FACT SHEET

Inspiring the Future of Ophthalmic Clinical Development

Retina, Glaucoma, Refractive & CED

Over the past 40+ years, Ora has played a significant role in the development of marketed ophthalmic products for the full scope of ophthalmic diseases. Ora's tenured experience in ophthalmology reaches far past the scope of our consulting and clinical trial history. We are the industry leader in both therapeutic experience and drug and device combination products that treat posterior segment diseases. In the last five years, we have conducted more than 45 clinical trials in retinal indications.

To ensure rapid recruitment of large retinal clinical trials, Ora has built a global operation, with teams operating in the North and South America, Europe, Asia, and Australia. Ora has the capacity to tailor your clinical trial experience to best suit your goals. Our expansive site network allows us to custom-build a clinical trial to your needs and ensure your investigator and recruitment prerequisites are met.

Areas of Expertise

Achromatopsia

Choroideremia

Cystoid Macular Edema

Diabetic Macular Edema

Diabetic Macular Ischemia

Diabetic Retinopathy

Dry Age-Related Macular Degeneration (Dry AMD), including Geographic Atrophy

Glaucoma & Neuroprotection

Leber Congenital Amaurosis (LCA)

Leber Hereditary Optic Neuropathy (LHON)

Macular Degeneration

Myopia Progression

Proliferative Vitreoretinopathy

Retinal Vein Occlusion (Branch [BRVO] and Central [CRVO])

Retinitis Pigmentosa

Retinoschisis

Stargardt Disease

Uveal Melanoma

Uveitis (Anterior, Intermediate, Posterior)

Vitreomacular Adhesion

Wet Age-Related Macular Degeneration (Wet AMD)

Thyroid Eye Disease

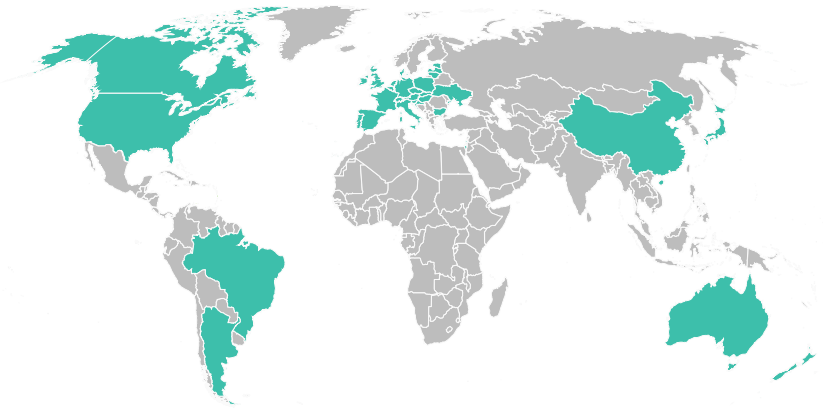
Keith Lane, MBA
Senior Vice President of Posterior Segment

With Ora since 2003, Keith Lane has dedicated his career to ophthalmology and played a key role in bringing multiple products to market. As Senior Vice President, Keith leads clinical operations and regulatory strategy activities of Ora's Posterior Segment division. He has overseen the successful conduct of over 80 ophthalmology trials ranging from First in Human Safety Studies to Global Phase 3 Pivotal Programs.

Prior to his current role, Keith held several senior management positions, including leading Ora's Research & Development department where he directed the creation and validation of clinical models, endpoints, and trial processes for nearly a decade. Keith also led the development, launch, clinical operations, and regulatory strategy of Ora's Visual Navigation Challenge (Ora-VNC™).

Keith has published numerous articles in peer reviewed journals and has spoken at many industry conferences. He received his MBA with Honors in Health Sector Management from Boston University and a BS in Biology from Bates College.

A globally experienced team in retina, across the clinical pipeline



Ora's fully dedicated retina teams in North America, Europe, Asia, and beyond bring forth substantial individual and collective regulatory and clinical trial management experience, positioning us to conduct your study.

Country Experience

In the past six years, Ora has worked on clinical trials in the following countries:

- **Europe:** Austria, Belgium, Czechia, Denmark, France, Germany, Hungary, Ireland, Italy, Lithuania, Netherlands, Norway, Poland, Portugal, Slovakia, Spain, Switzerland, UK, Ukraine
- **North America:** Canada, US
- **Latin America:** Brazil, Argentina
- **MENA:** Israel
- **APAC:** China, Japan, Australia, New Zealand

Beyond familiarity with many competent authorities and what they expect and require, a key benefit the Ora team provides our sponsors is the exceptional working relationship amongst our regional teams. We have strong forces in all regions proposed that collaborate to make sure we are efficiently meeting the needs of all regulatory authorities. These teams are on calls together to share information several times per week; their individual working knowledge within each domain complements one another and enables consistent cross-functional success.

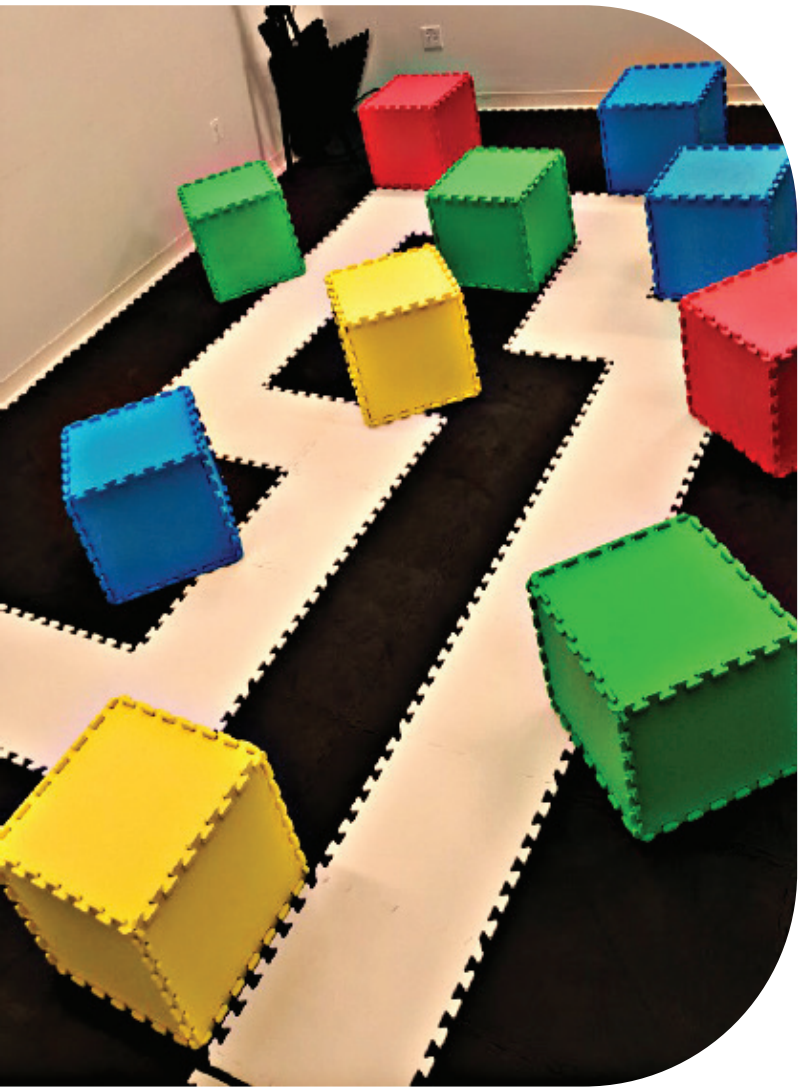
Clinical Phase Experience

Phase 1 **24%** → Phase 2 **43%** → Phase 3 **31%**

From healthy volunteer and unicentric phase 1 trials to large global phase 3 programs, Ora's experience spans all clinical development phases. Supporting you with deep scientific understanding in the early phases of your program, allowing you to de-risk your later phases of the study. By appointing a project management team that understands the needs of your trial at each phase, we can ensure the right coverage to ensure optimum project delivery at a budget that works for you.

Ora-VNC™ Mobility Courses

To address the need for functional endpoints in inherited retinal disease (IRD) patients, the Ora-VNC™ (Visual Navigation Challenge) mobility courses were created to evaluate gene therapies targeting IRDs and are used as functional endpoints in clinical trials worldwide. The Ora-VNC™ courses can be used to objectively assess changes in patient mobility that occur secondary to improvements in vision resulting from therapeutic intervention.



These courses also:

- Detect differences in visual function impairment specific to IRDs
- Enable clinically meaningful assessments of visual function through patient immersion in a 360-degree visual challenge environment
- Challenge specific aspects of vision that deteriorate with IRDs

Various Ora-VNC™ setups for different diseases and severities

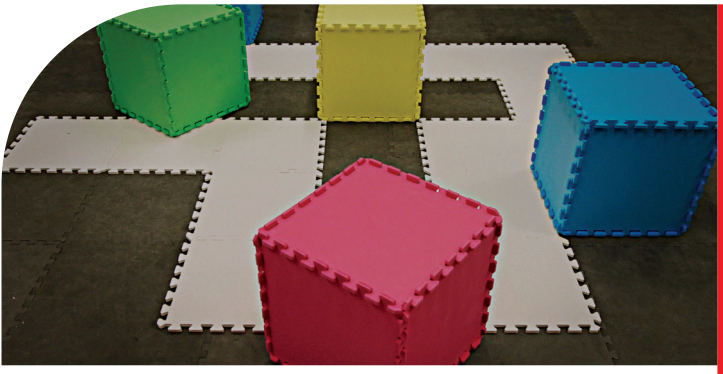
Ora offers multiple Ora-VNC™ mobility courses to accommodate various types of vision loss, as well as different severities, with courses appropriate for patients with vision levels ranging from mild visual field constriction (with preserved central acuity) to “light perception” only.

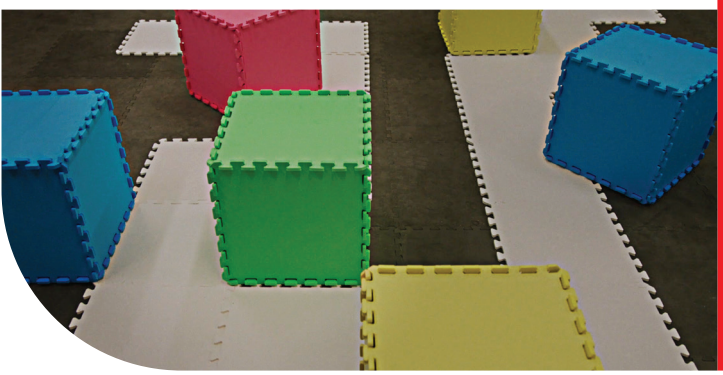
Multi-center capabilities

- Modular and designed for efficient set-up in any clinical center, without changes to site infrastructure
- Following course set-up and validation, we conduct robust training and certification for on-site technicians
- Mobility test sessions are recorded and sent to Ora's independent reading center, where certified, masked graders score patient performance in an FDA-compliant manner to ensure consistent and objective grading across all clinical sites

Standardization

- Standardized ambient light levels independent of room size and features
- Multiple course iterations to prevent patient memorization
- Presented to the FDA as integral endpoints in gene therapy, oligonucleotides, RNA therapy, and medical device development programs





Key Features

- Ability to assess the impact of therapies on IRDs
- Sensitive to changes in visual function
- Designed for use in multi-center studies
- Customizable to different difficulty levels to cater to a variety of patient populations
- Easy to use and highly mobile
- Includes a robust training system and standard protocol for use
- Incorporates a fully masked and independent reading center grading system for objective scoring of mobility test performance

Ora-VCF™ contrast test & Ora's low luminance tablet reading test

To address the need for more sensitive endpoints to assess changes in visual function in retinal diseases, including early stages of age-related macular degeneration (AMD) and non-proliferative diabetic retinopathy (NPDR), our goal is to develop validated, novel, and sensitive visual function endpoints that can identify underlying visual dysfunction and thereby can help evaluate therapeutic efficacy of novel therapies.

Study Overview

Ora is currently running IRB-approved research on over 100 AMD and age-matched normal control subjects over the age of 60. The subjects are screened and evaluated using many tests — 20 distinct tests and 50 variants. In addition, the team has evaluated test-retest reproducibility and repeatability.

VALIDATION OF VARIABLE CONTRAST FLICKER TEST

Test-retest repeatability and reproducibility

N = 21; 7 normals, 14 AMD

- *Repeatability:* Tests performed twice on the same day, 1 hour apart
- *Reproducibility:* Same tests done again 2 weeks later

Results: Percent Agreement

	REPEATABILITY	REPRODUCIBILITY
VCF	82.1 %	88.9 %

Software validation

- The VCF test is presented using a customized program
- Part 11 compliant software validation completed

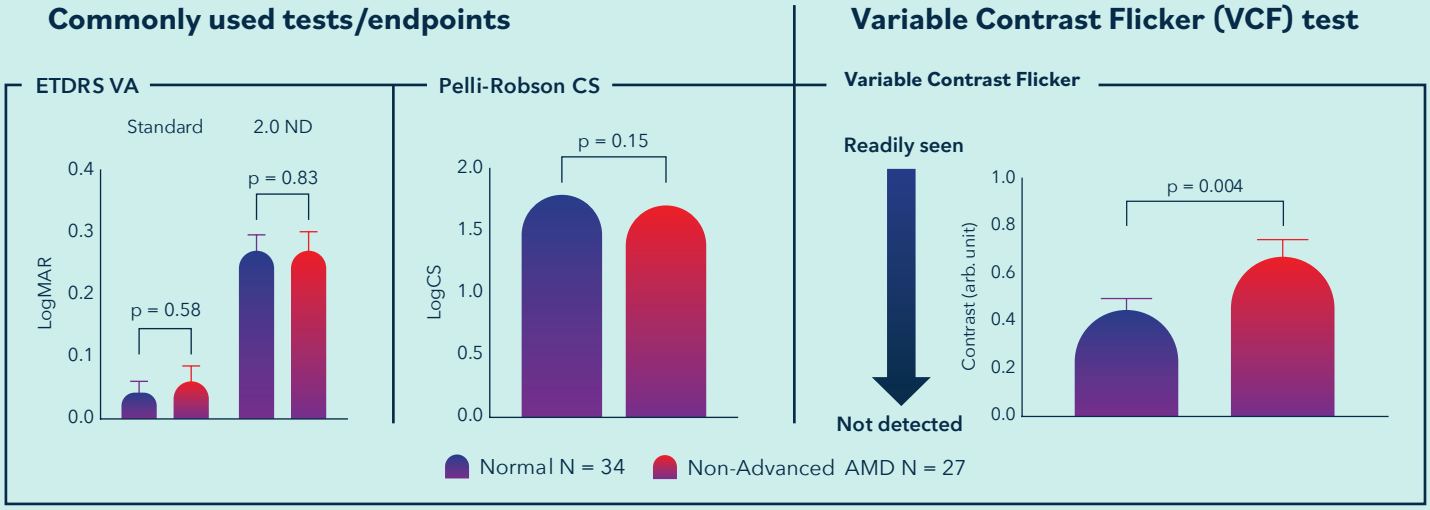
Summary

- VCF test was able to differentiate normal vs. nonadvanced AMD group, while some current common tests such as ETDRS VA and Pelli-Robson CS did not
- VCF test could be used to assess visual function in clinical trials
- VCF test could also be used to identify subjects with underlying visual dysfunction for screening

Key Results

Assessing some common tests/endpoints, such as ETDRS VA, 2.0 low luminance ETDRS VA, Pelli-Robson Contrast Sensitivity test, and MN Read test, it was found that there was no difference between AMD and normal subjects. In contrast, the Ora-VCF™ variable contrast flicker test and Ora's low luminance tablet reading test show significant visual dysfunction in AMD subjects compared to normal subjects.

RESULTS



Incorporation in a clinical trial

The Ora-VCF™ and low luminance tablet reading test can hold potential across a wide range of retinal diseases that impact visual function. Most efforts to date have focused on characterizing visual deficits in early to moderate dry AMD and NPDR. These tests are Part 11 Compliant, and all equipment, installation, and staff training are provided by our team.

Regulatory Strategy & Expertise

Ora has a full regulatory team that drafts and submits regulatory packages and manages interactions with US FDA, EMA, PMDA, NMPA, and other global regulatory bodies. Ora's in-house CMC (Chemistry, Manufacturing, and Control) and Preclinical teams can guide you through the early development journey, as we have strategic relationships with GMP manufacturers and GLP laboratories with favored pricing and scheduling. Working seamlessly with Ora's therapeutic experts, our medical writing group can draft clinical protocols that complement CMC and toxicology components based on comprehensive understanding of regulatory requirements to successfully deliver favorable regulatory interactions.

"Our goal at Ora is to ensure that we give our clients the best possible opportunity to experience successful clinical trial outcomes. That entails supporting both the scientific and operational aspects of study conduct at an elite level. When you marry comprehensive knowledge of the diseases and long tenured site relationships in ophthalmology, with a passionate and high performing operations team, you can really be efficient in performing a trial that gives the drug or biologic the best possible chance to work."

Ora

Ora is a global full-service ophthalmic drug and device development firm with vast capabilities through all steps of clinical research, including preclinical, clinical, CMC & regulatory, and patient and site evaluations. Through Ora's 40+ years of experience, the company has assisted in bringing more than 80 products to market. Ora's team of experts utilizes global regulatory strategies, integrated research operations, and extensive site and patient engagement to accelerate product development in anterior and posterior segment, as well as ophthalmic devices.