

eBOOK

# Advancing ocular therapeutics

Application book volume 1



• **Fortrea**



# Introduction

## Advancing ophthalmology clinical development across global markets

Ophthalmology research continues to evolve as sponsors pursue new approaches to address retinal disease, geographic atrophy, dry eye disease, progressive myopia and other vision-threatening conditions. As treatments become more sophisticated and development programs increasingly span multiple countries and regions, successful clinical trials require therapeutic knowledge, operational agility and the ability to navigate diverse healthcare environments. The stakes are high because every milestone achieved has the potential to move an innovative therapy closer to patients living with significant unmet needs.

Fortrea has supported ophthalmology studies across a wide range of indications, trial phases and product types, including pharmaceuticals, cell and gene therapies, medical devices and diagnostics. Our experience spans first-in-human to large-scale global Phase III programs, pediatric ophthalmology studies, regional APAC trials and complex retinal disease research requiring close coordination among sponsors, investigators/sites, patients (caregivers) and vendors. This breadth of experience provides valuable insight into the unique challenges that can influence study timelines, recruitment performance and overall trial execution.

What makes ophthalmology research distinct is the combination of scientific complexity and patient-specific considerations. Many studies rely on highly specialized investigators, advanced imaging requirements and detailed clinical assessments. Recruitment can be particularly challenging when patient populations are difficult to identify or when regional healthcare practices differ significantly from one market to another. In these situations, success often depends on thoughtful planning, proactive communication and the ability to adapt strategies as conditions evolve.

**The case studies in this eBook** highlight a range of ophthalmology clinical development challenges and the strategies used to address them. Sponsors encountered obstacles including compressed timelines, recruitment barriers, pandemic-related disruptions, complex regulatory requirements and evolving program objectives. Across each program, teams worked closely with stakeholders to develop practical solutions, maintain momentum and support critical development milestones, demonstrating how thoughtful planning, responsive execution and deep therapeutic understanding can help sponsors navigate complexity and achieve meaningful outcomes.



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# Unlocking biotech potential:

## A KEY QUESTION



How can a close sponsor-CRO collaboration meet a newly requested critical milestone?



## KEYWORDS

Ophthalmology, Geographic Atrophy (GA), Data Cut Request, Collaboration, Biotech

## An ophthalmology case study with Apellis

Apellis Pharmaceuticals, a growing biopharmaceutical company, wanted to investigate the efficacy of SYFOVRE® (pegcetacoplan injection) to treat patients with geographic atrophy (GA), an advanced form of dry age-related macular degeneration. A leading cause of blindness, GA affects more than five million people worldwide and one million in the United States alone. This targeted C3 therapy helps regulate excessive activation of the complement cascade within the immune system, a known contributor to the progression of many serious diseases. The implemented development plan for SYFOVRE® consisted of two global Phase III studies across 15 countries in over 200 sites worldwide, with an additional open-label extension study that was awarded later. The complexities of the trials required a contract research organization (CRO) collaborator with global reach, scalable solutions and excellent project and data management, which is why Apellis turned to Fortrea for support.

### Delivering on the data cut request

As the study approached a critical milestone, Apellis submitted a request to Fortrea for a data cut across the program. The request? Deliver data cut in a month. To meet this request, Fortrea leadership took immediate steps to develop a timeline with tight target delivery dates, increased staffing support for data management, organized daily internal and external meetings and collaborated even more closely with vendors and sites.

### KEY TAKEAWAYS

- Managed two full-service Phase III ophthalmology studies across 15 countries and over 200 clinical sites
- Satisfied sponsor request for data cut in a month
- Saved time in sponsor's New Drug Application for **first-ever treatment** for geographic atrophy patients who had no treatments available

The executed strategy included:

- Assessed routine deliverables to focus the full global team on the required critical data points of the data cut
- Tailored reporting to focus on the needs of the sponsor to reach the deliverable
- Frequent status updates among team members and leadership to support on-time delivery of the data cut
- Daily calls to the sponsor providing latest communication and status

Undaunted by the task, Fortrea scaled its global resources and engaged project management leads to collaborate tirelessly across worldwide time zones in support of the sponsor's request. The cut was delivered as requested by the target date, inspiring new confidence in Fortrea's capabilities and commitment to excellence.

According to Jason Raines, Senior Vice President of Development Operations at Apellis, "We requested tight timelines. We needed this data cut in the timing we asked for to support our mission and I appreciated the can-do attitude that was shown. Fortrea came to the table with problem-solving in mind."

### **Combining flexibility with operational agility for data-driven results**

Many biotech companies choose not to collaborate with global CROs due to concerns of deprioritization. However, this was not the case with the sponsor. Fortrea's mission to be more than a collaborator in the sponsor-CRO relationship drives dedicated collaboration, no matter the size or volume of business.

"Our concern when selecting a large CRO collaborator was that we wouldn't get as great of a service because of our size," Apellis said. "But we got the care we needed. Apellis and Fortrea built a true collaboration that has delivered multiple and critical milestones which simply could not have been done without great team communication, organizational agility, scalability in terms of people, processes, and systems and a global footprint."

**"Fortrea excels at planning, risk assessment and mitigation, and functional collaboration."**

**Apellis**

### **Pioneering life-changing treatment for patients**

Thanks to Apellis and Fortrea collaboration's speedy delivery of the data cut, Apellis successfully met its critical deadline and SYFOVRE® was approved by the FDA as the first-ever treatment for geographic atrophy. This collaboration highlighted how every day saved in clinical trials is not just a day saved in time and costs to the sponsor, but also a day closer to potentially delivering a medical breakthrough—and new hope—to patients in need of innovative healthcare solutions.

# Phase III Global Geographic Atrophy trial

## A KEY QUESTION



When patient recruitment depends on understanding diverse regional healthcare landscapes and local market dynamics, how do you support enrollment success across continents?



## KEYWORDS

Geographic Atrophy Clinical Trial, Ophthalmology Research, APAC, Patient Recruitment, Global Recruitment, Local Nuances

## Introduction

In a registrational Phase III geographic atrophy trial spanning eight countries and 50 sites across the U.S., Europe and APAC, Fortrea encountered an unexpected recruitment challenge that could have affected study timelines. While U.S. and European sites progressed as anticipated, APAC enrollment lagged significantly—not due to lack of patients, but because of fundamental differences in regional healthcare practices. In countries without established standard of care pathways for the ophthalmology disease, patients simply weren't presenting to clinics regularly, making traditional site-based recruitment strategies ineffective. Through agile leadership response, strategic vendor collaborations and sustained regional engagement, we transformed these obstacles into opportunity—completing enrollment one month ahead of schedule and randomizing 530 patients versus the 500 target. Here's how we turned geographic complexity and local healthcare nuances into pathways for global trial success.

## Addressing enrollment and retention challenges

This Phase III geographic atrophy trial presented unique patient recruitment challenges that required deep understanding of regional healthcare systems and flexible, tailored solutions. To meet the sponsor's registrational goals, the trial needed to randomize 500 patients while maintaining data quality across diverse global sites. However, what worked in Western markets proved insufficient in APAC regions:

### **Absence of standard care pathways in key**

**APAC markets:** In certain APAC countries, geographic atrophy had no established standard of care (SoC) treatment, fundamentally changing patient behavior. Unlike in the U.S. and Europe where patients with this disease typically maintain regular ophthalmologist visits for monitoring and emerging treatment options, as APAC patients lack a SoC treatment pathway, they had no clinical reason for routine appointments. This meant the traditional investigator referral model—where existing patients in clinic databases provide the recruitment foundation—wasn't a practicable model. Investigators rarely encountered these patients in their day-to-day practice, and when they did, these patients often weren't engaged in ongoing care. This created a recruitment paradox: Sites were selected for their ophthalmology experience, but the patient population existed outside their regular clinical flow.

### **Site engagement and motivation challenges:**

When investigators consistently fail to identify eligible patients despite significant effort, frustration and disengagement naturally follow. This risk was particularly acute in APAC, where sites had invested in study start-up activities, training and preparation, but were unable to leverage this due to patient availability issues rather than site capability problems. Maintaining investigator enthusiasm and preventing site attrition in underperforming regions required proactive communication and tangible solutions, not just encouragement.

## Solutions to boost enrollment

When slower than expected enrollment trends emerged, Fortrea didn't wait for problems to escalate. We promptly organized leadership meetings to analyze regional data patterns and develop rapid-response solutions. This proactive approach enabled us to identify root causes at affected sites and implement targeted interventions before rates could threaten trial timelines and integrity.

**Local recruitment vendor collaboration:** In China and select APAC countries where recruitment vendors are widely used and culturally accepted, Fortrea recommended a local, qualified vendor with proven experience in ophthalmology trials and verifiable patient identification capabilities. This wasn't about outsourcing recruitment—it was about accessing patient populations through channels that matched local healthcare realities. Once approved, this vendor conducted systematic outreach to hospitals and ophthalmology clinics, identifying patients with geographic atrophy diagnoses in medical records who weren't actively seeking care. This approach effectively created the patient database that didn't naturally exist through regular clinic flow, enabling sites to screen candidates who would likely not have been identified through traditional methods.



**Cross-site collaboration and learning:**

We implemented regular meetings among all sites globally to share lessons learned, discuss ongoing recruitment challenges and foster collaborative problem-solving. During these sessions, high-performing sites provided best practices that were working well for them—such as specific messaging that resonated with patients, effective physician referral approaches or screening process efficiencies—enabling rapid adoption across the network. This governance structure helped turn individual site successes into network-wide improvements and helped to support APAC sites in not feeling isolated in their recruitment challenges.

**Targeted site support with regional engagement:**

At Fortrea we have a strong APAC delivery team. We maintained close collaboration and communication between Fortrea, investigators and recruitment vendors through weekly meetings and onsite booster visits. In Taiwan, we worked closely with investigators to support patient screening despite high screen failure rates. In Australia, we conducted regular meetings with investigators and study coordinators to help maintain motivation and engagement throughout the study duration.

**Real-time monitoring and proactive intervention:**

We programmed Quality Tolerance Limits (QTLs) to closely monitor enrollment rates, screen failure patterns and protocol deviations across all sites. This enabled data-driven decision-making about where to focus support resources, which sites needed additional training or encouragement and when enrollment strategy adjustments were necessary. Early warning systems were critical to maintaining enrollment targets and preventing small regional delays from becoming major timeline threats.

**Results: Ahead-of-schedule enrollment and global study success**

By completing last patient randomization one month ahead of schedule, Fortrea successfully exceeded the sponsor's timeline expectations despite significant regional recruitment challenges. The trial randomized 530 patients versus the 500 target, helping to provide an additional buffer against attrition and protecting data integrity for registrational submission.

Perhaps most importantly, we successfully activated and maintained engagement across 50 sites in eight countries spanning the U.S., Europe and APAC—proving that with flexible, regionally tailored approaches and proactive problem-solving, even complex global ophthalmology trials can deliver on aggressive timelines.

# Ophthalmology gene therapy trial:

Project Manager

Knowledge and  
essential to driving  
sensors.



## Clinical project management is fundamental to ophthalmology research

In the evolving landscape of ophthalmology clinical research, the role of the clinical project manager is pivotal. These professionals serve as the linchpin between sponsors, sites, vendors and patients—ensuring that complex studies are delivered efficiently, compliantly and with a focus on quality. Their ability to coordinate multidisciplinary teams, navigate regulatory requirements and maintain clear communication is essential to the success of any clinical trial.

### Adam Sgarlata



**Adam Sgarlata, Senior Clinical Project Manager,** is a clinical research leader with over 15 years of experience managing ophthalmology trials across Phases I-IV; whose leadership and experience have played a key role in expanding our ophthalmology gene therapy trial portfolio. With deep experience in driving site engagement, patient recruitment and vendor oversight, he is passionate about translating scientific innovation into operational execution.



### Questions & Answers with Adam Sgarlata



**Adam, can you provide an overview of the ophthalmology gene therapy program and your background?**



Absolutely. I've been in clinical research for 15 years, with a focus on retinal studies and global project management. Our current program is a suite of gene therapy studies for neovascular age-related macular degeneration, all running across about 90 sites in the U.S. What's unique is that many of these sites participate in multiple studies, which lets us drive real efficiencies.



**What was the biggest challenge you and your team faced in launching the ocular gene therapy trial?**



The studies kicked off right in the middle of the pandemic, and we were asking sites—many of them completely new to gene therapy—to take on this large gene therapy dosing program. The regulatory and practical hurdles were significant—not just Institutional Review Board (IRB) approvals, but also institutional biosafety committees, complex storage and administration protocols, and a steep learning curve for everyone involved.



## Questions & Answers with Adam Sgarlata



### How did Fortrea help sites overcome these challenges?



We leaned into our long-standing relationships with high-performing retina sites. Because we'd worked with many of these clinics before, we knew their capabilities and could move quickly through the start-up process. But the real difference was our hands-on support. Our in-house and field CRAs spent hours working with and training site staff, helping them get certified on imaging and study procedures, and making sure they had the equipment and confidence to run these studies effectively with everything they needed. Our start-up team worked closely with study coordinators to help educate and navigate the National Institutes of Health (NIH) Institutional Biosafety Committee (IBC) registration process from start to finish—especially as staff turnover was high during the pandemic and communication was complex.

We also built a robust communication network. Sites always knew who to call, and I made sure my number was available if they needed help fast. It's a small-team feel with big-team backing—agile, responsive and always ready to jump in and solve problems.



### What differentiates Fortrea in managing complex ophthalmology gene therapy trials like this?



Adaptability and collaboration. We started with just one study and quickly scaled to six, adding new cohorts, increasing sample sizes and complexities as the program grew. Our teams are nimble—we pivot fast to reduce the burden on sites and keep the lines of communication open. We also work closely with vendors, from imaging to equipment, to make sure every piece fits together seamlessly and sites are able to receive, manage and properly administer the test material, which, in terms of gene therapy studies, required a lot of additional cold-chain logistics, safety protocols and education to the site staff.



### Can you share a moment where collaboration made a real difference?



There were plenty, but one stands out. When sites faced sudden staff change, our team jumped on calls with each of the sites to train new coordinators and staff to get them up to speed with the studies and quickly got them certified. That kind of responsiveness kept the trial and site on track and built trust with our clients.



### What advice would you give to sponsors planning similar trials?



Invest in relationships and communication. The science is complex, but it's the people and the process that make or break a study. Be ready to support sites and the patients at every step, and don't underestimate the value of a team that's willing to roll up their sleeves and solve problems together.

**“ We leaned into our long-standing relationships with high-performing retina sites...we knew their capabilities and could move quickly. ”**

A. Sgarlata



### Any final thoughts on the patient experience in gene therapy trials?



Gene therapy brings new hope, but it also brings complexity—especially for patients. Some routes require surgical administration and extra aftercare, while others are less invasive. Our job is to reduce the burden wherever possible, making sure patients and their caregivers are informed and feel supported every step of the way. At the end of the day, vision is everything for these patients, and we never lose sight of that.

# Accelerating APAC region

ials

## A KEY QUESTION



How can sponsors accelerate clinical trial timelines when unexpected challenges arise?

## KEYWORDS

Ophthalmology, APAC, Dry Eye Syndrome, Clinical Development, Patient Enrollment, Site Engagement, Operational Agility

Drawing on our 30+ year CRO heritage of Fortrea, formerly as part of Covance and Labcorp Drug Development, including all of the ophthalmology experience gained during the 2017 acquisition of Chiltern, we collaborated with a rapidly growing biotech in China to advance their ophthalmology program. This case study illustrates how our ophthalmology experience, great engagement with local sites and investigators and agile approach to regional operations provided the multifaceted capabilities to facilitate our collaborator's dry eye syndrome pipeline development.

## Key highlights

In this ophthalmology trial, several key learnings emerged, highlighting the importance of transparent communication, the role of flexibility at a global level and foundational elements of follow-through and trust.

- **Effective communication:**  
Maintaining open communication with the sponsor and being sensitive to their commercial strategy is vital
- **Agile approach:**  
Fortrea's ability to adapt processes and mobilize resources swiftly is crucial in navigating unexpected challenges
- **Trusted collaboration:**  
Building trust through swift, personalized attention and action is essential for success in clinical trials

## The challenge

Fortrea faced several challenges during this collaboration:

- 1. Restrictions and shortages during COVID-19 lockdown:** Enrolling patients became challenging during the COVID-19 lockdown period, with on-site visit restrictions and site resource shortages. As this was an ophthalmology study, patients needed to access the clinic in order to undergo the assessments and tests required for patient monitoring and the study endpoints.
- 2. Last patient in (LPI) impact:** The national COVID-19 outbreak in China from November 2022 to January 2023 significantly affected the study's LPI target.
- 3. Sponsor's commercialization strategy shift:** Our client's timelines changed due to critical go-to-market strategies for their current pipeline, which would determine the success of commercialization in the local market. Major changes included moving the clinical study report (CSR) final submission deadline to three months ahead of the original plan.

## Customer focus: Our unwavering commitment

These challenges required quick thinking and a laser-like focus on customer needs:



## Fortrea's actions and solutions

Fortrea's team responded to these challenges with agility and efficiency, proactively managing the situation to minimize disruption to the LPI target. Additionally, in response to the sponsor's strategy shift, Fortrea mobilized cross-functional teams, optimized internal processes and customized procedures to meet the accelerated CSR submission timeline.

**Close communication and engagement with ophthalmology sites and staff:** With considerable planning and supervision, clinics were made accessible to patients for assessments and monitoring visits were conducted, thus maintaining the project momentum despite the COVID-19 restrictions.

**Excellence in local operation:** A strong, capable ophthalmology-experienced team, based in China, took responsibility and with a "make it possible" attitude and scrupulous execution planning, the team successfully delivered the project.

## Strategic guidance and services provided

In response to the sponsor's request for an accelerated CSR submission, Fortrea provided critical strategic guidance and services:

- Escalated to senior management and functional heads for timely support
- Developed a detailed daily work breakdown and feasibility evaluation
- Collaborated with the sponsor to achieve the database lock (DBL) target ahead of schedule
- Adjusted data management, clinical monitoring and CSR timelines to expedite the process
- Facilitated budget negotiations to achieve agreement

## The success story

Fortrea's collaborative efforts supported the timely CSR submission, accelerating the product launch for our APAC collaborator. Our client expressed extreme satisfaction with the study delivery—particularly the final CSR delivery. This collaboration has built a trusted relationship between Fortrea and our Chinese collaborator.

## Conclusion

In summary, our ophthalmology capabilities, agility and commitment to customer experience proved essential to our collaborator's success. Through swift and sure adjustments achieved through collaborative efforts, Fortrea and our APAC region collaborator overcame challenges, expedited timelines and delivered results. This case stands as an example of both our operational capabilities and dedication to advancing ophthalmology trials—no matter the obstacles.



# Progressive myopia treatment evaluation

## A KEY QUESTION



How can sponsors successfully recruit diverse pediatric patients and manage global sites to advance progressive myopia medical device trials?

## KEYWORDS

Medical Devices, Pediatric Patient Recruitment, Patient Diversity, Site Management, Progressive Myopia, Global Ophthalmology Trial



Unlike regular myopia (shortsightedness), progressive myopia worsens over time and leads to increasingly severe visual impairment. It often begins during childhood or adolescence and can continue into adulthood if left untreated. Asian ethnic children are disproportionately affected by progressive myopia. Studies show a higher prevalence in this population compared to the general population.

Running trials that target this affected population requires not only detailed knowledge of medical device development, but also pediatric patient recruitment and its associated complexities including anticipating and accommodating the needs of multi-national regulatory authorities.

## Patient population and size

The subject sample in the clinical study is myopic children between the ages of 7 to <13 years (at the time of enrollment) randomized in a 2:1 ratio. Number of randomized patients participating is 145. Countries participating in the trial: Canada, Hong Kong, U.S. and Singapore.

Due to anticipation of future submission to the NMPA (Chinese Regulatory Authority), the requirement of at least 30% of the population from all sites to be native Chinese was also followed and metrics reported.

### Timelines

- **Start date:** March 5, 2021
- **LPI:** September 2022
- **LPO:** December 2025
- **End date:** March 2026
- **Enrollment rate:** 13 subjects per month (varied by site)

### Critical milestones

- 12 month interim analysis for determination of crossover/treatment change November 2023
- To prepare the sites for crossover, DM and CTL implemented document with set guidelines
- CTLs trained the CRAs, and the CRAs work 1:1 with the sites when their first crossover visit window is upcoming

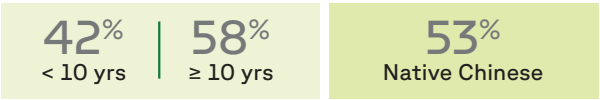


### Challenges

As well as the anticipated challenges of a trial involving children across multiple countries and sites, the trial also faced unforeseen challenges with both international ethics committees and COVID-19 shut downs and restrictions. These included:

- Site start-up in APAC countries (Hong Kong and Singapore) was extensive
- Hong Kong sites approved by CFDA were limited to four sites
- One Hong Kong site EC would not approve study design unless atropine was used as comparator and was not included in trial
- Many of the sites were research naïve optometry sites with no clinical trial experience
- Study start during COVID-19 shut down—impacted recruitment in Canada due to limitations to on-site visits
- High number of screen failures due to the inclusion/exclusion (I/E) criteria resulted in protocol amendment
- Defined variables involved as secondary endpoints at the beginning of the study, as well as well-established subgroups, therefore aiding in final analysis
- CRF data capture developed to help determine variables that may affect the Myopia progression and treatment response such as genetic or environmental factors

## Demographic diversity breakdown



|                            | <10 years | ≥10 years | Total |
|----------------------------|-----------|-----------|-------|
| 101—Canada                 | 1         | 3         | 4     |
| 102—Canada                 | 4         | 11        | 15    |
| 203—Hong Kong              | 19        | 31        | 50    |
| 204—Singapore              | 1         | 11        | 12    |
| 301—U.S. Chicago, IL       | 6         | 3         | 9     |
| 302—U.S. New York City, NY | 7         | 2         | 9     |
| 303—U.S. Houston, TX       | 22        | 23        | 45    |
| 304—U.S. Fresno, CA        |           | 1         | 1     |
| GRAND TOTALS               | 60        | 85        | 145   |

## Successful outcome

Fortrea met the evolving needs of the trial by being agile with design and requests.

This challenging patient population meant that we expanded the countries in the study, and modified our strategy to recruit successfully and meet diversity requirements. We also updated inclusion/exclusion criteria to reduce screen failures, and leveraged Facebook to boost enrollment. We also worked with our Site network to accommodate children and their school schedules by running the studies during evening hours and on Saturdays.

The Data and Safety Monitoring Board (DSMB) charter was also modified to meet requests to outline expectations and support an efficient review process.

Before the trial was completed, we were also able to provide data at the sponsors request to support industry meeting updates.

# Conclusion

## Supporting innovation across the ophthalmology development journey

The ophthalmology landscape continues to advance rapidly, creating new opportunities to address diseases and conditions that affect vision and quality of life for millions of people worldwide. As innovation accelerates, sponsors are increasingly challenged to manage complex study designs, recruit specialized patient populations, navigate regional differences and maintain momentum toward important development milestones.

The case studies in this eBook demonstrate how these challenges can be overcome through careful planning, operational flexibility and close collaboration among all stakeholders involved in the clinical research process. Whether accelerating a first-in-class geographic atrophy treatment, overcoming recruitment barriers across multiple regions, supporting gene therapy studies during a period of unprecedented disruption, advancing development programs in APAC markets or managing pediatric medical device research, each example reflects a commitment to solving problems and keeping studies moving forward.

Collectively, these stories highlight the value of combining global capabilities with local insight. They show how understanding patient needs, site requirements and regional healthcare dynamics can contribute to stronger recruitment performance, more efficient studies and successful delivery against ambitious timelines. They also reinforce the importance of maintaining clear communication and adapting quickly when circumstances change.

As the future of ophthalmology continues to evolve, the need for effective clinical development strategies remains constant. The experiences shared throughout this eBook reflect the dedication, scientific understanding and operational capabilities required to support innovative treatments from development through key milestones. Most importantly, they demonstrate how focused execution can help bring new possibilities closer to the patients and communities that stand to benefit from advances in vision care.



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