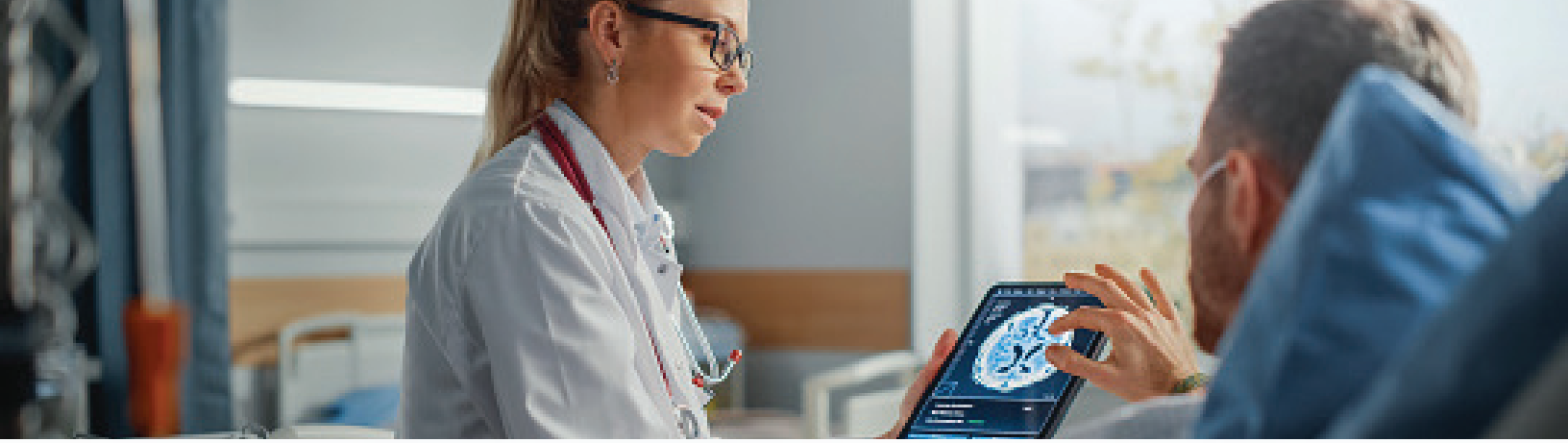
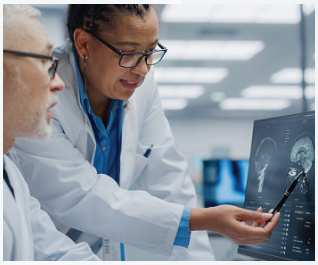


Advancing precision medicine to improve health outcomes in rare neurological diseases

Precision medicine offers the promise to treat a variety of conditions, especially rare diseases, with targeted approaches. But developing more personalized medicines can introduce new complexities in the clinical trial process, which can hold back drug developers on the road to commercialization. **Find out the factors that make rare neurological diseases a prime target for precision medicine, the unique challenges of clinical trials for these conditions, and how choosing the right contract research organization (CRO) can help small and midsize biopharma companies develop these life-changing treatments.**

3.5-5.9%
OF THE GLOBAL POPULATION IS AFFECTED BY THE MORE THAN
6,000
KNOWN RARE DISEASES[1]



The unique demands of rare neurological disorders

According to some estimates, approximately 3.5 to 5.9% of the global population is affected by the more than 6,000 known rare diseases.[1] Of these, nearly half are neurological, with a disproportionate impact on pediatric populations: Over 50% of rare disease patients are children, and the vast majority of pediatric rare diseases have a significant neurological component.[2] Conditions impacting the central nervous system (CNS) can have a rapid and debilitating impact on patient development, quality of life, and ultimate survival, making earlier diagnosis and treatment critical for young patients.

For many rare diseases, clinical trials represent the sole lifeline for understanding and treating a patient's condition. However, the natural history and variations of many rare diseases are not fully understood, making clinical trial planning particularly challenging. For rare CNS diseases, in particular, drug development is complicated by genetic complexity, clinical variability, and difficulty in accessing affected tissue for biomarker discovery, drug delivery, or clinical endpoint measurement. Rare CNS disease trials present operational complexities as well, as many patients face significant disease-related physical or developmental disabilities and thus require specialized care, transport, and more. This is especially salient for pediatric trials, where the demands of clinical trial participation often impact an entire family.

[1] https://www.nature.com/articles/s41431-019-0508-0
[2] https://pharmaphorum.com/patients/global-genes-rare-neurological-disorder-research/

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Taking a precision medicine approach

The advent of precision medicine has opened new avenues for the development of rare CNS disease treatments that target the right mechanism for the right patient at the right time. By leveraging resources such as next-generation sequencing, detailed clinical phenotyping, and patient-derived stem cell models, developers can better understand variation within a disease, both on a mechanistic and phenotypic level.[3] By identifying reliable biomarkers, drug developers can conceptualize subgroups within a given condition to create effective, targeted diagnostics and therapies.

Informed screening and diagnostic approaches are especially vital for rare CNS diseases. With a means of identifying preclinical or early-stage cases, patients can receive individualized intervention earlier in disease progression to improve their prognosis and quality of life. Biomarker identification can also facilitate the identification of underlying drivers of disease, informing targeted drug development or drug repurposing. High-throughput screening and artificial intelligence are thus critical tools in selecting drug candidates for rare diseases. By capturing and understanding the genotypic and phenotypic heterogeneity of a disease, developers can identify reliable patient biomarkers and design potential drugs that are more likely to be effective. For rare CNS diseases, where each day of progression matters, moving forward with optimal diagnostics and drug candidates can make all the difference.

How partnering with a CRO can optimize the development of precision CNS therapies

CNS drugs in Phase 2 and 3 clinical trials fail at a rate of roughly 85% due to a lack of efficacy, which has driven many major pharmaceutical companies to divest their CNS development programs.[4] While this opens new opportunities for small and midsize biopharma companies to join the development fight, these organizations can benefit immensely from the resources and support available through partnership with a CRO. Working with a CRO can ensure that each step of drug development is optimized for the sponsor and, more importantly, the patients.

Some key areas where CRO partnership can improve rare CNS therapy development include:

Clinical pharmacology modeling & simulation — These studies aim to evaluate what the body does to the drug and what the drug does to the body, understand patient variability, and relate that back to benefit, risk, and dosing. For precision therapy development, clinical pharmacology modeling is crucial. CROs can support sponsors in leveraging preclinical studies, published data, and model-informed approaches to develop dosing strategies, study practices, and patient selection criteria.

Clinical pharmacology modeling is especially valuable to optimize dosing in the complex circumstances of pediatric studies, where a safe and effective dose range must encompass neonates to adolescents.[5] Experienced CROs can help sponsors best leverage these tools in planning PK/PD studies for young populations in rare disease trials.

[3] https://www.sciencedirect.com/science/article/pii/S1934590918302376
[4] https://www.wcgclinical.com/insights/cns-trial-failure-rates-high-as-need-for-new-drugs-grows/#:~:text=The%20failure%20rate%20of%20CNS,to%20pass%20through%20that%20barrier

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Natural history studies — Because many rare diseases and affected populations are poorly understood, natural history studies can help developers elucidate disease mechanisms and hallmarks for better clinical trial design. Partnership with an experienced CRO can offer better access to patient populations, quality data collection, and streamlined planning for both retrospective and prospective natural history studies.

Protocol design and development — By providing broad expertise and experience in protocol development, working with a CRO can ensure that protocols are optimized from the start to run smoothly and collect quality data. CROs can also leverage relationships with patient advocacy networks to identify clinically meaningful study endpoints for a particular rare disease.

Patient recruitment — CROs like Allucent are experienced in finding the right trial sites and pathways to reach an optimal patient population, which is especially valuable for rare diseases. For example, Allucent uses multiple channels to maximize patient identification and recruitment, including KOL referrals, patient advocacy groups, clinical databases, patient registries, and investigator experience and patient relationships.

Clinical trial operations and patient retention — CRO partnership can also simplify the logistics of a clinical trial to ensure that all processes are properly coordinated and that patient participation is as easy as possible. Allucent's Patient Direct Trial approach removes logistical barriers to participation through home nursing visits and patient concierge services, support caregivers, and supportive new technologies through established vendor relationships.

Regulatory support — A CRO can offer expert regulatory support to design studies that yield high-quality, persuasive data packages and align with regulatory guidance. When navigating the complex landscape of orphan drug development, it's crucial to proceed with the best regulatory knowledge at every step.

[5] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/general-clinical-pharmacology-considerations-pediatric-studies-drugs-including-biological-products

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Case study: A natural history study of CDKL5 Deficiency Disorder

CDKL5 deficiency disorder, or CDD, is a rare genetic disorder that typically manifests within the first three to six months of life. Those afflicted by the condition experience seizures and issues with neurological and cognitive development, producing lasting effects on motor function, speech, and more.[6] A drug development client approached Allucent for assistance in carrying out a natural history study to better understand the progression of CDD. Facilitating this study introduced several notable challenges. Because the disease occurs in only 1 of approximately 60,000 live births, identifying and recruiting eligible patients for the study required a significant global reach. Allucent collaborated with CDD advocates throughout trial planning to ensure feasibility for patients and recruit a suitable pediatric population. After identifying appropriately equipped sites in Europe and the United States, Allucent developed a comprehensive plan to facilitate cross-country study participation.

Making the trial as smooth as possible for patients and their families demanded a network of support from Allucent partners. For on-site visits, families were provided with funds for travel, lodging, and food rather than reimbursement to eliminate any upfront costs. Additionally, childcare services were provided for other children in the family, and in-home nurse visits were used when possible, to minimize patient travel. For families traveling internationally for on-site visits, appropriate translation services were in place.

Especially because this was a natural history study, the client's overall goal was to make participation easy for families of children with CDD who dedicated their time just to understand the condition. By working with Allucent, they were able to coordinate a complex global trial while sparing no detail in patient support. The outcome was excellent: The study met its enrollment goals, participating families were engaged, and attrition from the study was low, demonstrating the success of Allucent partnership in overcoming the challenges of a pediatric rare disease trial.

About Allucent

Allucent is a CRO striving to bring new therapies to light by solving the distinct challenges of small and mid-size biotech companies. We boast extensive experience in both CNS and rare disease research, with more than 20 years of successful clinical development in each therapeutic area. Allucent has supported over 120 rare and orphan disease clinical trials and 16 product approvals across a variety of novel therapy classes and precision medicine, including gene therapies, GMOs, stem cell therapies, and mRNA and antisense therapies. We've also been at the forefront of CNS research, involving more than 150 clinical trials across 20+ indications. Our expertise includes movement, demyelinating, and seizure disorders, as well as neurodegenerative and neurovascular diseases.

We interact extensively with regulatory agencies in the U.S., Canada, and Europe to keep pace with the stipulations and advances in CNS and rare disease trials and treatments. Allucent understands the drive and passion behind developing crucial treatments for these conditions and is devoted to supporting organizations in this mission.

To learn more about Allucent's CNS clinical trial experience and capabilities, visit https://allucent.com/Allucent-Rare-Diseases-Expertise

[6] https://www.epilepsy.com/causes/genetic/cdkl5-disorder

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