

Transforming vision with end-to-end phase 3 execution for a novel presbyopia therapy

Operational excellence in 1,000+ subject US presbyopia program



Advancing a new pupil modulating therapy for presbyopia

Presbyopia is a near universal condition affecting adults over age 45 and impacting daily activities such as reading, device use, and near task productivity. Ora recently partnered with a biotechnology company to initiate a complex large-scale program for an innovative, pupil modulating ophthalmic therapy designed to improve depth of focus safely and noninvasively.

Ora partnered with this sponsor to deliver a fully integrated, end-to-end Phase 3 program evaluating efficacy and safety —spanning protocol development, regulatory support, site activation, monitoring, data management, medical oversight, CMC coordination, and final CSR delivery. The program included three Phase 3 US based studies evaluating a daily topical drop, including randomizing a total of 1,059 subjects across 71 enrolling sites.

Challenges in conducting presbyopia clinical trials

Presbyopia trials face inherent scientific and operational challenges because the condition involves a complex combination of lenticular stiffening, ocular biomechanics, and dynamic pupil behavior. Pharmacologic presbyopia treatments rely heavily on pupil modulation, yet determining the optimal pupil size that balances improved depth of focus with adequate retinal illumination remains a major uncertainty. Recent modeling work shows that smaller pharmacologically induced pupils enhance depth of focus but may compromise light throughput, and the clinically effective range is still under debate, creating difficulties in endpoint selection and response characterization within trials.

Establishing consistent, reliable efficacy endpoints introduces additional complexity. BCVA and near vision assessments are sensitive to lane setup, lighting, examiner training, and calculation accuracy.

Experience from presbyopia programs demonstrates that LogMAR calculations are frequently prone to site error, requiring repeated retraining, additional monitoring, and standardized certification protocols. These issues reflect broader scientific challenges noted in the literature: pharmacologic drops often induce only modest improvements in reading ability unless they achieve a very small pupil (<2 mm), and the effect is short-lived, making timing of assessments critical and susceptible to variability. Even drugs that successfully modulate pupil size can introduce myopic shift or dimming effects that are not fully predictable, complicating endpoint interpretation and increasing the risk of inconsistent efficacy signals across sites.

Recruitment and patient selection also present obstacles. Although presbyopia is widespread, trials often need patients within a narrow age and severity range to produce meaningful pharmacologic effects, as early presbyopes respond differently than more advanced presbyopes. Clinical experience shows that only select patients benefit significantly from pharmacologic miosis, and patient satisfaction varies widely depending on pupil dynamics and tolerance of side effects such as dimming or headaches. Moreover, as highlighted in review articles, there are persistent concerns about long-term safety—including potential risks such as retinal complications—that require longer follow-up and strict monitoring, potentially deterring participation and increasing study burden.

The operational demands of presbyopia trials are heightened by the need for robust site selection, consistent lane certification, and tight control of visual acuity testing conditions. Program level learnings show the importance of unified feasibility planning across efficacy and safety studies, aligned expectations for BCVA certification, and precise execution of both remote and onsite setup activities. Without rigorous harmonization, variability in lane certification, examiner technique, and test environment can materially affect primary endpoints. These constraints are further compounded by the volume of near vision assessments and the need for multiday monitoring visits at high enrolling sites, elevating CRA workload and emphasizing the need for strong training and quality oversight.

Phase III studies for Presbyopia - 1059 subjects randomized

Full scope of services including Ora CMC and DM/Biostats

Efficacy 1

- 22 sites
- 469 subjects
- Enrollment
8.5 months

Efficacy 2

- 17 sites
- 229 subjects
- Enrollment
8.5 months

Safety

- 32 sites
- 361 subjects
- Enrollment
4 months

Ora's end to end execution

Ora managed every operational and scientific component of the program:

- Project Management
- Clinical Monitoring
- Data Management
& Biostatistics
- CMC oversight
- Safety and medical
monitoring
- BCVA oversight
- Regulatory and quality support
- Vendor management
- Medical writing (protocols,
amendments, IB updates, CSRs)

Consistent PM & CRAs remained on the program from hand off through database lock, ensuring exceptional continuity and efficiency.

Execution at scale with speed

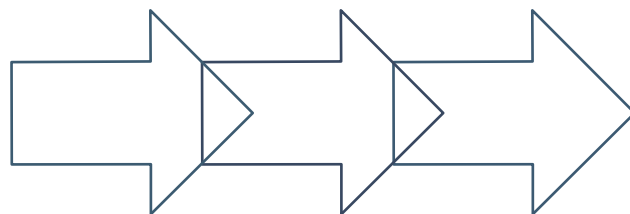
Despite the enrollment challenges introduced by strict inclusion and exclusion criteria, Ora successfully advanced execution across all three Phase 3 presbyopia studies through disciplined coordination and site level engagement. Recruitment momentum was strengthened early through three rounds of IRB approved screening reimbursement initiatives, which helped motivate sites to increase screening volume. Frequent Brief IMs provided continuous updates, reinforced best practices, and ensured study teams stayed aligned on enrollment strategies. These efforts, combined with targeted operational support for slower performing sites, positioned the program to meet the sponsor's yearend enrollment goal despite timelines extending approximately one month beyond initial projections.

Operational execution was underpinned by a unified site selection strategy that optimized efficiency across the entire program. A single feasibility assessment supported both efficacy and safety studies, enabling streamlined decision-making and consistent activation standards. By conducting a mix of remote and onsite SQVs—supplemented by SQV waivers for prequalified sites—Ora accelerated startup while preserving quality. Importantly, sites activated for efficacy studies were also set up for participation in the Safety Study, allowing screen fail subjects to roll over seamlessly when eligible and maintaining enrollment continuity across the broader program. This structured, cross study approach minimized redundancy, reduced activation delays, and created an integrated operational framework that strengthened overall execution.

As sites activated and enrollment progressed, Ora remained fully engaged to ensure data quality, endpoint fidelity, and monitoring efficiency. Alignment around BCVA expectations required expanded onsite lane certification, enhanced coordination with BCVA teams for timely supply distribution, and additional training to harmonize sponsor expectations with standard procedures. When LogMAR calculation errors emerged, Ora responded with targeted retraining, comonitoring, and supplemental IMVs to confirm correction of all impacted data. High enrolling sites received added monitoring days, and continuous SDV tracking enabled Ora to anticipate and resolve issues before they affected timelines. Combined with effective IP management—including securing supplemental refrigerators and prioritizing shipments—these efforts ensured smooth operational flow and supported successful delivery of all three studies through database lock.



Key takeaways for future presbyopia development



Prioritize program wide site strategy early
using a combined feasibility and aligned SQV plan



Ensure alignment and set clear site training goals for BCVA certification



Require CRA competency validation for LogMAR and other critical endpoints

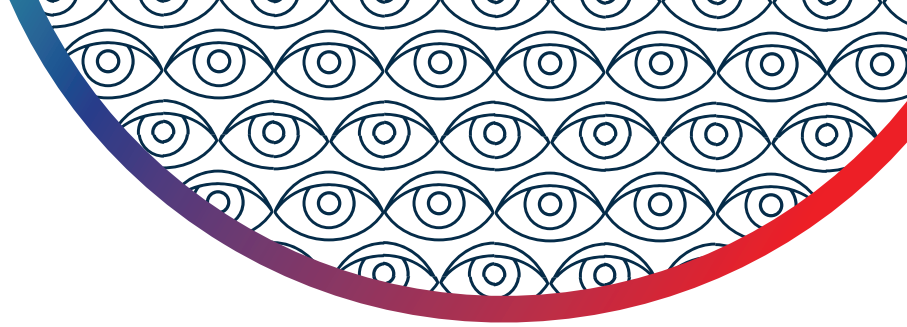


Plan multi day IMVs for complex ophthalmic endpoints



Preserve staffing continuity—PM and CRA consistency dramatically improves quality and efficiency

Future Presbyopia trials will demand not just operational rigor, but trust, foresight, and innovation. Ora's success in this pivotal program shows how an engaged network, continuous learning, and sponsor alignment can overcome execution challenges and advance the field toward approval of next generation Presbyopia therapies.



References

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