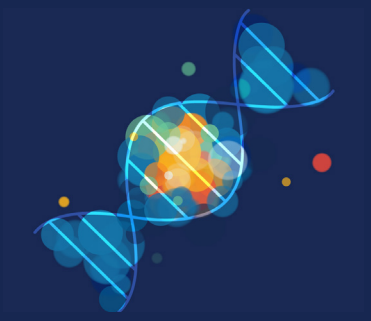
Case Study:

SUCCESSFUL APPROACHES IN GLOBAL PHASE III ULTRA-RARE DISEASE TRIAL FOR THE TREATMENT OF NIEMANN–PICK DISEASE TYPE C (NPC)



A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED GLOBAL PHASE III CLINICAL TRIAL FOR THE TREATMENT OF NIEMANN–PICK DISEASE TYPE C (NPC), AN ULTRA-RARE LYSOSOMAL STORAGE DISORDER.

60 PATIENTS

13 SITES

8 COUNTRIES*

*(Australia, Czech Republic, Germany, Netherlands, Slovakia, Switzerland, United Kingdom, and United States)

CHALLENGES

Recruitment Challenges

- NPC is an ultra-rare disease with a prevalence of 1:120,000. In addition, a short recruitment window was set, requiring all subjects to be enrolled within a 3-month period.

Subject Randomization and IP Management

- A system was required for allocation of subjects to a treatment arm and IP supply management across various countries globally.

Endpoint Protection

- Primary endpoint as well as other efficacy endpoints rely on consistency of the subject performing structured neurological assessments accurately at each visit as well as regulatory requirement to maintain investigator consistency in assessing the outcome across all study visits to ensure accurate ratings of changes in patients.

Maintaining Timelines For Database Lock

- A target milestone was provided for Database Lock allowing only 2 weeks for data review and cleaning prior to database lock.

RESULTS

- Despite ultra-rare recruitment challenges, recruitment was complete in 3 months and over-enrolled the study 130% of the target patients.
- Database was locked within 10 days of LPLV.
- All primary and secondary endpoints were successfully met, and New Drug Application was filed with the FDA.
- FDA approval after priority review.

SOLUTIONS

Recruitment Challenges

- Strong relationships with patient advocacy groups were utilized to share awareness of the study among the patient population.
- Strong relationships with Key Opinion Leaders enabled these investigators to 'champion' the study with advocacy groups and across their referral networks.
- A competitive recruitment strategy was applied with sites regularly updated on recruitment progress and reminded of remaining slots for enrollment.

Subject Randomization and IP Management

- Randomization performed with the use of computerized interactive response technology (IRT).
- Medpace ClinTrak® IRT is customized to provide the exact level of functionality required for your study including real-time subject status/visit tracking, drug supply/shipment management, and randomization.

Endpoint Protection

- Investigators were provided with training and guidance documents on expectations for performing efficacy assessments and requested to ensure investigator availability when planning subject visits.
- Medpace closely monitored for any inconsistencies in efficacy data or changes in assessors and quickly initiated follow-up actions such as re-training and reminders of expectations.
- Medpace CRAs prioritized review of efficacy data during monitoring visits and were able to swiftly escalate concerns to the Clinical Trial Manager for further actions/follow-up.
- Sponsor was informed in real-time of any protocol deviations regarding efficacy endpoints, to support with investigator follow-up as required.

Maintaining Timelines For Database Lock

- Sponsor worked closely with Medpace in a 'one-team' approach to discuss in advance the required timelines and expectations for the database lock.
- Medpace was able to initiate various strategies to minimize risks to meeting the deadline, including:
  - Ensuring sites were kept up to date with data entry and queries throughout the study, avoiding the risk of any last-minute backlogs.
  - Working closely with sites in advance to share timelines and expectations as well as discussing and supporting as issues arise, e.g., postponement of Last Patient Last Visit (LPLV).
  - 'Front-loading' activities as far as possible, i.e., increased cleaning activities ahead of the database lock and scheduling additional Routine Monitoring Visits.
  - Regular communication and planning calls with Sponsor and vendors to ensure alignment in advance and share updates during database lock.

"Medpace has been the dynamic, collaborative partner we needed to achieve clinical and regulatory success. We are a small but highly involved Sponsor, and Medpace has always been flexible in understanding exactly what support we need to successfully execute our development program. The quality of their expertise is unmatched to any other CRO our team has worked with. We feel extremely fortunate – and a sense of relief – to have such a wonderful partner to help us continue to achieve a shared goal of urgently bringing new therapies to patients with extremely high unmet medical needs."

– Chief Development Officer, Biotechnology Company