MERIT

CASE STUDY

Imaging Solutions for Ophthalmic Gene Therapy Clinical Trials

OVERVIEW

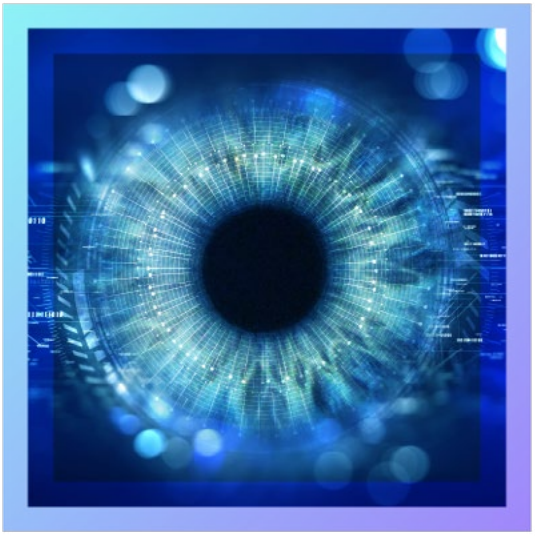
The first FDA-approved ocular gene therapy, voretigene neparvovec-rzyl (Luxturna, Spark Therapeutics), approved in 2017, uses an adeno-associated virus (AAV) vector to deliver a functional copy of the *RPE65* gene for the treatment of Leber Congenital Amaurosis (LCA) type 2. Luxturna was also the first directly administered gene therapy that targets a disease caused by mutations in a specific gene approved in the U.S. Since that time, gene therapy in ophthalmology has continued to advance at a rapid pace.

The eye has been recognized as an immune-privileged organ since the 1940s, contributing to its popularity as a target for gene therapy. It also offers easily accessible anatomy that can be examined with high-quality imaging techniques. The following is a small sample of the vectors, drug candidates, and diseases under study in the field of ophthalmic gene studies, as well as some of the companies currently sponsoring clinical trials:

- **Adeno-Associated Virus vectors**
  - ADVM-022 by Adverum Biotechnologies for neovascular Age-Related Macular Degeneration (nAMD)
  - RGX-314 by REGENXBIO Inc. for nAMD and Diabetic Retinopathy
  - AGTC-501 by Applied Genetic Technologies Corp for X-linked Retinitis Pigmentosa (XLRP)
  - GT-005 by Gyroscope's Therapeutics for dry AMD
  - HMR59 by Hemera Biosciences for dry AMD
  - 5-OPTIRPE65 by MeiraGTx UK II Ltd. for LCA2
  - EDIT-101 by Editas Medicine Inc, CRISPR-Cas9 for CEP290 mutations for LCA10
- **RNA-based antisense oligonucleotides**
  - Sepofarsen by ProQR Therapeutics for LCA10
  - QR-421a by ProQR Therapeutics for RP USH2A

EXAMPLE STUDY

MERIT's imaging expertise and proprietary software play a vital role in gene therapy clinical trials such as the example described below.



SITUATION

A leading biotechnology company sponsors a Phase 2 clinical study to evaluate the efficacy and safety of subretinal delivery of an innovative gene therapy for nAMD.

As a pivotal trial, enrollment and screening of patients has a goal of randomizing over 100 subjects across many study centers.

CHALLENGES

Conducting a large Phase 2b/3 gene therapy trial with multiple sites presents many challenges. This study presents the following potential issues:

- **SPECIALIZED RETINAL SENSITIVITY AND VISUAL FIELD MEASUREMENTS**
- **NUMEROUS TIME POINTS FOR A VARIETY OF IMAGING MODALITIES** including:
  - Fluorescein Angiography (FA)
  - Spectral Domain-Optical Coherence Tomography (SD-OCT)
  - Autofluorescence (AF)
  - Color Fundus Photography (FP)
  - Microperimetry
  - Ocular instability test
  - Pupillometry
- **RAPID TURNAROUND TIME REQUIRED** for processing and reading of images for Inclusion/Exclusion Criteria
- **COMPLEX PROTOCOL** with extensive inclusion/exclusion criteria and long duration (up to 24 months)
- **STRICT REGULATORY AND DATA PRIVACY REQUIREMENTS.** FDA-approved drugs and medical devices for gene therapy face rigorous regulatory requirements from HIPAA to 21 CFR Part 11, to GDPR.

SOLUTION

MERIT's comprehensive portfolio of ophthalmic services provides seamless support for gene therapy trials. Our EXCELSIOR™ platform allows immediate transfer of data directly from qualified sites to a central database for review and storage as well as masked reading. MERIT's team of experts assure high-quality, consistent reading.

MERIT proactively addresses the potential issues of gene therapy studies by:

- **LEVERAGING OUR EXPERIENCE IN SUPPORTING 29 GENE THERAPY STUDIES**, providing valuable knowledge of specialized modalities such as microperimetry and static visual field
- **FACILITATING THE TASKS OF MANAGING MULTIPLE IMAGING MODALITIES** through our cloud-based EXCELSIOR software makes it possible to handle numerous time points and imaging modalities efficiently. The technician and equipment certification, image upload, archiving, viewing, and evaluation are all managed through EXCELSIOR's configurable workflows
- **DELIVERING RAPID TURNAROUND TIME** for processing and reading of images is supported by our team of experts. Our tenured staff provide efficient management of services with Reading Center and CRO partners, supporting quick reading of images according to the trial protocol
- **SUPPORTING TRANSPARENCY AND ACCESSIBILITY** of image submissions in the workflow process providing greater accessibility for CROs and Sponsors
- **PROVIDING THOROUGH, STUDY-SPECIFIC TRAINING** is necessary to support complex protocols. Training covers inclusion/exclusion criteria; primary and secondary endpoints and objectives; ocular data collection and evaluation requirements per time point; and evaluation procedures as detailed in the Imaging and Grading Charter
- **MAINTAINING QUALITY ASSURANCE & COMPLIANCE:** Adherence to regulatory controls and quality policies and procedures reduce the risk of manual error and increase the transparency and reliability of trial data

TAKEAWAYS

- **EXPERIENCE WITH 29 GENE THERAPY TRIALS:** MERIT's tenured staff is well-versed in gene therapy trials, providing the domain expertise required for your program
- **RAPID TURNAROUND TIME:** Efficient, quick turnaround times for image processing and reading, including 3–5-day turnaround for eligibility
- **COMPLEX COORDINATION OF SERVICES, EQUIPMENT, AND IMAGING MODALITIES:** MERIT successfully manages multiple Reading Centers, harmonizing imaging data from many manufacturers, and evaluating various imaging modalities

It's important to have a team of domain experts for complex gene therapy studies to assure high-quality, consistent data review and interpretation. With MERIT, your critical endpoints are safe in our hands.

MERIT

Connect with us to learn more about how our expertise and approach can support bringing your product to market on-time and on-budget. Your success is our priority.

START A CONVERSATION

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