Ora Creating vision beyond what we see

Research & Development

At Ora, we do research on clinical research to optimize and enhance our sponsors' future clinical trials. When your product has promise, let's prove it.

Ora R&D consists of a team of MDs, ODs, PhDs, and clinical experts with a proven track record of ophthalmic experience and excellence. The five pillars of the R&D team include:

1. Understanding the pathophysiology of the disease
2. Clinical research compliance
3. Protocol optimization and modification
4. Implementation of the technological toolset
5. Visual techno-scientists

Ora Technology

- Controlled Adverse Environment (CAE®)
- IVAD
- OPI 2.0
- EyeCup™

Ora Calibra® Scales

- Lissamine Green Staining
- Fluorescein Staining
- Redness
- Discomfort

The Goal of Ora R&D:

To turn down the noise in our sponsor's clinical data to improve statistical power, increase likelihood of success, and give better therapy-placebo differentiation. Ora R&D believes in the continual evolution of our technologies and methodologies to match the best endpoints for each potential therapy.

Historically used endpoints and clinical designs often lack precise control of confounders. As a result, such studies are subject to more "noise" which increases sample size requirements or have low sensitivity to changes within early stages of the disease. Ora R&D is on a quest for constant improvement of clinical endpoints and approaches to ensure we:

1. **Accurately measure product efficacy.**
2. **Fully understand therapeutic impact.**
3. **Streamline clinical designs and sample requirements.**

R&D Pilot Study

Ora's stationary Allergen BioCube® (ABC) had been previously validated and used to conduct studies assessing the efficacy of drugs in the treatment of allergic rhinitis[1-2]. Yet, the stationary nature of the ABC limited its use across multiple ophthalmology and allergy centers. Therefore, the Ora R&D team worked to create a mobile Allergen Biocube (mABC) to solve this technological shortcoming. A pilot study that was presented at ARVO 2022 titled, "Clinical Validation of the Mobile Allergen Biocube (mABC) in Subjects with Seasonal Allergic Conjunctivitis (AC) or Rhinoconjunctivitiis (RAC)."

The mABC was effective in inducing clinically relevant ocular and nasal allergic signs and symptoms in subjects with a history of AC or ARC over a 90-minute exposure period. Importantly, a single 90-minute exposure period was enough to

qualify most subjects without priming visits. The study clinically validated the mABC for both ragweed and timothy grass pollen exposure.

In conclusion, this pilot study proved the mABC could serve as an important tool to evaluate potential allergy therapeutics in clinical studies requiring a consistent environmental allergy model across multiple ophthalmology and allergy centers. Furthermore, the mABC may help reduce sample size and study duration requirements in ocular and nasal allergy clinical trials. Thus, providing a competitive advantage to Ora's research partners and sponsors.

R&D Analysis of Previous Clinical Studies

Beyond pilot studies, the R&D team performs data analysis on previous clinical studies with the goal to:

1. **Develop better ways to recruit and screen subjects.**
2. **Highlight potential trends underlying high screen failure rates.**

The rigorous analysis by the R&D team is performed to increase the efficiency and cost-effectiveness of the Ora clinical research process with the goal to better meet the needs of our partners to accurately show the effectiveness of their treatment and reduce the time to market.

A poster to be presented at ARVO 2024 titled "Factors Affecting Screen Failures in Clinical Trials for Dry Eye Therapies" is a perfect example of a detailed analysis done by the Ora R&D team. The screening and pre-randomization data from two identically designed DED clinical trials (Phase 2 and Phase 3) were combined into one data set totaling 1049 subjects. Of the 1049 subjects, 494 (47.1%) subjects met the screening criteria, and 555 (52.9%) were screen failures.

Mobile Allergen BioCube®

Results from the 2024 study provided insight into demographic factors (age, race, and eye color) that influenced screen failure. Additionally, data from Visit 1 and Visit 2 inclusion and exclusion criteria (Schirmer's test and Lissamine Green staining) helped shed light on the fact that only 1.8% of subjects screen failed due to Lissamine based inclusion criteria. While 29.7% of subjects screen failed due to Schrimer's based inclusion criteria. Overall, Lissamine Green staining provided a higher probability of being enrolled into a DED clinical trial compared to Schirmer's test.

By taking our R&D study results into consideration for future studies, Ora Clinical will be better able to modify our inclusion criteria. Thus, reducing the amount of screen failures and increasing the chances of success of our sponsor's clinical trial. By reducing the noise, we will improve the statistical power, increase likelihood of success, and give better therapy-placebo differentiation for our current and future sponsors.

References

1. *Gomes PJ, Lane KJ, Angjeli E, Stein L, Abelson MB. Technical and clinical validation of an environmental exposure unit for ragweed. J Asthma Allergy. 2016 Dec 14;9:215-221.*
2. *Angjeli E, Gomes P, Lane KJ, Stein L, Abelson MB. Technical and clinical validation of the Allergen BioCube® for timothy grass. Immun Inflamm Dis. 2017 Feb2;5(1):78-84.*

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.