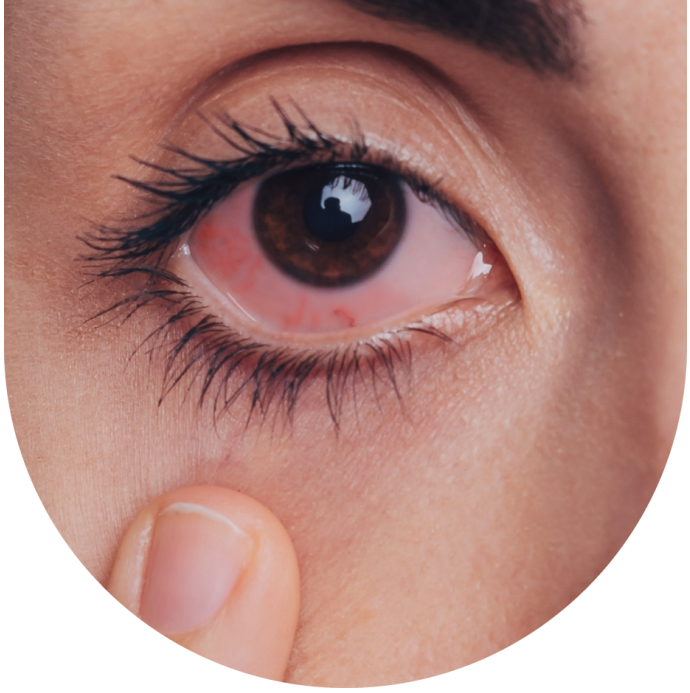
Ora The Ophthalmology Research Company™

CASE STUDY

Rewriting the Playbook in Dry Eye Development

A case study in first-in-class execution from Phase 2 to approval

Mastering the intricacies of Dry Eye clinical development



Dry Eye Disease (DED) is one of the most common yet persistently undertreated ocular surface conditions, affecting over 30 million adults in the U.S[1] and hundreds of millions globally[2]. Despite decades of research, it remains a therapeutic challenge. Encompassing tear film instability, inflammation, and neurosensory dysfunction, the multifactorial nature of DED makes both diagnosis and treatment complex[3].

In the clinical setting, DED presents a unique set of hurdles. Trials often suffer from a mismatch between subjective symptoms and objective signs like Schirmer's scores or staining[4], a discordance that can undermine endpoint reliability. This challenge is compounded by high placebo response rates in ocular surface trials, which can obscure treatment signals and increase the risk of trial failure[5]. Tight procedural timing windows, extreme sensitivity in test methods, and a saturated trial landscape further limit site performance and slow patient enrollment. To succeed, programs require more than operational rigor—they need deep therapeutic expertise and a proactive, solutions-focused partnership from start to finish.

Key challenges in Dry Eye trials

1

Symptom–sign discordance
Patient-reported discomfort often doesn't align with objective measures like Schirmer's or staining, undermining endpoint reliability and masking true efficacy.

2

High placebo response
Ocular surface trials are prone to elevated placebo effects, making it harder to differentiate treatment impact and increasing the risk of trial failure.

3

Complex procedures & recruitment friction
Tight timing windows, procedural sensitivity, and a saturated trial landscape limit site performance and slow patient enrolment.

A full-spectrum development partnership

This case study highlights a novel program that broke new ground: the development and approval of a first-in-class treatment for tear-deficient dry eye. The program set out to validate a new mechanism of action and deliver the first meaningful therapeutic advancement in years. This was the first therapy to target TRPM8 sensory nerves on the ocular surface to stimulate natural basal tear production.

Unlike traditional anti-inflammatory drugs, this neuromodulatory approach directly addressed the underlying tear-production deficit in aqueous-deficient and mixed dry eye subtypes[3]. This first-in-class status meant the regulatory path was less defined—and the stakes were higher. Convincing regulators required demonstrating biological plausibility, endpoint sensitivity, and reproducible efficacy. The sponsor needed more than execution. They needed leadership.

Ora became the partner. Across four integrated studies—a Phase 2b, two pivotal Phase 3 trials, and an extension study—Ora guided the program from early does exploration through long-term validation, enrolling 930 patients across 60+ sites.

Ora key contributions

- **Expert endpoint training:** Ora standardized notoriously variable assessments like Schirmer's test and symptom reporting across investigative sites.
- **Purpose-built site network**: Top-tier dry eye investigators were activated swiftly through Ora's specialized network.
- **Accelerated recruitment:** 1,200+ candidates were screened through targeted, modern outreach.
- **Embedded oversight:** Real-time issue resolution and sponsor alignment ensured seamless execution.
- **Submission-ready data:** Integrated across all phases for a smooth regulatory handoff.

What made the difference?

Built for Dry Eye. Trusted for execution.

Specialized site network
Activated top-tier dry eye investigators through Ora's purpose-built site network.

Accelerated recruitment
Screened 1,200+ candidates with modern outreach tactics, driving efficient enrolment.

Endpoint rigour and training
Delivered custom training that transformed the notoriously messy Schirmer test into tight, reliable data.

Operational oversight
Embedded liaisons enabled real-time problem-solving and fostered seamless collaboration with the sponsor.

Ora didn't just manage trial operations. It led a novel therapeutic approach through one of the most complex approval gauntlets in ophthalmology. The Schirmer data generated was so consistent it helped influence FDA negotiations.

The label language secured enabled Day-1 marketing claims about natural tear production. The program also delivered biological insights that helped set this therapy apart in a crowded market.

This wasn't just regulatory success. It was commercial readiness.

This program proved that innovation can succeed in Dry Eye. Ora proved it can lead the way.

Proven approach. Repeatable success.

Ora has completed more than 150 Dry Eye trials across Phase 1 through 4. Its purpose-built model includes:

Deep therapeutic focus

Expertise in aqueous-deficient, evaporative, and mixed DED subtypes.

Precision processes

Tailored recruitment, endpoint reconciliation, and data integrity protocols.

150+ Dry Eye

Spanning Phase 1 to Phase 4, across a wide range of mechanisms. Proprietary models and training frameworks trusted by regulators.

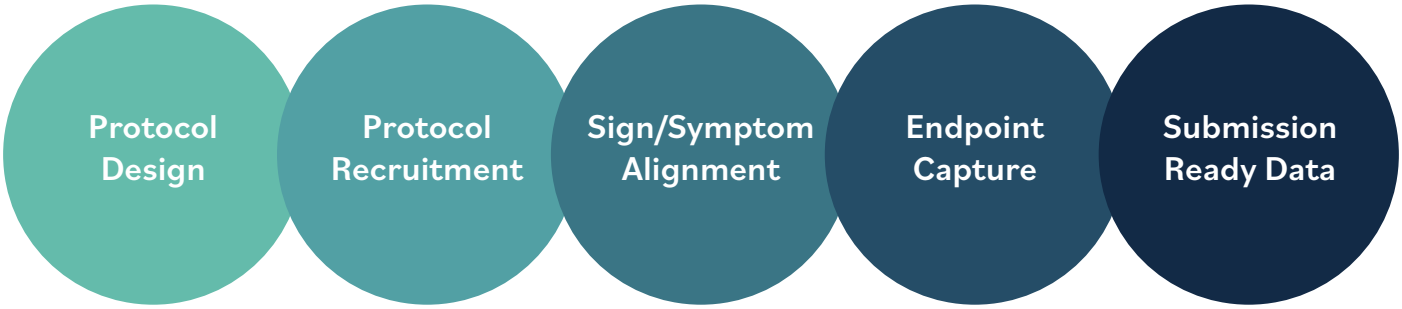
Run the gauntlet with a partner that's done it all before

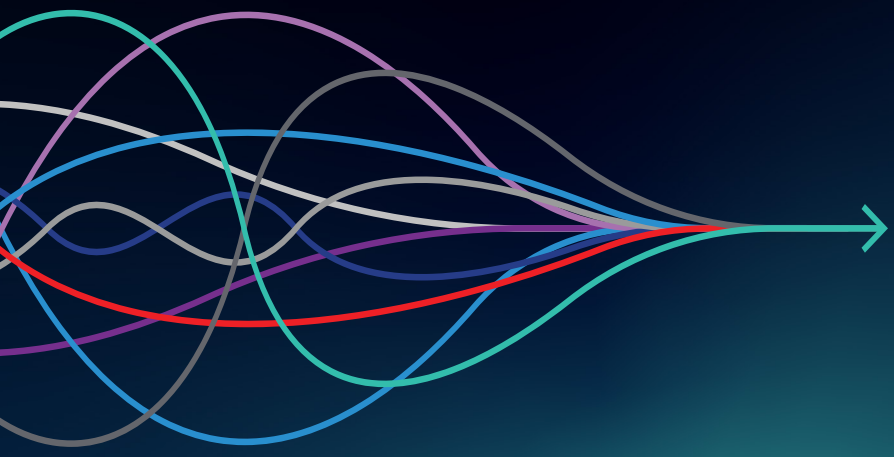
When the path is complex, the right partner makes all the difference

Dry Eye trials are among the most deceptively difficult in ophthalmology. Protocol complexity, recruitment competition, placebo effects, and sign/symptom discordance can derail even promising therapies. That's sponsors choose Ora.

We don't just manage timelines; we lead programs through the high-stakes moments that make-or-break outcomes.

With deep therapeutic expertise, a trusted network, and proven processes, we help innovators go the distance.





Most CROs can manage a trial. Ora guides you through the gauntlet. We anticipate risks, turn down the noise, and deliver results that withstand regulatory and commercial scrutiny.

In Dry Eye, there's simply no substitute for experience.

References

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2. Sullivan DA, Hammitt KM, Schaumberg DA, et al. Report of the TFOS/ARVO Symposium on Global Treatments for Dry Eye Disease: An unmet need. Ocul Surf. 2012;10(2):108–116.
3. Craig JP, Nichols KK, Akpek EK, et al. TFOS DEWS II Definition and Classification Report. Ocul Surf. 2017;15(3):276–283. doi:10.1016/j.jtos.2017.05.008.
4. Sullivan BD, Crews LA, Messmer EM, et al. Correlations between commonly used objective signs and symptoms for the diagnosis of dry eye disease: clinical implications. Acta Ophthalmol. 2014;92:161–166. doi:10.1111/aos.12040.
5. Montecchi-Palmer M, Wu M, Rolando M, et al. Possible Strategies to Mitigate Placebo or Vehicle Response in Dry Eye Disease Trials: A Narrative Review. Ophthalmol Ther. 2023;12:1827–1849. doi:10.1007/s40123-023-00720-1.

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 85 product approvals. We support a wide array of innovators and organizations, from start-ups to global pharmaceutical and device companies, to efficiently bring new products from concept to market. Ora's clinical models, unique methodologies, and global regulatory strategies have been refined and proven across thousands of global projects. For more information, please visit www.oraclinical.com and follow us on LinkedIn.