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How Biotechs Can De-Risk CNS Development Through Early Modeling, **Simulation and Study Design**

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A guide to accelerating neuroscience programs with data-driven insights, targeted populations, and regulator-ready evidence

Few areas of drug development are as scientifically rich and operationally daunting as neuroscience. Developing therapies for the central nervous system (CNS) demands patience, precision, and persistence, as the brain remains one of the least understood organs in human biology, and its disorders among the hardest to treat.

Yet a surge of innovation is reshaping this field, powered by new modalities, deeper biomarker understanding, and sophisticated modeling approaches that can turn data into actionable insights.

For small and mid-sized biotech companies, the true engine of CNS innovation, the path to success often depends on the partners they choose. Allucent, a global contract research organization (CRO), has carved out a reputation for helping sponsors navigate the scientific and regulatory complexity of neuroscience development and clinical trial execution.

Through its Clinical Pharmacology Modeling and Simulation team, Allucent integrates translational science, clinical pharmacology, and advanced analytics to design smarter studies, de-risk programs, and accelerate therapies for a broad range of indications including amyotrophic lateral sclerosis, schizophrenia, Huntington's disease, and other neurological indications.

"The biology of the brain is still not necessarily fully understood," says Teresa Nunes, MD, Chief Medical Officer at Allucent. "Even within a single indication, patients can respond very differently. That makes it harder to know which subpopulation to target and which endpoints to use. These are fundamental challenges that shape every part of study design."

The Complex Landscape Of CNS Trials

Unlike oncology or immunology, neuroscience rarely offers validated biomarkers or short trial durations. Neurodegenerative diseases progress slowly, requiring lengthy studies to demonstrate any meaningful change. Psychiatric disorders are heterogeneous and susceptible to high placebo responses. And for both categories, the blood–brain barrier (BBB) remains a challenge to therapeutic success.

"Getting a drug into the brain is a special challenge compared to most other disease areas," says Alex MacDonald, PhD, VP Model-Informed Drug Development, at Allucent. "For neurodegenerative diseases, trials often need to run for long durations just to see a signal. That means you need large numbers of patients, and that creates additional recruitment, retention, and analytical hurdles."

Dr. Nunes adds that the patient experience itself can become a limiting factor.

"These studies often involve dozens of assessments, and the patients, especially those with advanced disease, can experience real fatigue," she says. "Retention becomes difficult when participants don't see immediate improvement, and that can threaten statistical power at the very moment when you're trying to detect subtle efficacy effects."

The practical implications are clear: successful CNS trials demand designs that minimize burden, select appropriate endpoints, and build in flexibility for heterogenous populations.

Designing Smarter Trials Earlier

In many programs, the roots of later-stage challenges lie in early development. Allucent emphasizes integrating clinical pharmacology at the earliest possible point to anticipate issues of BBB penetration, target engagement, and dose feasibility before they jeopardize a study's success.

"As we move into the clinic, it's vital to understand the likely translation from preclinical to human data, particularly for small molecules or antibodies that need to reach the brain," Dr. MacDonald says. "Modeling those dynamics early gives sponsors a higher probability of success once dosing begins."

This principle supports Allucent's approach to model-informed drug development (MIDD). The company's scientists use pharmacokinetic (PK) and pharmacodynamic (PD) models to simulate how a molecule will behave before, during, and after it crosses the BBB. These insights not only refine first-in-human dose selection but also guide the inclusion or exclusion of concomitant medications that could alter CNS exposure. The payoff is real: sponsors can enter the clinic with data-driven confidence in their design assumptions, potentially shortening timelines and avoiding costly protocol amendments.

Turning Complexity Into Clarity

Allucent's scientists are redefining neuroscience development through advanced modeling and simulation. The team's work has enabled sponsors to optimize dosing, support regulatory filings, and eliminate the need for additional clinical trials.

One example involved a program for a rare neurodegenerative disease, where regulatory authorities questioned potential drug–drug interactions mediated by a specific liver metabolizing enzyme. Allucent built a custom physiologically-based pharmacokinetic (PBPK) model to simulate both plasma and CNS exposure of the parent molecule and active metabolite. The analysis predicted the impact of co-administered inhibitors of the specific enzyme, allowing the client to adjust dosing safely without running a new clinical trial.

Another had orphan drug status designation to treat the symptoms of a rare neurodevelopmental disorder. Using a population PK model, the sponsor and Allucent scientists evaluated exposure–response relationships across age and weight groups and the team's simulations informed the patient populations to be included in the marketing application.

A further project involved pediatric dosing for a treatment for narcolepsy, where Allucent's model-based extrapolation from related pediatric populations proposed safe, effective dose ranges based on achieving similar systemic exposures which supported regulatory approval for lower-weight children. Additionally, an exposure–response analysis revealed an effective and better patient-oriented regimen to treat schizophrenia than the clinical trial design had tested, enabling a label change.

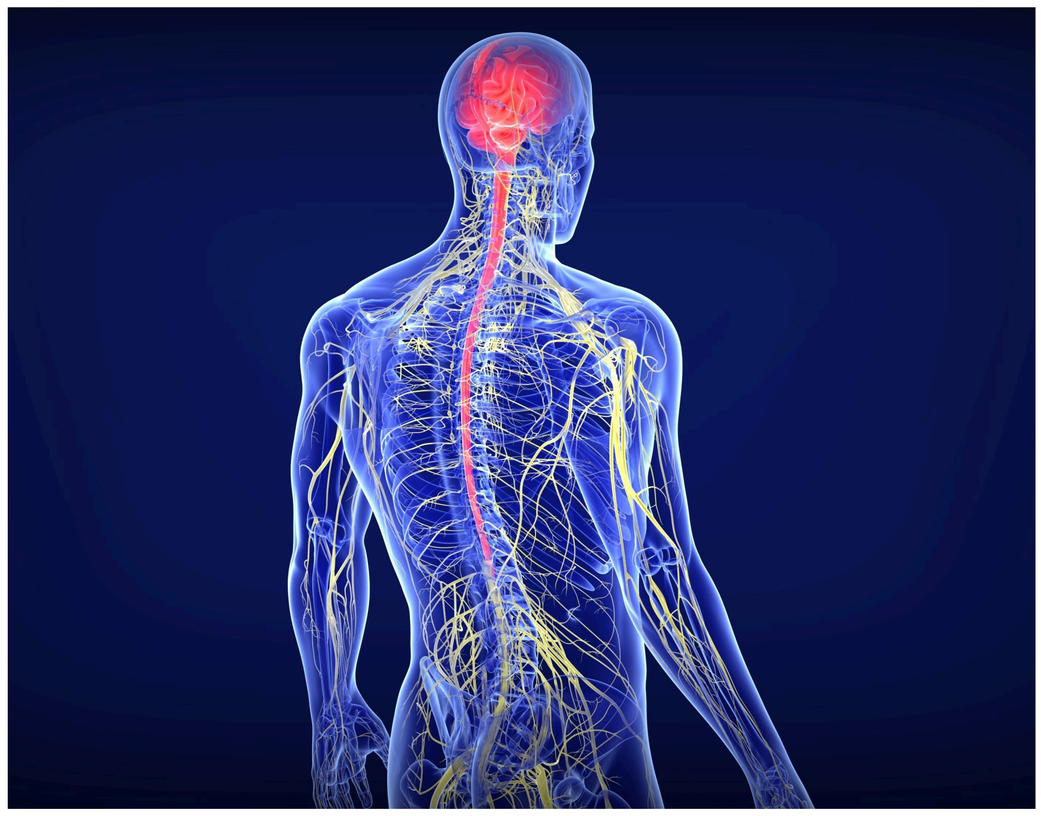
By converting uncertainty into quantifiable probabilities, Allucent's MIDD practice helps sponsors make faster, more defensible decisions at every stage of the development continuum.

> "Modeling can clarify where clinical data alone are ambiguous. PK and pharmacostatistical models let you test hypotheses virtually, predicting CNS penetration, assessing drug-drug interaction risks, and quantifying placebo responses before committing patients and resources."
>
> Alex MacDonald, PhD, VP Model-Informed Drug Development, Allucent

Early Engagement And Designing With The End In Mind

Still, even the most sophisticated modeling must align with regulatory expectations. For neuro-focused biotechs, uncertainty around acceptable endpoints, surrogate markers, or composite scales can derail progress late in development.

Early engagement with regulators is absolutely critical," Dr. Nunes says. "We help clients prepare for their first FDA or EMA meetings and understand what evidence the agencies will expect, which endpoints can be justified, and how to structure studies that will stand up to later scrutiny."



Of course, differing regulatory perspectives across regions require careful alignment, particularly for Alzheimer's, Parkinson's, and other neurodegenerative diseases.

"Even within a single disease, endpoints used for early-stage patients may not apply to late-stage populations," she says. "That directly affects how you plan your development plan and potential approvals."

Allucent's MIDD approaches are increasingly serving as the bridge between scientific reasoning, optimal dosing regimens, and regulatory confidence. By quantifying dose–exposure–response relationships, the company equips clients to defend dose selection, support inclusion criteria, and justify labeling recommendations. For small biotechs, this level of preparedness can make the difference between a productive FDA interaction and a costly program delay.

Beyond study design, regulatory success depends on recruitment strategy and feasibility planning, two often-overlooked pillars of CNS research.

"Patients may be scattered globally, especially in rare neurodegenerative diseases," Dr. Nunes says. "You need to understand the patient pathway, where they are, how to reach them, and which sites can actually deliver. Our feasibility assessments and experience in CNS help clients build that map before the first patient is screened."

Addressing Special Populations

CNS drug development isn't limited to adults. Many devastating neurological disorders begin in childhood, where the ethical and physiological stakes are even higher.

"The brain is not static," Dr. Nunes says. "Extrapolating from adults to children is possible in select cases but is rarely sufficient on its own. In pediatric populations, you have to think about development and behavior, and you often have a limited window of opportunity to intervene before development milestones are lost."

Allucent's pediatric expertise demonstrates how modeling can substitute for infeasible trials and/or optimize data collection in a smaller patient population to confirm dose and modeling results. Population PK models can simulate how dosing must be adjusted for body size, age, and metabolism, while limiting invasive procedures such as lumbar punctures or large blood draws.

"In children, you can't always perform the same procedures you would in adults," Dr. Nunes says. "Modeling lets us minimize the number of assessments and still maintain the scientific integrity of the study."

These approaches align with regulators' increasing emphasis on quantitative medicine and model-based extrapolation to reduce pediatric trial burden.

Translating Science Into Operational Success

Allucent's impact extends beyond algorithms and simulations. The company's integrated teams combining clinicians, modelers, statisticians, and regulatory experts help clients translate strategy into execution.

In one neurodegenerative program, Allucent worked with a biotech sponsor in early-stage development. "Before execution, our medical, clinical operations, clinical pharmacology, and statistics experts evaluated the indication and existing approaches to determine the appropriate patient population," Dr. Nunes says. "You need a thin line between selecting a subpopulation likely to show a signal and still being able to recruit."

The team also optimized clinical outcome assessments, balancing scientific rigor with feasibility. "Early-stage studies tend to include too many assessments, which can make them unmanageable," Dr. Nunes says. "We helped the client decide what could be done at home versus on site and developed a

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>
> Teresa Nunes, MD, Chief Medical Officer, Allucent

plan to train raters and reduce variability in scoring, a well-known issue in CNS trials."

In another example, Dr. MacDonald describes a psychiatric program that progressed from Phase I to Phase III with Allucent's continuous support.

"We started with Phase I in healthy adults, then transitioned to children for Phase II and Phase III," he says. "We used modeling to adjust doses, manage drug-interaction risks, and support the regulatory submission. That partnership has lasted eight years, and we're still working with them through their submission process."

Such long-term, embedded relationships, often spanning multiple programs, exemplify Allucent's business model. The company measures success not by transactions but by trust and continuity: partnerships that grow with the client's science and accelerate it across clinical and regulatory milestones.

The Future Of Neuroscience

Looking ahead, both Drs. Nunes and MacDonald see neuroscience entering a new era, one defined by smarter stratification, digital health integration, and a renewed industry focus after years of underinvestment.

"I think we'll see more biomarker-driven approaches like we did in oncology," Dr. Nunes says. "Sponsors are asking which biomarkers can help stratify populations, not necessarily for approval but to find the subgroups where the drug will truly work."

She also anticipates breakthroughs in neuroimaging and AI-driven analytics.

> "There's enormous potential in using AI to analyze big datasets and correlate markers with outcomes ... It's about connecting dots we couldn't see before."
>
> Teresa Nunes, MD, Chief Medical Officer, Allucent

Another area gaining traction is digital health. With wearables and remote-monitoring devices increasingly in use, chronic-disease trials can collect continuous, real-world data while reducing patient travel, although full regulatory acceptance of some of these digital solutions is still developing.

"Especially for Parkinson's or sleep disorders, being able to track movement, behavior, and sleep patterns at home is transformative," Dr. Nunes says. "It can reduce burden and improve participation."

Dr. MacDonald agrees, noting that after years of retrenchment, neuroscience is once again attracting robust scientific and commercial interest.

"Just 10 or 15 years ago, big pharma was shutting down its neuroscience divisions," he says. "After a period of reduced activity, neuroscience is seeing renewed scientific and commercial interest. Successes in Alzheimer's and multiple sclerosis have proven the biology can work. The field has re-established itself as a place where real progress is possible."

Science, Strategy, and Partnership

CNS drug development will never be simple. But by integrating advanced modeling, thoughtful trial design, and proactive regulatory engagement, the barriers become more manageable. Allucent's experience shows how data, collaboration, and patient-centered design can turn complexity into opportunity.

Across programs in neurodegeneration, psychiatry, and rare pediatric disorders, the company's model-informed strategies have enabled sponsors to predict CNS exposure, justify dosing, and secure regulatory approvals, often faster, with fewer patients, and even fewer trials than traditional pathways.

The lessons are clear for emerging biotechs navigating the neuroscience frontier:

- Start early with modeling and clinical pharmacology. It sets the foundation for efficient design and informed regulatory dialogue.
- Design around the patient. Feasibility, retention, and real-world relevance determine success as much as endpoints do.
- Engage regulators proactively. Early conversations, backed by quantitative evidence, build confidence on both sides.

"Our goal is to make every study scientifically sound, operationally feasible, and patient-centered from the start," Dr. Nunes says.

Through that combination of science and empathy, Allucent continues to help its partners bring hope to patients with some of medicine's most complex conditions and to advance the next generation of CNS therapies.

Allucent

Helping bring new therapies to light

Allucent is on a mission to help bring new therapies to light by solving the distinct challenges faced by biopharma and government clients. A global provider of comprehensive drug development solutions, including consulting, clinical operations, biometrics, and clinical pharmacology across a range of therapeutic areas, Allucent brings more than 30 years of experience in over 70 countries. With an A-Team of former regulators, leading scientists, and clinical experts, Allucent's individualized partnership approach delivers deep insights and hands-on expertise to help clients navigate the complexities of bringing innovative treatments to patients.

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