CASE STUDY

Inspiring the Future of Ophthalmic Clinical Development

Driving Success in Global Study Start-up

A Case Study in Myopia Progression Demonstrating Enrollment Success

An area of considerable focus for ophthalmic treatment innovation today is the growing pandemic of progressive pediatric myopia. This disease affects approximately 20% of children worldwide, typically manifests between the ages of 7 to 10 years old, and continues to progress over the next 10 to 15 years of their life[1]. While the cause of myopia is unknown, its prevalence is growing around the globe, particularly in Asian countries[2-4].

Myopia has been described as the sixth most common cause for vision loss in the world[5]. Despite this, there are limited treatments for progressive myopia in pediatric patients. Muscarinic receptor antagonists, such as atropine, have been shown to successfully slow the progression of myopia[6] and are approved for use in some Asian markets. However, the need for innovative treatments across the world is still substantial. Without future research into new therapeutics, myopic children around the globe will continue to develop vision threatening diseases such as retinal detachment, glaucoma, cataracts, and myopic macular degeneration[7].

Clinical research for new therapies for progressive pediatric myopia comes with inherent complexities, especially considering the long study timelines and the age of the subjects. Ora has been working with a pharmaceutical partner and has successfully enrolled many pediatric patients in a complex phase 3 global study. This study is a great example of how Ora's people, processes, and technologies work together to accelerate enrollment and set large phase 3 global studies up for success.

Obstacles/Challenges for Global Pediatric Myopia Trials

01 **Pediatric Studies:** Difficult to enroll due to parental concern that their children will be randomized into the placebo group for a study with a 4 year long follow-up period.

02 **Previous investigational therapeutic usage:** 70-80% of pediatric myopia patients need to "wash out" other investigational drugs for 6 months prior to their screening appointment.

03 **Limited access to pediatric myopia patients in China:** Season limitation only allows access during summer/ winter holiday (only 2-3 months/year).

In 2021, Ora partnered with a sponsor to conduct the world's first multi-regional phase 3 pediatric myopia clinical trial for low-concentration atropine that included patients within the US, UK & Europe and China.

- A total of 678 subjects from 48 sites in the US (267), UK & Europe (241), and China (170) have been enrolled in the study.
- Ora enrolled the Phase 3 global trial in a little over two years (start: April 2021/end: June 2023) and the study will be completed in June 2027.

Ora Success Factors

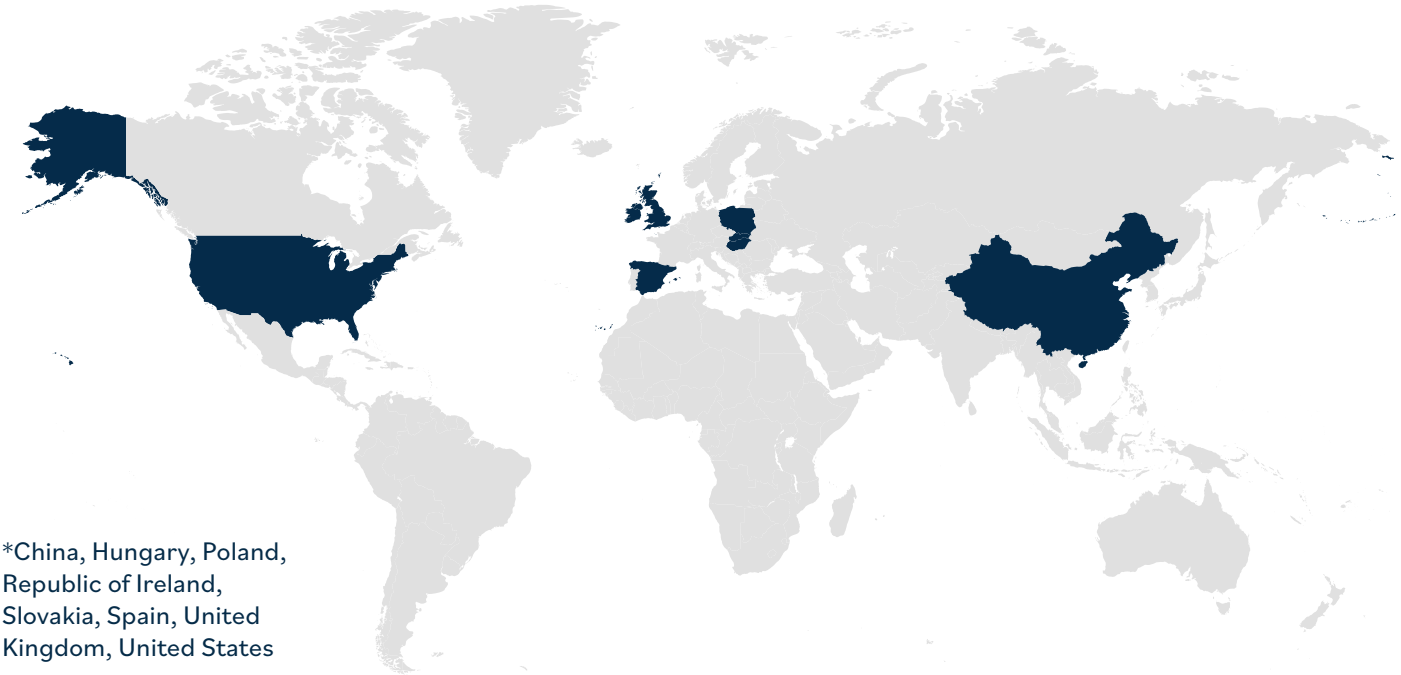
- Experienced local teams in China, UK & Europe, and the United States to ensure local implementation.
- Tried and tested approaches to cross-functional and global working.
- Problem solving attitude of the team to mitigate Covid-19 and logistics delays.

Study Details

678 Patients | **48** Sites

Global Reach

8 Countries* | **3** Continents



*China, Hungary, Poland, Republic of Ireland, Slovakia, Spain, United Kingdom, United States

Global Pediatric Myopia Progression Study – Teamwork Drove a Successful Start

Ora has local teams around the world with the ophthalmology experience you need for successful product development. Regional and in-country Ora clinical ophthalmology experts with substantial experience understand and adapt to local nuances, ensuring regulatory, investigator, and patient success on the ground from day one through completion of your global study.

Ora goes above and beyond what a typical CRO will do for their partners to ensure a successful study. We put you and your study subjects FIRST!

01 **Cascading communication between countries:** In the pediatric myopia study, enrollment started in the US, then in the UK and Europe and finished in China. Open communication between the different Ora site teams allowed for the enrollment process to be improved and optimized as the study progressed to achieve enrollment on time.

02 **Global-to-local approach:** Ora will never use a "one size fits all" model. In the pediatric myopia study, we tailored our overarching strategies, frameworks, and systems to specific global communities. Thus, ensuring that Ora's high-level goals and strategies were effectively molded to meet the specific needs of different countries, communities, and cultures.

03 **Customized patient recruitment:** Ora's in house marketing team worked with the pediatric myopia study team to craft customized recruitment materials (brochures, videos, social media advertisements, etc.) centered around educating/putting parents and their children at ease about joining the clinical trial.

04 **Further study expansion to meet clinical trial criteria:** Ora actively expanded the pediatric myopia trial to include Poland and Hungary to ensure 30% of the enrolled study subjects had light eyes (blue or green). Our extensive global site network allowed us to make this addition seamlessly.

Ora Global Operational Success Factors

KOLs Ophthalmic Networks and Site Selection

Focused Site and Patient Engagement

"One Team" Mentality with Sponsor

Risk/Issue Identification Mitigation and Escalations

Global Pediatric Myopia Progression Study: China Details

By incorporating the feedback received from the US, UK and Europe enrollment strategies, the China team was able to optimize their enrollment. Despite the fact enrollment started in China later than in the other regions, we were able to enroll 170 subjects in just 10.5 months with only 12 sites activated. The enrollment rate (subject/month/site) in China was an impressive 1.5 compared to 0.6 in the US and 1.0 in the UK and Europe.

The Ora Difference in China

During Covid-19, cities like Shanghai were locked down for a long period of time. During lock down, no people or vehicles were allowed to enter the city. The China team found a vendor who had a special truck which had the ability to travel into locked down cities during Covid-19 to ensure the IP was delivered on time to sites/ subjects throughout China. When you work with Ora, we will do everything in our power to help get your therapeutic to market.

General China Capabilities

- OraNet™ Global Research Community includes access to 35+ sites across major cities in China, including sites with prioritized access.
- Stable, knowledgeable, and experienced China leadership/ team members.
- Ora's China team works hard to streamline operations and navigate regulatory pathways to accelerate clinical trials from start to finish.
- Clinical trial execution in China is aligned with Ora Global SOPs, trainings, and technologies for the delivery of data of the highest quality and integrity.

Study Details

170	10.5	12	1.5
Subjects	Month Enrollment Time	Active Sites	Enrollment Rate (subject/month/site)

Global Pediatric Myopia Progression Study: Europe Details

Enrollment in the Pediatric Myopia study in the UK and Europe tallied 241 subjects, spanning over 6 countries including: the United Kingdom, Poland, Hungary, Republic of Ireland, Slovakia, and Spain. Communication of successful enrollment strategies among the European countries allowed the teams to optimize their enrollment in real-time to meet their deadline. Additionally, passionate and engaged investigators ensured the enrollment of high-quality pediatric subjects in the study.

The Ora Difference in Europe:

As enrollment in the pediatric myopia progression study went along, team leaders quickly realized a problem. One of the parameters listed in the protocol stated that 30% of the study subjects needed to have light eyes (blue or green). Yet, with the initial countries included in the study, it proved difficult to enroll a high volume of light-eyed subjects. Therefore, Ora reached out and actively involved Poland and Hungary to be part of the study. As a result, enrollment was completed on time, with 33% of subjects having light eyes.

General Europe Capabilities

- The OraNet™ Global Research Community in Europe provides our partners with prioritized access to 240+ sites with strong patient diversity across ethnicities.
- High-profile Key Opinion Leaders (KOLs) who are internationally respected with global influence.
- Principal Investigators maintain a strong network resulting in a consistently expanding referral capacity.
- In country CRAs are local to specific sites and are experts in local regulatory nuances and country/site contract requirements.
- Ora Europe Monitoring Coverage and Standards-Monitoring coverage in 44+ countries across Europe, the Middle East, and Caucasus Regions that leverage experienced/local resources.

Study Details

241	10	22	1.0
Subjects	Month Enrollment Time	Active Sites	Enrollment Rate (subject/month/site)

References

1. Morgan I, Rose K. How genetic is school myopia? Prog Retin Eye Res. 2005; 24(1):1-38.
2. Pararajasegaram, R. (1999)."VISION 2020-the right to sight: from strategies to action" Am J Ophthalmol 1 2 8 (3): 359-360.
3. Wong, T. Y., P. J. Foster, J. Hee, T. P. Ng, J. M. Tielsch, S. J. Chew, G. J. Johnson and S. K. Seah (2000). "Prevalence and risk factors for refractive errors in adult Chinese in Singapore" Invest Ophthalmol Vis Sci 4 1 (9): 2486-2494.
4. Fredrick, D. R. (2002). "Myopia" BMJ 3 2 4 (7347): 1195-1199.
5. Morgan, I.G.; He, M.; Rose, K.A. Epidemic of pathologic myopia: What can laboratory studies and epidemiology tell us? Retina 2017, 37, 989-997.
6. Song YY, Wang H, Wang BS, Qi H, Rong ZX, Chen HZ. Atropine in ameliorating the progression of myopia in children with mild to moderate myopia: a meta-analysis of controlled clinical trials. J Ocul Pharmacol Ther 2011;27(4): 361-368.
7. Wong, T.Y.; Ferreira, A.; Hughes, R.; Carter, G.; Mitchell, P. Epidemiology and disease burden of pathologic myopia and myopic choroidal neovascularization: An evidence-based systematic review. Am. J. Ophthalmol. 2014, 157.

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.