

# MODERNIZING GLAUCOMA TRIALS: EMERGING TRENDS SHAPING CLINICAL DEVELOPMENT

Authors: Karen Klugo, MD, and Tracy Huiet, MS



## ABSTRACT

Glaucoma, a globally leading cause of irreversible blindness, presents significant challenges in both detection and management due to its asymptomatic nature and progressive visual impairment. This whitepaper delves into the complexities of the current glaucoma landscape, emphasizing the need for early detection and the limitations of traditional intraocular pressure (IOP) lowering therapies, which often lead to compliance issues and optical nerve damage.

The standard of care in glaucoma treatment has traditionally relied on a stepwise approach, starting with topical IOP-lowering drops. However, advancements in selective laser trabeculoplasty (SLT) and minimally invasive glaucoma surgery (MIGS) are reshaping treatment strategies, offering alternatives to patients who struggle with compliance or require surgical intervention due to insufficient effect of topical therapies. These developments underscore a pivotal shift from symptom management to disease modification, paving the way for innovative therapies.

Emerging trends in glaucoma therapeutics are moving beyond IOP reduction and towards addressing the underlying disease mechanisms. Innovations such as long-acting formulations, neuroprotective strategies, and personalized medicine are set to revolutionize patient care by enhancing adherence and targeting the disease more holistically.

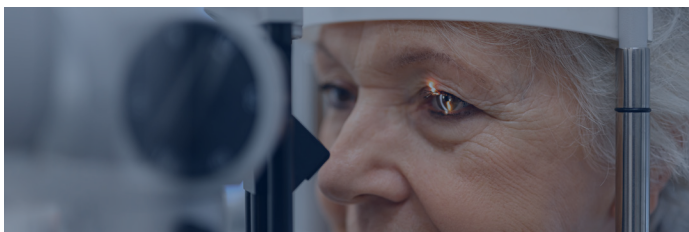
The evolution of clinical trial design is critical to these advancements, with a growing emphasis on precise patient selection, endpoint selection, and the use of imaging biomarkers besides functional outcomes. Nonetheless, operational challenges, like extended study durations and data variability, pose significant hurdles in clinical trials, necessitating robust quality control measures, and strategic planning.

Regulatory and market access considerations are essential in navigating the complex landscape of glaucoma drug development. Understanding global regulatory requirements, safety requirements, and market drivers is crucial for achieving successful outcomes in clinical trials, drug approvals, and ultimately access to patients.

In conclusion, this whitepaper outlines strategic recommendations for Sponsors, emphasizing the importance of partnering with a full-service, global ophthalmology CRO to optimize clinical development and enhance the success rates of glaucoma therapies. By leveraging these insights, stakeholders can better navigate the evolving landscape and contribute to meaningful advancements in glaucoma treatment and patient care.

## UNDERSTANDING THE CURRENT GLAUCOMA LANDSCAPE

Glaucoma remains one of the leading causes of irreversible blindness worldwide. It is characterized by a group of optic neuropathies including primary open-angle (the most prevalent form), angle-closure glaucoma, normal tension glaucoma, and secondary glaucoma that stem from causes like steroid use, trauma, or uveitis. All forms are characterized by progressive retinal ganglion cell loss and corresponding visual field loss. Early detection is critical as the damage from glaucoma is irreversible; however, a challenge remains because patients are often asymptomatic, potentially resulting in significant structural loss before symptoms of functional loss prompt intervention. The traditional mainstay of treatment, topical intraocular pressure lowering drops, introduces several challenges for patients who are required to use them to preserve their sight. Chronic use of topical IOP-lowering drops, especially those with preservatives, increase incidence of ocular surface disease, which can increase patient discomfort and ultimately affect compliance.



## CURRENT STANDARD OF CARE

The current standard of care in glaucoma generally follows a sequential treatment plan, beginning with topical IOP-lowering drops as the first line of therapy. Selective laser trabeculoplasty (SLT) may be used when drops alone are not sufficiently effective to lower the IOP, or adherence becomes an issue. Some surgeons may also use SLT as a first-line option for a newly diagnosed patient who may struggle with compliance. For patients who progress further, minimally invasive glaucoma surgery (MIGS) offers a lower-risk alternative to traditional incisional surgery while reducing dependence on chronic drop therapy. MIGS is also frequently combined with cataract surgery, allowing the opportunity to address IOP control in a patient that has visually significant cataracts. Trabeculectomy and tube shunts remain the traditional surgical approaches for advanced or refractory disease, but they carry a higher complication rate and require intensive post-operative management.

The adherence and treatment burden challenges discussed are shifting the dynamics of glaucoma research from relying on IOP lowering to more complex targets of disease modification and direct neuroprotection. Earlier, more precise diagnostics and a growing focus on gene therapy are further shifting the field from disease management to true disease modification. This evolving environment creates opportunities for new therapeutic approaches currently being developed.

## EMERGING TRENDS IN GLAUCOMA THERAPEUTIC DEVELOPMENT

The glaucoma therapeutic landscape is evolving beyond conventional IOP reduction toward addressing other components of the disease, including potentially modifying the underlying course of the disease. Emerging strategies include long-acting, daily formulations, neuroprotection, and therapies targeting retinal ganglion cell dysfunction and optic nerve degeneration.

Long-acting formulations reduce treatment burden and improve adherence. This is planned with sustained-release implants, injectable depots, and bio-erodible formulations that enable controlled drug releases over days to months. This addresses limitations of topical therapies such as poor compliance, administration errors, and variable exposure.

The devices can provide localized drug delivery with continuous ocular surface dosing.

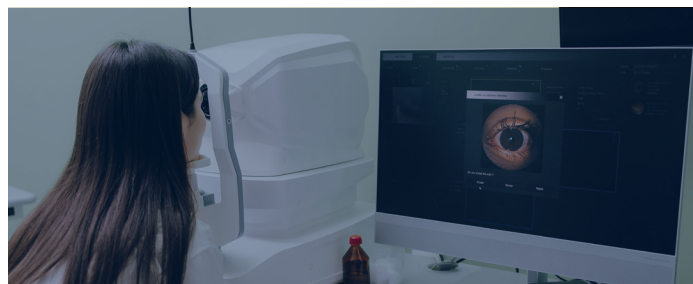
Furthermore, gene therapy is on the innovative horizon for the treatment of glaucoma, offering potential long-term beneficial effects by targeting the disease's underlying cause at a molecular level. Gene therapy for glaucoma aims for two key targets to cure the disease: lower IOP and prevent retinal ganglion cell degeneration.

## OPERATIONAL CHALLENGES IN GLAUCOMA TRIALS

There are operational challenges that can be unique to glaucoma clinical trials such as long study durations, site and patient burden as well as data variability and quality control.

Glaucoma can be a slow progressing disease which can make it difficult to demonstrate a treatment effect on visual function in a clinical trial of short follow-up duration, especially for treatments targeting neuroprotection or disease. Studies focused on IOP lowering can be conducted in a short timeframe.

Differences in technique for visual assessments can cause increased variability in data. It is important to ensure proper training of site staff and technicians by completing visual assessments for each study. IOP can also be varied and is influenced by time of day, corneal properties, and measurement techniques. Variability can be decreased when ensuring consistency in the technicians completing assessments from visit to visit and in time of measurements at the visits.



## MARKET ACCESS CONSIDERATIONS

Market access for new glaucoma treatments can be challenging because the treatment landscape is mature and inexpensive, with many topical agents to lower IOP such as prostaglandin analogues,  $\beta$ -blockers, carbonic anhydrase inhibitors,  $\alpha$ 2-agonists and fixed-dose combinations. Procedural alternatives such as selective laser trabeculoplasty (SLT) are increasingly used, also in newly diagnosed patients. Therefore, new treatments should provide sufficient incremental value over existing treatment to justify its price and secure reimbursement. As a consequence, more IOP reduction than topical standard of care drops is not sufficient, a new innovative treatment that demonstrates reduced glaucoma progression and improved visual function outcomes such as visual field maintenance over a long period of time has a much stronger value proposition. This distinction between IOP lowering effect and reduced progression should determine the clinical development program from the beginning. It is furthermore important to identify the population in which the unmet need is greatest, such as patients inadequately controlled on multiple medications, or patients with poor adherence. Finally, defining the right comparator is one of the most important issues in clinical development. In general, the comparator should reflect actual treatment pathways in the intended markets, rather than simply the comparator that makes the clinical trial easiest. To summarize, a health technology evidence package that contains advanced clinical efficacy, patient benefit, and economic consequences of the new treatment compared to the optimal standard of care treatment in the aimed markets is required for market access and adequate pricing and reimbursement.

## WHAT ADVANTAGES DOES MEDPACE OFFER SPONSORS AS A CRO PARTNER FOR SUCCESSFUL GLAUCOMA CLINICAL DEVELOPMENT?

In conclusion, the landscape of glaucoma clinical development is rapidly evolving, necessitating strategic approaches that optimize study efficiency and outcomes. For Sponsors, prioritizing a partnership with a full-service global ophthalmology CRO like

Medpace can be pivotal. Medpace's integrated Central Lab, Bioanalytical Lab, ECG, and Imaging Core Lab services offer a holistic approach to clinical studies, enhancing efficiency and streamlining communication and management. This single-vendor strategy significantly reduces operational complexities and fosters a cohesive study environment.

Furthermore, Medpace's flexible resourcing ensures that as development programs progress, the necessary global, in-house resources are allocated to meet project deliverables. This adaptability is essential in accommodating the dynamic nature of clinical trials, allowing for seamless scaling and resource management.

Lastly, maintaining continuity with Medpace across your program ensures that your assigned team remains consistent, fostering strong team chemistry, optimizing performance, and minimizing disruptions. This continuity is instrumental in delivering high-quality results, ultimately contributing to the successful development of glaucoma therapeutics. By leveraging these strategies, Sponsors can navigate the complexities of glaucoma clinical trials with confidence and precision, setting the stage for breakthroughs in disease management and patient care.

## FULL-SERVICE CLINICAL DEVELOPMENT

Medpace is a scientifically-driven, global, full-service clinical contract research organization (CRO) providing Phase I-IV clinical development services to the biotechnology, pharmaceutical and medical device industries. Medpace's mission is to accelerate the global development of safe and effective medical therapeutics through its high-science and disciplined operating approach that leverages local regulatory and deep therapeutic expertise across all major areas including oncology, cardiology, metabolic disease, ophthalmology, endocrinology, central nervous system and anti-viral and anti-infective.

Visit our [website](#) to learn more about our ophthalmology capabilities, and how we can help with your future clinical development plans.

---

MAKING THE COMPLEX  
**SEAMLESS**

