Worldwide Clinical Trials

Case Study

A United CRO-Biotech Partnership: How strong collaboration in an ALS study expedited recruitment, enhanced retention, and benefitted scientific methodology

Introduction

An emerging biopharma company was exploring the expansion of their asset into amyotrophic lateral sclerosis (ALS) and required the services of a full-service, global CRO capable of delivering a Phase III study in such a relentlessly progressing and ultimately fatal condition. Worldwide Clinical Trials was selected because of our personalized approach and extensive experience operationalizing global neuroscience and rare disease studies. Together, we needed to develop a supportive, multifaceted partnership and a flexible, patient-optimized study plan from recruitment through completion.

Study Facts

245 Patients

30 Sites

12 Countries
Distributed across NA and EU

18-Month
Treatment Period

Primary Endpoints:

Combined Assessment of Function and Survival (CAFS)

Secondary Endpoints:

Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R), survival, and slow vital capacity (SVC)

The Challenges

1 Small Biotech With Limited Resources

This emerging biotech company was on a typical small to midsize enterprise growth journey supported by their vision to expand the use of their lead asset into multiple neurological disorders in accordance with the "pipeline in a molecule" strategy. They had no corporate and only limited personal experience with ALS clinical development and began the study with lean staffing and no clinical trial system infrastructure. They needed a CRO with global resources, strong scientific expertise in ALS, a cross-functional operational team, and the ability to adapt to the biotech's growth journey.

"Pipeline in a molecule"
A strategy in which sponsors who have a molecule that has proven efficacious for one indication explore efficacy in other indications to increase the product's ultimate market size.

2 Disease-Specific Impacts on Recruitment & Retention

The study had a 12-month recruitment period to enroll patients who were less than 18 months from their first symptom onset. With the typical diagnosis for ALS taking around 12 months, many patients were only eligible to enroll during a small window of time. The study's 18-month observation period* presented further challenges to enrollment and retention, since this is a significant amount of time for patients in the control group to receive the placebo alongside a modestly effective standard of care.

The small enrollment window, long study duration, and inclusion of a placebo arm would make patient recruitment and retention challenging. To appropriately test the study's hypothesis, the study needed to retain the enrolled patients to minimize missing data, which could have a significant confounding effect on the analysis and interpretation of the study outcome.

*This 18-month duration was designed in agreement with ALS thought leaders and verified through data modeling and regulatory scientific advice meetings. In today's current landscape, a study of this duration would be unlikely to gain support from regulators, ethicists, and the advocacy community.

"We were looking for an experienced CRO that could appreciate the growth journey we were on as a biotech serving the ALS community. **It was important we could trust the CRO teammates to be a knowledgeable sounding board as we took our first steps into this indication.** We were laser-focused on ensuring that all external stakeholders had a good impression of the study, from the security and trust of the day-to-day conduct to the scientific and empathetic style in which we went about it."

Clinical Project Manager
Biotech Sponsor

3 Unexpected Events

The latter part of the study period overlapped with the onset of the COVID-19 pandemic, intensifying the challenges of working with such a respiratory-compromised patient population.

The Worldwide Solutions

Our strategic and operational neuroscience and rare disease teams developed multiple strategies to mitigate the risks of these challenges and drive study success.

Partnering for Success

We approached the program as a united team with the sponsor, establishing a harmonized working relationship built upon respect, scientific dedication, and enjoyment in collaboration.

Supporting Our Sponsor's Growth Journey

We adapted our support as the emerging sponsor evolved. When the partnership was established, our sponsor required extensive specialist support from us. Thanks to the open communication and strong partnership, we periodically revised the team structure to suit the changing needs of our sponsor as they grew. The study team ultimately consisted of pairs of specialist counterparts for shared, detailed decision-making and sponsor oversight.

Working in Harmony

Our sponsor came into the partnership with an established protocol, enabling us to conduct a thorough feasibility review. Together with our sponsor, we developed a list of target investigator sites. We completed the detailed site capabilities evaluation, making recommendations to our sponsor about clinical site involvement. Our final selection of world-renowned ALS investigators brought additional credibility to the study, fulfilling our sponsor's goal of collaborating with high-quality research sites and leading investigators who could positively represent the study within the ALS community. In parallel, we established the operational solutions and leveraged our vendor partnerships to fulfill the protocol requirements, specifically for collecting outcome measures and easing patient burden.

United in Purpose

The true collaboration stemmed from a mutual dedication to advancing the program and commitment to involving patients as research partners. This unity was especially evident when coordinating communication with the investigator sites and the wider ALS community. We led the day-to-day site relationships throughout the study and supported our sponsor's relationship with key community stakeholders.

Together we presented at meetings for investigators and at industry and scientific events. The shared tone, tenor, and approach to stakeholder communication transcended a transactional relationship, building the trust of investigators through a harmonized and high-quality study conduct.

"We came together as one team, through mutual respect of each other's experience and recognition that each team member was making a critical contribution to a study that would make a huge difference — either by bringing to market a new therapy for an ultimately fatal condition or through the lessons we collectively learned by undertaking the challenge."

Clinical Project Manager
Biotech Sponsor

Patient-Centric Operational Solutions

Our sponsor considered the patient journey during the study design phase, including a disproportionate randomization ratio, limited/optional invasive measures, use of telemedicine, and an increasing interval between study visits to accommodate the progressive functional decline of the participants. All efforts were intended to increase the attractiveness of study participation while reducing the associated burden for a population with significant morbidity.

We implemented a patient-optimized, flexible approach to operations that was commensurate with the study design requirements. Many of these patient-centric operational solutions also served as prospective risk mitigations for COVID-19 restrictions. For more on how we navigated the COVID-19 pandemic during this study, **check out our white paper**.

Patient-focused features included:

Patient Information & Recruitment

- Dedicated study website for providing detailed information required to consider study participation
- Study app for patients and caregivers for sharing essential information about the study, visit reminders, etc.
- Study portal for facilitating communication with investigators

Data Integrity & Patient Retention

- Direct-to-patient shipment of study drug
- Incorporation of home health services
- Use of telemedicine for remote visits
- Integration of portable spirometry
- Automated participant payment system
- Concierge travel service

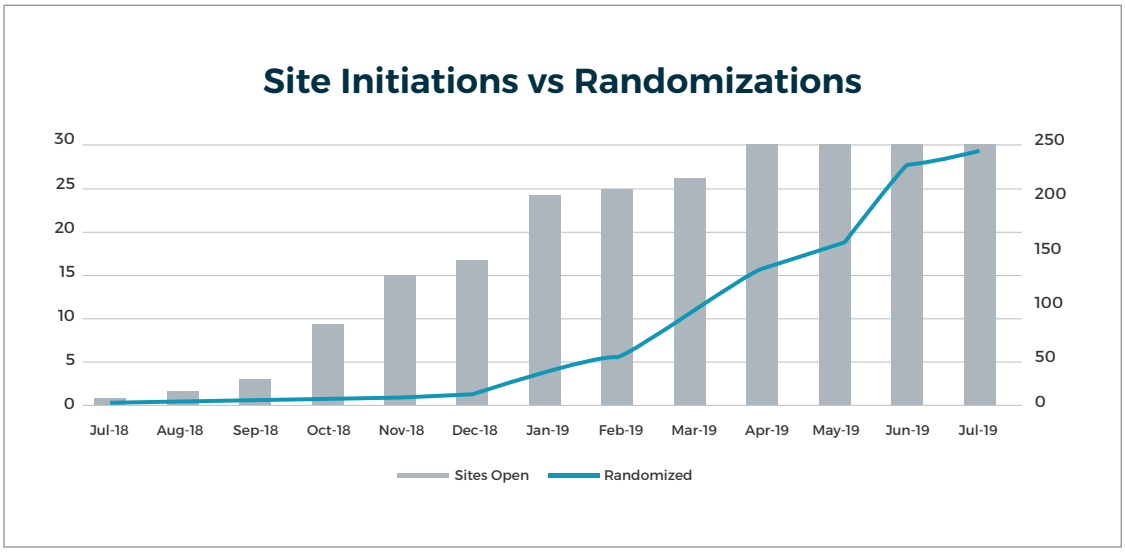
Community Engagement

Our patient-centric operational solutions were the primary feature in conversations between our sponsor and the research community. These conversations helped establish the positive intentions of the industry in an arena that was predominantly academic dialogues at the time.

Our sponsor's appointment of a full-time director of patient advocacy enabled meetings to be held at regular intervals with numerous prominent ALS advocacy organizations. Additionally, our teams presented posters at ALS conferences and consortia meetings to showcase the study's design and operations. This study was one of the first to be included on the ALS Signal Dashboard and received a four-star accolade from the **Patient-Centric Trial Design (PaCTD) Rating Criteria**.

We also took an innovative approach to selected site initiation visits, holding a four-way conversation that included the investigator, our sponsor, a national advocacy representative, and our team. These visits provided an opportunity to strengthen relationships, discuss the patient-centric operational solutions available, and share information among all stakeholders in the study ecosystem. These meetings also provided opportunities to discuss the specific profile of patients who would qualify for the study, building relationships between site and advocacy to bolster the support available in a patient's decision whether to participate.

The Results



12
Recruiting Months

0.68
Recruitment Rate
(Patients/Site/Month)

14.6%
Screen Failure Rate

22.0%
Drop-out Rate

While the study results were negative, it was not a "failed study" due to the high level of data integrity that produced consistent results across all clinical endpoints. **Our patient-centric approaches and close CRO-biotech collaboration has informed the future of ALS study operations and expectations for ALS community engagement across the industry**.

We met the 12-month recruitment goal, and the study retained an adequate number of randomized patients over the 18-month treatment period, ensuring a robust test of the study's hypothesis. **All major study milestones were achieved, fulfilling the commitment to the biotech's investors and enabling several significant inflection points on their growth journey**.

We have applied the lessons learned across subsequent studies in our ALS portfolio and nurtured the strong relationships built with patient stakeholders and investigators. Additionally, this study has informed how we approach research across a variety of rare neurological disorders.

We continue to emphasize operational solutions intended to recruit and retain patient partners by reducing the burden of participation and improving the quality of study information.

Why Worldwide?

Worldwide is a leading CRO in the field of neuroscience clinical research with deep experience in neurodegenerative and neuromuscular studies. Our team members draw on their previous experience holding various roles across the ALS research community to inform Worldwide's approach to ALS clinical development and partner closely with our rare disease methodology experts to deliver tailored study solutions.

Talk with our team about how we can support your neuroscience study.

Contact Us ⟶

Worldwide Clinical Trials