

Driving **CNS** **Clinical Trial** **Success** Through Data Confidence



Clinical research in central nervous system (CNS) therapies presents unique challenges that require specialized solutions.

Nearly half of Phase III CNS studies fail, primarily due to challenges in demonstrating efficacy, leaving sponsors with at-risk R&D investments and delays in getting vital treatments to patients with significant unmet needs. **These efficacy demonstration hurdles stem from multiple fundamental issues inherent in CNS clinical trials:**



High placebo response that masks true treatment effects, compromising endpoint signal detection



Variability in complex clinician-reported outcome measures, making it difficult to see treatment effects among the noise



Baseline score inflation resulting in inappropriate eligibility and amplifying placebo response

Signant's solutions are purpose-built to overcome these challenges by blending deep clinical expertise with specialized technology and services. Our comprehensive set of solutions empowers sponsors to design, conduct, and monitor CNS trials with unprecedented control over endpoint reliability, generating high-confidence data that maximizes signal detection potential and increases the chance of study success.

Proven best-in-class expertise in CNS clinical trials

1,280+
studies

60+
countries

380,000+
patients

70+
indications

68,000+
sites

Critical pillars for CNS trial success

Each component of our solution set targets a specific challenge of clinician-reported outcomes, while collectively and seamlessly working in concert to address the fundamental complexities of CNS trials. Together, these solutions create a robust foundation for driving confident, reliable endpoint data even in the most challenging indications.

DRIVING ENDPOINT SIGNAL DETECTION

TRIAL DESIGN CONSULTING

Optimizing protocols for signal detection



RATER TRAINING

Standardizing ClinRO assessments



PURESIGNAL ANALYTICS

Early detection of assessment quality risks



PLACEBO RESPONSE MITIGATION

Limiting the impact of placebo effect



SITE SELECTION

Leveraging site performance data



RATER STATION®

Powering consistent electronic clinician ratings



CENTRAL RATING & CENTRAL REVIEW

Reducing variability with independent experts



① TRIAL DESIGN CONSULTING

Optimizing protocols for signal detection

Signant's world-renowned CNS thought leaders, with decades of hands-on clinical and investigator expertise in patient care, help sponsors develop study designs that maximize signal detection potential.

- Strategic guidance on patient populations, endpoint selection, and study design to increase treatment-placebo differentiation and align with the clinical profile of investigational drugs
- Expert recommendations for inclusion/exclusion criteria and screening methodologies to ensure appropriate patient populations

② SITE SELECTION

Leveraging site performance data

Signant's Site Selection service leverages advanced analytics to help sponsors verify, identify, and select clinical trial sites with proven track records of generating high-quality CNS endpoint data.

- Evaluation of historical performance metrics to prioritize sites demonstrating excellence in ClinRO data quality
- Selection or verification of proposed sites aimed at optimizing endpoint signal detection potential

③ RATER TRAINING & QUALIFICATION***Standardizing ClinRO assessments***

Reduction of intra- and inter-rater variability through best-practice training programs ensures standardized administration and scoring of complex clinical outcome assessments across sites and raters.

- Scale-specific education and qualification methodologies addressing common administration errors and scoring nuances
- Integration with Rater Station to ensure only qualified raters access relevant scales

④ RATER STATION®***Powering consistent electronic clinician ratings***

Our purpose-built technology platform for CNS assessments, Rater Station®, eliminates administration and scoring errors and improves data quality through intelligent guidance and standardization.

- Pre-set workflows, on-screen guidance, and customizable edit checks to ensure accurate scale administration, scoring, and patient eligibility
- Audio/visual recording capabilities to support rigorous quality control and monitoring and drive highest quality data

⑤ CENTRAL REVIEW & CENTRAL RATING***Reducing variability with independent experts***

Our global network of CNS expert raters delivers independent assessment, review, and quality control, tailored to the needs of each study to drive consistent endpoint quality.

- Central quality review of audio/video recorded site-based assessments and subject eligibility verification to prevent errors, inconsistencies and baseline score inflation
- Independent central ratings or scoring to standardize complex ClinRO endpoint measures

⑥ PURESIGNAL ANALYTICS***Early detection of assessment quality risks***

Proprietary, clinician-defined algorithms and data scientists proactively identify and mitigate risks to study endpoint data quality.

- Clinically driven central statistical monitoring tailored to study-specific endpoints to derive deeper insights across all levels
- Timely, targeted interventions to mitigate quality concerns delivered directly by Signant's in-house clinicians

⑦ PLACEBO RESPONSE MITIGATION***Limiting the impact of placebo effect***

Evidence-based strategies to minimize the placebo response that compromises accurate signal detection in CNS studies.

- Comprehensive training for investigators, site staff, and patients on key techniques and appropriate trial participation expectations
- Targets both genuine placebo effects and data quality issues that mimic placebo response

Therapeutic expertise

Signant Health brings proven expertise across the full spectrum of CNS indications.

NEUROLOGY, including:

- Alzheimer's Disease
- Parkinson's Disease
- Multiple Sclerosis
- Mild Cognitive Impairment
- Myasthenia Gravis
- Huntington's Disease
- Epilepsy and Seizure Disorders
- ALS
- Non-Alzheimer's Dementia
- Rare Neurological Disorders

PSYCHIATRY, including:

- Major Depressive Disorder
- Schizophrenia
- Bipolar Disorder
- Generalized Anxiety Disorder
- ADHD
- Autism Spectrum Disorder
- Tourette Syndrome
- Substance Abuse/Addiction
- PTSD
- Borderline Personality Disorder



The Signant 4S advantage: A synergistic approach to CNS trials

Signant Health uniquely embeds CNS scientific knowledge throughout our technology platform and operational infrastructure, infusing every aspect of your evidence generation with deep therapeutic expertise. Going beyond simply facilitating electronic clinician ratings, our science-led approach fundamentally enhances their quality, reliability, and consistency across the complete study lifecycle.

Signant SmartSignals perfectly addresses the Four S's needed for successful CNS trial implementation: Solution, Science, Scale, and Service.



SOLUTION: CLINRO TECHNOLOGY PLATFORM

Signant's Rater Station solution is a purpose-built platform, specifically designed by our expert raters to address the complexities and nuances of CNS clinician-rated outcome assessments. Intelligent workflows with embedded logic guide clinicians through proper administration and scoring procedures, enhancing endpoint reliability and facilitating consistent, accurate measurements across all study sites and raters.



SCIENCE: WORLD-CLASS SCIENTIFIC LEADERSHIP

Signant's in-house team comprises renowned psychiatrists, neurologists, and CNS clinical scientists who have pioneered assessment methodologies and shaped industry standards. Our experts include key opinion leaders who developed many of today's gold-standard rating scales, supported by advisory boards of international authorities. This expertise is further complemented by our global network of expert raters enabling consistent, high-quality assessments across diverse trial settings.



SCALE: GLOBAL REACH

Signant has proven experience managing trials across over 60 countries. Our infrastructure supports any scale ranging from targeted rare disease studies to large-scale worldwide trials, standardizing complex assessments across diverse research environments and site capabilities.



SERVICE: PROVEN OPERATIONAL EXCELLENCE

Signant's operational delivery ensures tailored client service with expert teams implementing comprehensive CNS solutions — from customized rater training and site support to best-in-class project management. Our specialists understand the unique challenges of CNS trials, delivering exceptional support throughout the entire study lifecycle.

Trusted partner for CNS evidence generation

Our comprehensive solutions work synergistically across the entire study lifecycle, delivering endpoint data confidence and streamlining workflows to optimize signal detection—even in the most challenging CNS indications. **The Signant difference is built on:**



Scientific leadership with decades of renowned CNS expertise driving continuous innovation



Purpose-built technology designed specifically for complex CNS assessments



Global operational excellence with demonstrated success spanning diverse geographies and languages



Proven track record supporting top biopharmaceutical companies in challenging CNS indications



Intimate partnership working alongside sponsors, investigators, and regulators

Affiliations

Signant maintains active scientific and clinical relationships with leading neurological and psychiatric advocacy organizations. In collaboration with these groups and sponsors, our science and medicine team actively assists with training, designing eCOA for study-specific needs, and developing endpoint quality safeguards. A selection of memberships and relationships include:



WHO IS SIGNANT HEALTH?



Signant Health is the evidence generation company. We are focused on leveraging software, deep therapeutic and scientific knowledge, and operational expertise to consistently capture, aggregate, and reveal quality evidence for clinical studies across traditional, virtual, and hybrid trial models. For more than 25 years, over 600 sponsors and CROs of all sizes – including all Top 20 pharma – have trusted Signant solutions for remote and site-based eCOA, EDC, eConsent, RTSM, supply chain management, and data quality analytics. Learn more at www.signanthealth.com.