IXICO CLINILABS THE CRO FOR CNS

Executing a Multi-Arm Phase 1 Alzheimer's Disease Global Clinical Trial

With Clinilabs and IXICO

clinilabs.com | IXICO.com

Introduction

In the realm of Central Nervous System (CNS) clinical trials, the expertise in science and technology is constantly being pushed to new boundaries. This case study focuses on a groundbreaking collaboration between a biotechnology company and its development partners, Clinilabs and IXICO, to conduct a complex Phase 1 multicenter, multi-arm Alzheimer's disease (AD) clinical trial.

The goal was to generate rich data that would support the safety, tolerability, and potential efficacy of a new investigational drug aimed at treating Alzheimer's disease.

The study was designed to assess the safety and tolerability of single and multiple doses of a monoclonal antibody investigational drug and to estimate its serum pharmacokinetics (PK) following intravenous (IV) administration in patients diagnosed with Alzheimer's disease. The inclusion of AD patients necessitated a strategic approach involving specialty investigator sites with access to the patient population and the capability to perform complex biomarker assessments.

As a global, full-service CRO dedicated to the development of CNS therapeutics, Clinilabs' project team identified high performing investigator sites and best-in-class providers to conduct the study. IXICO was selected to participate because of its neurological imaging expertise, and its leadership in brain imaging. MRI scans on this trial were centrally read by neuroradiologists and used to monitor the occurrence and progression of Amyloid Related Imaging Abnormalities (ARIA). Detection and management of ARIA was critical to ensuring diagnostic accuracy and the success of the trial.

Study Objectives

This Phase 1 study utilized a single ascending dose (SAD) and multiple ascending dose (MAD) placebo-controlled design. It aimed to evaluate the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of the investigational drug in participants with Mild Cognitive Impairment (MCI) or Mild Dementia due to Alzheimer's disease.

Synergy Between Clinilabs and IXICO

The synergy between Clinilabs and IXICO proved to be a significant asset, particularly in navigating the complexities of a multi-arm Alzheimer's disease study. The collaboration was rooted in synchronized clinical and imaging site qualification processes, and rapid site activation, which ensured alignment with study recruitment schedules and timeline priorities.

Seamless communication, supported by interconnected systems like Clinilabs' Electronic Data Capture (EDC) systems and IXICO's proprietary platform, TrialTracker, optimized the experience for both clinical and imaging site users.

This close integration extended to streamlined reporting capabilities, providing the sponsor's study teams with clear, actionable insights. The agility and fluidity with which both organizations operated allowed for quick adaptation to meet study needs, efficiently managing challenges such as protocol amendments and subject reads.

Clinical Operations and Imaging

Clinilabs accelerated the study start-up by employing a personalized approach to investigator site feasibility assessments, while IXICO confirmed imaging capabilities. Rapid site qualification enabled the enrollment of the first subject within nine days of the first site activation. The Clinilabs and IXICO project teams held regular meetings with the sponsor to prioritize daily tasks, which allowed Clinilabs to screen, enroll, and secure database lock nine days prior to the target completion date and within budget, even with the need to adapt to eight protocol amendments throughout the term of the study.

IXICO was responsible for managing the end-to-end imaging services for this U.S.-based, multicenter Phase 1 study. This included ensuring that imaging site qualifications and staff training were completed on time, in line with the clinical site initiation visit (SIV) timelines. A total of 1,000 image datasets were processed, achieving complete accuracy.

- Amyloid PET (Positron Emission Tomography) visual reads confirming amyloid positivity for inclusion.
- Amyloid PET Standard Uptake Value ratio (SUVr) assessments.
- Magnetic Resonance Imaging (MRI) visual reads for exclusion and ongoing safety monitoring.

IXICO CLINILABS

Methodology

Key Clinical Operations

Clinilabs' meticulous project management was pivotal in collecting high-quality, actionable data from the onset of the trial. IXICO's project managers proactively planned and coordinated imaging site qualifications, maintained rigorous data quality assurance despite the complexities of protocol amendments, and ensured the timely transfer of imaging data.

The early insights gained from this data led to the implementation of multiple protocol amendments, including the addition of cerebrospinal fluid (CSF) sampling and the collection of end-of-study (EOS) data. These changes were made because the close collaboration between Clinilabs and IXICO provided a high level of scientific expertise to support the project and identify how the study could obtain the optimum data for its aims.

The study enrolled participants aged 55-90 years old with mild cognitive impairment or a confirmed diagnosis of Alzheimer's disease, across 17 clinical centers in the United States. Of the 260 subjects screened, 65 were randomized, and 60 completed the study within an 18-month period.

Top-line results were released within six days following database lock, allowing the client to present the findings at a major industry conference.

Key Imaging Analysis and Operations

IXICO utilized a centralized team of highly skilled MRI and PET readers, each with specialized expertise in radiology and nuclear medicine. This team deployed reader training and read methodologies that had been fully endorsed by the tracer manufacturers, ensuring technical confidence in the robust read process. For the PET eligibility reads, IXICO implemented a hybrid quantification and visual read approach, where the SUVr was first used to make an initial classification. Only borderline cases required a visual read, ensuring both speed and accuracy in results.

17 clinical centers in the United States.

Results

The successful execution of this Alzheimer's disease clinical trial provided rich data and insights critical for the investigational drug's development, with minimal stress and burden on patients and sponsors. IXICO's centralized, standardized read process using experienced readers ensured accuracy in read outcomes.

The study's imaging read results offered high-dimensional insights, enabling the sponsor to gain a deeper understanding of amyloid-related imaging abnormalities (ARIA-E) and the impact of amyloid-directed therapy. Clinilabs' ongoing management of the study enabled the project teams to stay on schedule, offering an advantage over industry norms.

Additionally, the early adaptation and protocol modifications allowed the sponsor to present preliminary validation of an amyloid-directed therapy at an industry conference, shaping the future development of the investigational drug, which is now advancing in clinical development.

Conclusion

This case study underscores the importance of selecting the right partners in executing complex and challenging CNS clinical trials. The collaboration between IXICO and Clinilabs not only ensured the successful delivery of the Phase 1 Alzheimer's disease study but also provided the sponsor with critical insights, facilitating informed decision-making for the drug's further development.

IXICO is dedicated to delivering insights in neuroscience to help transform the advancement of investigational therapies for neurological diseases, such as Huntington's disease, Parkinson's disease, and Alzheimer's disease. The Company's purpose is to advance medicine and human health by turning data into clinically meaningful information, providing valuable new insights in neuroscience by supporting pharmaceutical companies across all phases of CNS clinical research. IXICO's goal is to be a leading advocate of artificial intelligence in medical image analysis.

IXICO has developed and deployed breakthrough data analytics, at scale, through its remote access technology platform, to improve the return on investment in drug development and reduce risk and uncertainty in clinical trials for the Company's pharmaceutical clients.

More information is available on **www.IXICO.com**

Clinilabs is a global, full-service contract research organization (CRO) focused exclusively on central nervous system (CNS) drug and device development. With deep expertise in CNS, we are committed to the development of therapeutics that treat a range of psychiatric, neurological, and substance use disorders, as well as rare and ultra-rare CNS diseases.

Clinilabs partners with pharmaceutical and biotechnology companies to deliver a complete, first-in-human through Phase 3 spectrum of high-quality, timely, and cost-effective clinical drug and device development services, with the shared goal of speeding new CNS medicines to market.

Clinilabs has conducted more than 750 CNS clinical trials since 2000 and has played a pivotal role in approving 22 new therapies across 13 CNS indications to help transform patients' lives worldwide.

More information is available on **www.clinilabs.com**

IXICO plc
4th Floor, Griffin Court
15 Long Lane
London
EC1A 9PN

IXICO.com

Clinilabs
4 Industrial Way West
Eatontown,
NJ 07724

CLINILABS.com

clinilabs.com | IXICO.com