAV capsids with targeting properties and transduction efficiency for specific tissues or cells can be efficiently obtained through novel virus capsid screening and modification technologies.

• Dual AAV Vector Delivery Technology

Through the splicing effect of intronic peptides, the peptide fragments delivered by AAV vectors can be spliced together to form complete and functional proteins, thereby overcoming the load limitation of AAV.

AAV Gene Therapies

The AAV-based gene therapy product developed by G* Biotech has undergone clinical trials involving over 100 patients, demonstrating excellent safety and efficacy profiles.

Asset	Target	Phase	Indication
PTH-0565	VEGF	Phase 1/2a	Neovascular Age-related Macular Degeneration; Diabetic Retinopathy; Diabetic Macular Edema
PTH-0566 ★	Retinoschisin 1	Phase 1/2a	X-linked Retinoschisis
PTH-0567	Dystrophin	IIT	Duchenne Muscular Dystrophy
PTH-0568 ★	-	IIT	Oculocutaneous Albinism Type 1
PTH-0569	-	IIT	Alzheimer's Disease
PTH-0534 ★	ABCA4	Preclinical	Stargardt Disease

PTH-0566: A Novel AAV Gene Therapy for X-Linked Retinoschisis

X-linked retinoschisis (XLRS) is an X-linked recessive genetic disease caused by mutations in the retinoschisin 1 (RS1) gene. Clinical treatment mainly consists of follow-up observation for complications and drug therapy, such as carbonic anhydrase inhibitors. There is currently no effective clinical cure.

PTH-0566 is an adeno-associated virus (AAV) gene therapy injection currently under development. Through systematic design of target serotypes and gene expression elements, PTH-0566 can efficiently restore the expression of RS1 protein in retinal cells, thereby improving the retinal structure and function of patients.

- AAV Serotype: Self-complementary AAV8, achieving rapid efficacy
- Administration: Subretinal injection, achieving efficient infection of photoreceptor cells
- Target protein: Independently-designed hRS1, enhancing the protein expression level and expression specificity
- Promoter: RSP with good safety and strong expression level

Improving the Retinal Structure and Function in the IIT

In the investigator-initiated trial (IIT), all 12 patients showed good tolerability, with no SAEs or DLTs reported. The results indicated that PTH-0566 had a favorable safety and tolerability profile and was effective at a low dose.

Following a single administration without the need for concomitant therapy, improvements in retinal structure and function were observed, including reduction or even complete closure of the schisis cavity, improvement in best-corrected visual acuity (BCVA), and a significant decrease in central retinal thickness (CRT).

PTH-0565: An AAV Gene Therapy for Durable Anti-VEGF Control in Retinal Disorders

Neovascular age-related macular degeneration (nAMD), diabetic retinopathy (DR), and diabetic macular edema (DME) are common retinal disorders characterized by a lack of spontaneous recovery and continuous progression. Current treatments are dominated by monoclonal antibodies and fusion proteins that require long-term administration, and frequent intravitreal injections reduce patient convenience, adherence, and persistence. In addition, repeated antibody dosing may induce immune tolerance, leading to diminished long-term efficacy.

PTH-0565 was developed using a multi-target strategy, featuring an innovative expression cassette design and coordinated codon optimization, resulting in markedly improved expression efficiency. Compared with similar treatment strategies, PTH-0565 could achieve up to a 19-fold increase in anti-VEGF protein expression, supporting substantial clinical improvements in dosing and safety while reducing overall treatment costs.

Significant Visual Gains Observed in nAMD Patients

PTH-0565 is being evaluated for the nAMD indication in a multicenter Phase I/IIa clinical trial, with available data demonstrating clinically meaningful efficacy. The first treated patient has been followed for more than one year, showing an improvement of over 10 letters in BCVA. The second patient has been followed for more than 40 weeks, with a BCVA gain of over 15 letters.

R&D COMPANY OVERVIEW

G* Biotech is a biotechnology company dedicated to the development of new AAV gene therapy drugs for ophthalmic diseases, neuromuscular diseases, genetic metabolic diseases, etc.

G* Biotech has built a 3000-square meters research and development production base integrating AAV gene drug research and development, pilot-scale preparation and quality control. It has formed a highly integrated and perfect AAV gene therapy "technology chain".

SEEKING OPPORTUNITIES

- Out-licensing
- Co-development
- Financing

About Protheragen

Headquartered in New York, Protheragen is a US-based company specializing in the global pharmaceutical and biomedical sectors. Our core services aim to precisely connect innovative pharmaceutical assets with potential partners worldwide, efficiently facilitating diverse strategic collaborations including, but not limited to: Licensing-out, Financing, Co-development, and Mergers & Acquisitions.

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