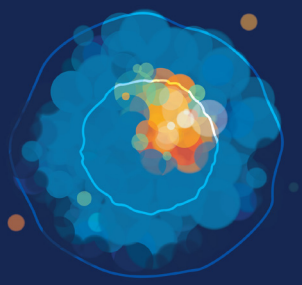
Case Study:

GLOBAL RARE BLOOD DISORDER STUDY ACHIEVES MARKET APPROVAL AND 100% PATIENT RETENTION



OPEN-LABEL, SINGLE-DOSE, MULTI-CENTER MULTINATIONAL, GENE THERAPY TRIAL IN ADULT SUBJECTS WITH A RARE BLOOD DISORDER

66 PATIENTS
Phase I/IIb, Phase IIb, Phase III

28 SITES

9 COUNTRIES
US, UK and EU

SERVICES PROVIDED

- Project Management
- Regulatory Submissions
- Clinical Monitoring
- Clinical Safety
- Medical Monitoring
- Central Lab

CHALLENGES

- Hub and Spoke Model: Pharmacy Set-up and Dosing Day Preparation
- GMO/RS Submissions
- Patient Enrollment for Rare Disease Indication
- Patient Retention up to 15 years Post-dosing
- Study Endpoints Protection and Centralized Data Review

RESULTS

- Key milestones were successfully met
- FDA, EMA, and MHRA marketing approval
- Multiple regulatory inspections without critical findings
- 100% retention in Long Term Follow Up (LTFU) up to 8 years Post-dosing

SOLUTIONS

Hub and Spoke Model: Pharmacy Set-up and Dosing Day Preparation

- A hub and spoke model was implemented. In this model, selected sites were divided into three categories based on the qualification and capacity of their pharmacies: central dosing sites, local dosing sites and non-dosing sites. Central dosing sites supported multiple geographically dispersed non-dosing clinical sites (also located in different countries).
- Pharmacies qualified and equipped to store, prepare, administer, and discard gene therapy and with trained and experienced pharmacy teams were carefully selected after onsite pharmacy qualification visits.
- Clinical sites and central dosing sites were trained extensively by Medpace Clinical Research Associates (CRAs), including mock runs completed with the sites before dosing day. This ensured a clear communication and transfer process between the pharmacies and the clinical team and between the local and central dosing sites and CRAs.
- Patient Transfer for Dosing Plan was written to detail the organization of patient dosing at clinical sites and patient transfers to a central dosing site. Patients' travel to central dosing sites was supported by patient travel concierge vendors.
- Medpace CRAs reviewed patient eligibility at screening and before dosing (lead-in – around 6-7 months after screening). They also reviewed IMP worksheets and all IMP documentation released by the pharmacy right after dosing.
- Scheduled patient dosing dates were closely tracked by the Medpace study team. Medical Monitors were informed of each dosing date in advance to ensure 24-hour coverage before and after the patient dosing.

GMO/RS Submissions:

- GMO submissions and regional and national regulatory requirements for gene therapy products were carefully assessed and planned as part of the global start-up strategy in order to achieve timelines.
- Since the coordination of IMP release is critical, the setup of site activation had to be timed perfectly. To ensure a flawless setup, Medpace generated a site activation checklist that included GMO-specific provisions and central dosing requirements.

Patient Enrollment for a Rare Disease Indication:

- Enrollment was supported by an engaged and involved community. Patients were educated on the indication and were motivated to enroll by the prospect of helping younger generations, as the rare blood disorder is inherited.

- Medpace and the Sponsor maintained direct communication with Investigators to ensure Investigators clearly informed patients of the study requirements, the risk of lack of efficacy, and the irreversible nature of gene therapy. This required a good relationship between the Investigators and patients. Selecting the right patients for participation was key to the success of the study.

Patient Retention up to 15 Years Post-dosing:

- Individual Patient Transfer Plans were created for each patient transfer between different sites within a country or between different countries, when required.
- Sponsor allowed operational flexibility to keep patients on the study, regardless of costs, opening and closing sites due to changes in patient location or arranging intercontinental travels, translations, regulatory approvals for cross-border patient transfers and insurance. These extreme measures allowed for 100% patient retention up to 8 years post dosing (current time).
- Clinical site nurses visited patient homes near the clinical site when onsite patient visits were restricted due to COVID-19, when possible.
- Home nursing and patient travel to local lab facilities were implemented when patients could not travel to their sites for safety visits.
- Local laboratory vendors were set up to ensure samples of relocating patients were collected and shipped to MRL locations.

Study Endpoints Protection and Centralized Data Review:

- Gene therapy trials rely on data collected through patient's follow-up visits. Other than patient visit compliance, a strict strategy for endpoint protection should be implemented. Studies conducted within rare disease populations are rather small in size and any data lost can significantly impact the final data set.
- Centralized data review activities have been implemented to ensure real-time insight into study data quality to improve safety, and to ensure proper operational oversight, risk assessment and mitigation.
- Automatic EDC and MRL alerts were set up to flag out of range values, with a particular focus on values from liver samples. Medpace Medical Monitors followed up directly with clinical sites to review the values, when needed.
- Immediate actions were implemented in case of missed visits or procedures/samples not performed or collected.