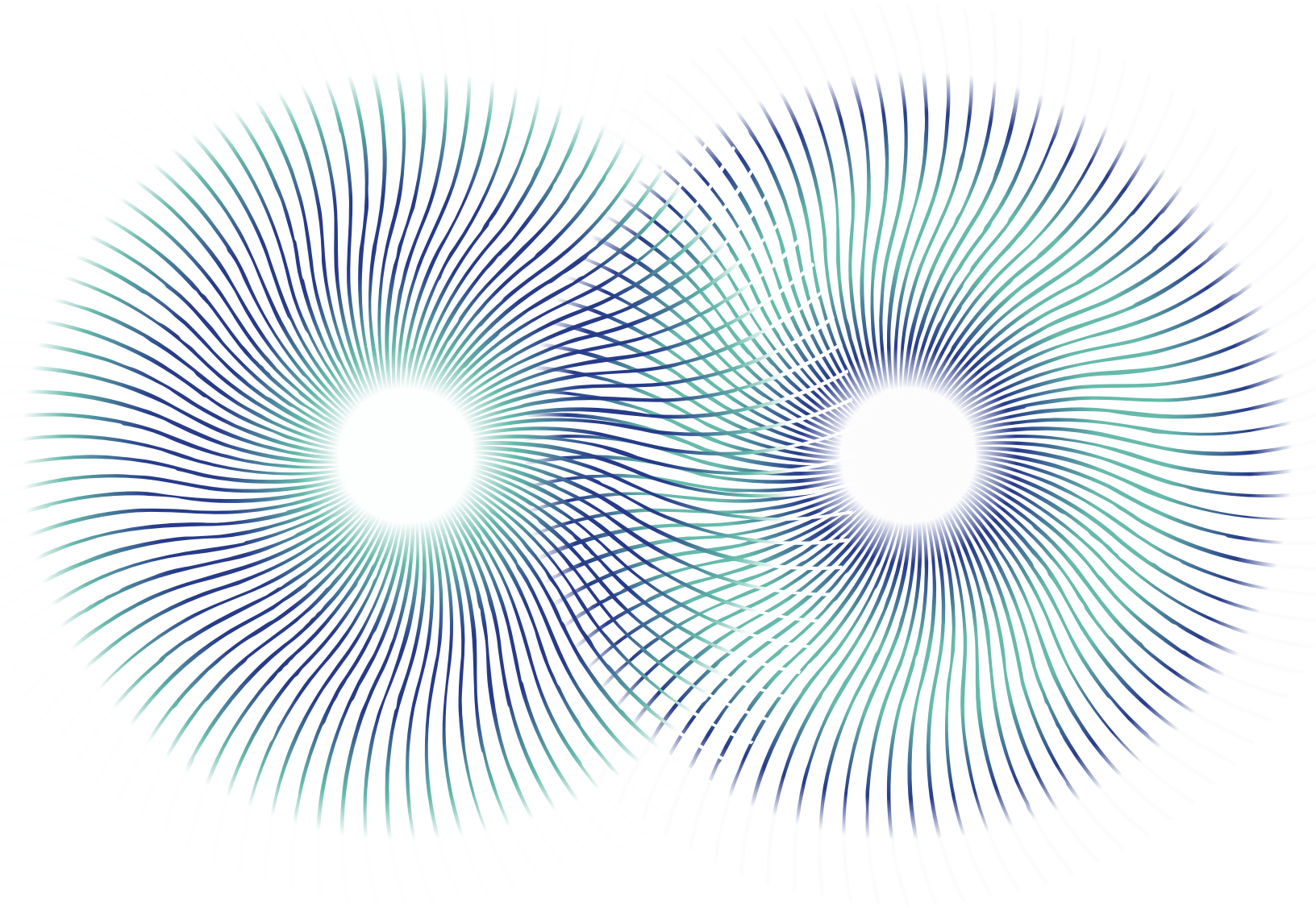
Ora The Ophthalmology Research Company®

CASE STUDY

From prescreening to approval: Two pivotal Demodex trials

Ora's focused prescreening model, block enrollment, and onsite support enabled execution of two parallel Phase 3 Demodex studies – supporting a successful NDA

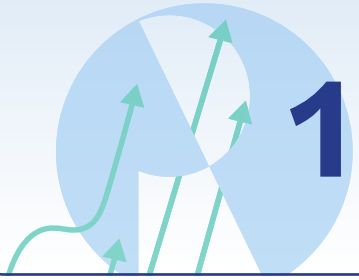


Program at a glance

830
Subjects

35
Active Sites

1,000+
Patients Prescreened



1.5x enrollment boost from prescreening

Two Phase 3 pivotal Demodex trials

Ora recently partnered with a leading ophthalmic pharmaceutical company to execute two simultaneous Phase 3 registration trials for a first-in-class treatment for Demodex blepharitis. The parallel program was designed to generate the replicated efficacy and safety dataset required for an NDA submission — a high bar that demanded both operational precision and scientific rigor from day one.

Together, the studies enrolled 830 subjects across 35 active sites, with more than 1,000 patients prescreened upstream of formal enrollment. The sections that follow outline the challenges Ora encountered — and the approaches it implemented — to hit enrollment targets, protect data quality, and support a successful path to regulatory approval.

Ora's prescreening model can be applied to any anterior segment indication with a measurable eligibility threshold — quickly identifying candidates, filtering unqualified leads upstream, and carefully controlling data quality for primary endpoints.

The burden of Demodex Blepharitis

Demodex blepharitis is a chronic inflammatory condition of the eyelid margin caused by an overpopulation of Demodex folliculorum and Demodex brevis — microscopic mites that colonize the hair follicles and sebaceous glands of the eyelid. The condition is far more common than its name recognition suggests. Studies estimate that Demodex infestation affects between 45 and 58% of the general population to some degree, with clinically significant blepharitis developing in a substantial subset. Prevalence rises sharply with age, exceeding 70% in adults over 60.

Despite how widespread it is, Demodex blepharitis has spent decades as an underdiagnosed and poorly managed condition. Patients and clinicians alike tended to lump it in with other forms of blepharitis or dry eye disease, two conditions it resembles in its presentation. The hallmark clinical finding is cylindrical dandruff, or collarettes: waxy, sleeve-like debris accumulating at the base of the eyelashes, formed from mite waste and egg casings. Associated symptoms include eyelid itching, crusting, redness, and a persistent foreign body sensation. Left untreated, the condition can progress to anterior blepharitis, meibomian gland dysfunction, and chronic ocular surface inflammation.

Until recently, there was no FDA-approved treatment for Demodex blepharitis. Patients cycled through lid hygiene regimens, warm compresses, and lid scrubs that managed symptoms without addressing the underlying mite burden. The unmet need was real, and it made the development of a targeted therapeutic both compelling and consequential.

Challenges in Phase 3 Demodex trials

Designing and executing pivotal Phase 3 studies in Demodex blepharitis is inherently difficult. The condition had never been the subject of a successful large-scale registration trial before, which meant there was no established playbook for site training, patient identification, or endpoint validation. Ora and its sponsor partner were, in important respects, building the infrastructure as they went.

The patient identification challenge was central. Demodex blepharitis is prevalent, but finding patients who meet precise eligibility criteria, including minimum mite density scores and collarette thresholds, requires something more than a standard referral pipeline. Anterior segment sites were experienced in treating blepharitis broadly, but the specific paradigm of scoring for Demodex density was new to most investigators. Even high-performing sites encountered early friction. Patients presenting with blepharitis symptoms did not uniformly meet the mite density thresholds required for study entry, and without an upstream identification strategy, screen failure rates would have been difficult to control.

Endpoint standardization presented its own risks. Mite density assessment and collarette grading are inherently subjective clinical measurements. Variability in how different assessors across different sites score the same patient can introduce noise into the primary endpoint data; noise that narrows the statistical window for detecting a true treatment effect. In a novel indication with no prior precedent for endpoint reliability, the stakes of getting this wrong were high.

Running two parallel pivotal programs simultaneously added a further layer of complexity. Site resources, patient flow, and operational oversight all needed to be coordinated across both studies at once, without allowing either program to cannibalize the other's enrollment momentum.

Two pivotal trials executed at scale

Despite these challenges, Ora successfully enrolled 830 subjects across 35 active sites, completing both programs on time and supporting a successful NDA submission. What made that possible was a combination of novel prescreening infrastructure, rigorous training investment, and the kind of real-time operational decision-making that a novel indication demands.

Ora ran two concurrent Phase 3 trials across...

830	35	1,000+
Subjects	Active sites	Patients prescreened

Prescreening Impact

- Prescreened patients were **1.5x more likely to enroll** than those who did not prescreen.
- Patients with mite density scores above 1.25 at prescreening were **2.6x more likely to qualify** than those who scored below that threshold.
- Screen-to-enrolled rate improved from **50%** in Study 1 to **69%** in Study 2 — a direct result of iterative operational learning between programs.

A new model for patient identification

The most consequential operational decision Ora made was to build a centralized prescreening program before formal enrollment began. Rather than relying on sites to identify Demodex-eligible patients through standard referral pathways, Ora established a structured system for scoring mite density and collarette presentation upstream — routing threshold-positive candidates directly into the study pipeline.

The results were measurable. Prescreened patients proved 1.5 times more likely to enroll than those who had not undergone prescreening. Among patients with mite density scores above 1.25 at prescreening, the likelihood of qualifying at formal screening was 2.6 times higher than for patients scoring below that threshold. The prescreening model reduced wasted site visits, improved conversion efficiency, and allowed investigators to focus their clinical resources on the patients most likely to qualify.

Endpoint rigor and the investment in training

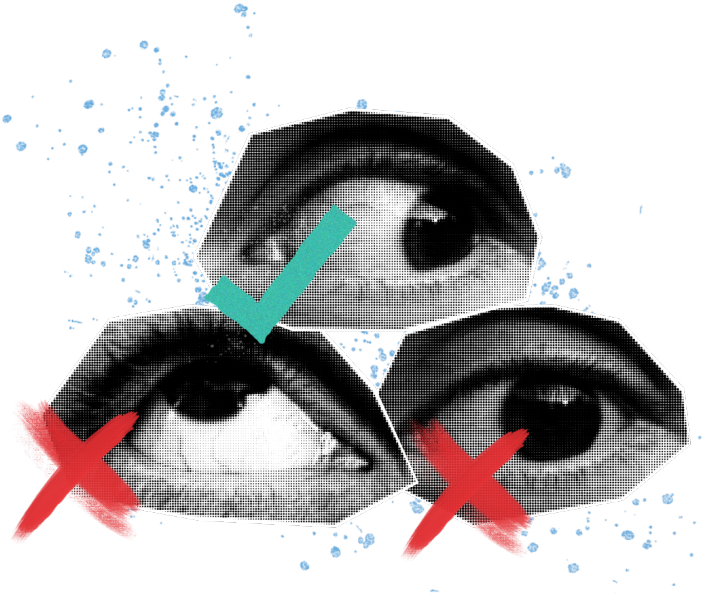
Ora mitigated the risk of endpoint variability through targeted, custom training programs delivered before and during enrollment. Mite density assessment and collarette grading — both notoriously difficult to standardize across sites — were transformed, through deliberate investment in assessor calibration, into consistent and reproducible measurements. The training infrastructure built for these trials directly supported the reliability of the primary endpoint data submitted to the FDA.

Ora also deployed a block enrollment strategy, carefully controlling the timing and sequencing of prescreening, testing, and study visits. This approach hyper-controlled the conditions under which key measurements were taken, reducing noise in the dataset and increasing sensitivity to the true treatment signal.

Learning across two programs

One of the distinctive features of running two parallel pivotal trials is the opportunity for real-time learning between them. Ora used it. Lessons from prescreening efforts and patient identification strategies developed during Study 1 were systematically applied to Study 2. The screen-to-enrolled rate climbed from 50% in the first study to 69% in the second — a 19-percentage-point improvement that reflected the iterative refinement of site communication, patient outreach, and enrollment workflows.

Regular touchpoints with sites to share enrollment approaches, combined with real-time data on prescreening performance, gave investigators and coordinators the information they needed to course-correct quickly. This continuous improvement mindset was essential in a novel indication where no established enrollment infrastructure existed at the outset.



Sponsor alignment and real-time triage

Executing two concurrent pivotal programs required more than operational competence — it required the kind of transparent, proactive communication between sponsor and CRO that keeps complex programs on track when things do not go as planned. Ora maintained close alignment with the sponsor throughout both studies, enabling rapid resolution of site-level issues and ensuring that enrollment decisions reflected both scientific and strategic priorities. That shared accountability, sustained over the full arc of the program, was a material factor in reaching the finish line.

Leveraging this approach for novel anterior segment indications, Ora can quickly identify eligible patients, direct them to participating sites, filter unqualified leads via prescreening, and rigorously control data quality for primary endpoints — from first patient screened through to NDA submission.

Key takeaways for future

This program demonstrated that large, complex anterior segment trials in novel indications succeed when operational precision is paired with genuine scientific investment in the endpoints. Key takeaways for future Phase 3 programs include the following.

1 Prescreening as a strategic asset

In indications with narrow eligibility windows and high screen-fail risk, upstream identification of likely qualifiers is not optional — it is foundational. Building the prescreening infrastructure before enrollment begins, rather than after the first screen failures arrive, is the difference between timeline recovery and timeline protection.

2 Assessor training as a regulatory investment

Subjective clinical measures require systematic calibration to achieve the inter-rater reliability that regulators expect. For novel indications without established scoring norms, this investment is especially critical. Done well, it does not just protect data quality — it builds the regulatory confidence that supports approval.

3 Iterative improvement across study phases

A concurrent or sequential multi-study program is also a learning opportunity. Ora's willingness to carry forward what was learned in Study 1 and apply it rigorously in Study 2 produced a 19-point gain in screened-to-enrolled rate. That kind of improvement does not happen without a culture of continuous refinement and a team willing to act on the data.

4 One-team accountability

Maintaining transparency and proactive communication so sponsor and CRO function as a unified team is not a soft benefit — it is an operational requirement for complex, high-stakes programs. Shared accountability protects trial integrity and sustains the momentum that novel indications demand.

Future Demodex and anterior segment trials will demand not just operational rigor, but trust, foresight, and a proven site network. Ora's success in this pivotal program demonstrates how prescreening innovation, endpoint discipline, and sponsor alignment can overcome the complexities of novel indication development — and advance the field toward the next generation of approved therapies.

Ora

Ora is the world's leading full-service ophthalmic drug and device CRO with employees in over 20 countries around the world. For over 50 years, we have proudly helped our clients earn more than 90+ product approvals. The Ora Cornea & Ocular Surface team has led 190+ programs in the past five years alone, supporting more than 60 product approvals in conditions including blepharitis, dry eye disease, ocular allergy, and ocular redness — including landmark therapies such as Xiidra®, Tyrvaya®, VEVYE®, Pataday®, and Lumify®. For more information, please visit www.oraclinical.com and follow us on LinkedIn.