

Neurology's Disease Modifying Moment

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Neurology is moving from a history of high-risk failures to a period of unprecedented therapeutic experimentation. For decades, the complexity of the brain, limited understanding of disease biology and the formidable blood-brain barrier (BBB) made central nervous system (CNS) drug development one of pharma's toughest challenges. That equation is now beginning to shift. Advances in neurobiology, neuroimmunology, precision medicine and drug-delivery technologies are opening new routes to diseases once considered largely untreatable. Recent approvals have introduced disease-modifying and genetically targeted therapies, while the Phase III pipeline is testing approaches aimed at Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), Dravet syndrome and other neurological disorders. Behind this momentum is a deeper change: developers are moving beyond managing symptoms towards targeting the biological mechanisms that drive disease. The question now is whether this scientific momentum can finally translate into durable clinical benefit and make disease modification a repeatable reality in neurology.



Neurology, once considered the graveyard of pharma development, is entering a new era. After years of high clinical failure rates, limited treatment options and formidable barriers to drug delivery, the field is beginning to produce therapies that address disease biology rather than simply manage symptoms. Recent approvals have introduced new mechanisms, genetic medicines, muscle-directed approaches and technologies designed to improve delivery to the brain. At the same time, a growing late-stage pipeline is testing disease-modifying approaches across Alzheimer's disease, Parkinson's disease, ALS, SMA, Dravet syndrome, multiple system atrophy (MSA) and stroke.

The significance of this resurgence goes beyond the number of new medicines. Neurology is undergoing a broader shift in how diseases are understood, targeted and treated. Advances in neurobiology, neuroimmunology, genetics, biomarkers and drug-delivery technologies are opening development pathways that were difficult to pursue a decade ago.

An enormous unmet need

More than 600 neurological disorders have been identified, spanning diseases of the brain, spinal cord and peripheral nervous system. They range from common conditions such as migraine and epilepsy to neurodegenerative diseases including Alzheimer's disease and Parkinson's disease, as well as stroke, multiple sclerosis (MS), ALS and cerebral palsy.

According to the World Health Organization (WHO), 3.4 billion people experienced health loss associated with neurological conditions in 2021, representing around 42 per cent of the global population. More than 80 per cent of this health loss occurred in low- and middle-income countries, highlighting persistent gaps in diagnosis, treatment, care and rehabilitation.

The scale of the burden is creating an equally large incentive for pharmaceutical innovation. For the industry, however, the opportunity is not simply the size of the patient population. The bigger opportunity lies in developing therapies capable of delaying progression, preserving function or altering disease biology.

From symptom control to disease modification

The most important change in CNS development is the move from symptom management towards disease modification. Historically, much of neurological treatment focused on controlling symptoms through established pathways. The newer generation of programmes is increasingly attempting to intervene in the mechanisms driving disease—whether pathological protein accumulation, neuroinflammation, genetic defects, neuronal signalling or other biological processes.

“This is an extremely promising moment in the development of therapies for neurological disorders. Both new and established modalities are breaking down longstanding barriers to treat complex diseases that previously lacked early interventions and disease-modifying approaches,” said **Arun Mistry, Chief Medical Officer, Minoryx Therapeutics**.

One of the strongest examples is the growing role of neuroimmunology. Researchers are increasingly examining microglia, astrocytes, complement pathways, inflammasomes and other components of the immune system in neurological disease.

“Our understanding of neurobiology has helped the field evolve beyond symptom management, with growing recognition that chronic neuroinflammation is a key driver of progression across many neurological disorders,” said Mistry.

This is expanding the target landscape beyond traditional dopamine- and serotonin-based mechanisms and creating opportunities for therapies designed to intervene in the biological processes underlying neuronal injury and degeneration.

Big Pharma returns to CNS

The scientific resurgence is being accompanied by renewed pharmaceutical investment. Neurology M&A activity increased from 10 deals in 2024 to 14 in 2025. Across 2024 and 2025, 24 neurology M&A transactions had a combined value of \$26.9 billion, according to DealForma.

Major transactions include Bristol Myers Squibb's \$14 billion acquisition of Karuna Therapeutics, AbbVie's \$8.7 billion acquisition of Cerevel Therapeutics and Johnson & Johnson's \$14.6 billion acquisition of Intra-Cellular Therapies. AbbVie subsequently acquired Aliada Therapeutics for \$1.4 billion, adding an Alzheimer's programme and brain-delivery technology to its portfolio.

The strategic focus is also changing. Companies are increasingly seeking not just individual drugs but platforms, delivery technologies and mechanisms that can support multiple CNS programmes.

Lilly's licensing agreement with Sangamo Therapeutics for neurotropic adeno-associated virus (AAV) capsid technology illustrates this shift towards platform-based investment. Lilly also agreed to acquire AtaiBeckley in July 2026, adding rapid-acting neuroplastogen programmes to its neuroscience portfolio.

According to Beacon Intelligence, Roche has 21 CNS projects, focused particularly on neurodegeneration and rare neurological diseases, while AbbVie has 16 projects across mental health, neurodegeneration and rare neurological conditions. Biogen has 10 neurology-focused asset-indication combinations, while Lundbeck has seven assets exploring areas including neuropeptide signalling, neuronal biology, protein aggregation and neuroinflammation.

A broader clinical development landscape

The renewed interest is reflected in clinical trial activity. According to IQVIA, 605 CNS clinical trials were initiated in 2024, representing 11 per cent of total industry trial starts and placing CNS third among therapy areas, behind oncology and immunology.

Alzheimer's disease, depression and Parkinson's disease each recorded more than 200 trial starts over the five-year period to 2024. Schizophrenia, epilepsy, MS, ALS, migraine, anxiety and muscular dystrophy also accounted for significant activity.

China is becoming an increasingly important contributor. A 2026 analysis published in *Molecular Psychiatry* identified 273 neuropsychiatric drugs under development in China's innovative drug pipeline, including programmes seeking first-in-class

opportunities.

The modality mix is also changing. Small molecules remain dominant, with nearly 3,000 assets and more than 1,000 in active clinical development, according to Beacon Intelligence. Their advantages remain significant, including scalability, oral administration and, for selected molecules, the ability to penetrate the BBB.

“Novel small molecules will remain as important as advanced therapeutic modalities due to their scalability, potential for oral administration, blood-brain barrier penetration, and ability to target intracellular inflammatory and neurodegenerative pathways,” said Mistry.

However, the pipeline is becoming increasingly diversified across antisense oligonucleotides, monoclonal antibodies, gene therapies, gene editing and RNA-based medicines.

“Newer technologies like gene therapies and gene-editing technologies have the potential to provide transformative benefits in genetically defined diseases,” Mistry added. “RNA-based therapeutics and targeted biologics are increasingly capable of addressing both disease-specific mechanisms and inflammatory pathways, supporting a more comprehensive disease-modifying approach.”

The market is responding

The commercial environment is also improving. The global CNS market was projected to exceed \$80 billion in sales in 2025 for the first time since 2013, making it the fifth-fastest-growing therapy area.

The revival is being driven by more than increased demand. GlobalData has attributed the resurgence in CNS drug development to advances in neuroimmunology and neurodegeneration, as developers move beyond conventional neurotransmitter pathways.

This creates an important feedback loop for the industry. Better understanding of disease biology encourages new investment; new investment supports more sophisticated technologies and clinical programmes; and successful approvals provide greater confidence for further investment.

Landmark approvals redefine CNS treatment

Recent regulatory milestones illustrate the breadth of the transformation.

In March 2026, the US Food and Drug Administration (FDA) granted accelerated approval to Denali Therapeutics' Avlayah (tvidenofusp alfa-eknm) for neurological manifestations of Hunter syndrome in eligible paediatric patients. Designed to cross the blood-brain barrier (BBB), it became the first FDA-approved biologic specifically designed for this purpose.

Ionis Pharmaceuticals' Zanvastro, approved in September 2025, became the first treatment for Alexander disease. The antisense oligonucleotide reduces production of glial fibrillary acidic protein (GFAP), addressing a molecular driver of the disease.

Takeda's Orzeyful (oveporexton), approved in August 2026, became the first medicine designed to treat the underlying cause of narcolepsy type 1, a disorder associated with loss of orexin-producing neurons.

SMA has also seen treatment diversification. Novartis' Itvisma, approved in November 2025, expanded one-time SMN1 gene replacement therapy to eligible patients aged two years and older. Scholar Rock's Isembyld, approved in September 2026, introduced the first FDA-approved muscle-targeted therapy for SMA.

In April 2026, Axsome Therapeutics' Auvelity received an expanded indication for agitation associated with Alzheimer's disease dementia, becoming the first FDA-approved non-antipsychotic treatment for the condition.

Taken together, these approvals demonstrate that innovation is occurring across multiple levels—from genetic correction and molecular targeting to new treatment mechanisms and delivery approaches.

The Phase III test

The most consequential test now lies in the late-stage pipeline.

Ionis Pharmaceuticals and Otsuka's ulefnersen is being developed for FUS-ALS and has reported positive Phase III FUSION results, including statistically significant improvement in functional impairment and survival. Its significance lies in its attempt to

address the underlying genetic cause of FUS-ALS.

Alzheimer's disease remains a major focus. Eli Lilly's remternetug is a next-generation anti-amyloid monoclonal antibody being developed for early Alzheimer's disease. Roche's trontinemab combines amyloid targeting with its Brainshuttle technology and has progressed into Phase III following encouraging Phase II findings.

Other programmes are testing different biological hypotheses. Annovis Bio's buntanetap is designed to reduce production of APP, tau and α -synuclein, while AriBio's AR1001 is an oral, once-daily phosphodiesterase-5 (PDE-5) inhibitor being studied in early Alzheimer's disease. Its Phase III POLARIS-AD study has completed its last patient visit after enrolling more than 1,500 patients.

In Parkinson's disease, Roche and Prothena's prasinezumab is targeting aggregated α -synuclein, while Lundbeck's amlenetug is being evaluated in Phase III for MSA, which currently has no approved disease-modifying treatment.

The pipeline extends to rare neurological diseases. Stoke Therapeutics and Biogen are developing zorevunersen for Dravet syndrome, targeting the SCN1A-related mechanism. Suven Life Sciences' masupirdine is being investigated for agitation and neuropsychiatric symptoms associated with Alzheimer's dementia. In stroke, China Medical System's loberamisol is testing a multi-target approach involving PSD95-nNOS and myeloperoxidase (MPO).

The breadth of this pipeline is significant because CNS innovation is no longer dependent on a single disease hypothesis or technology. Multiple biological approaches are now being tested in parallel.

Why neurology remains difficult

The progress should not obscure the underlying risks. CNS disorders remain highly heterogeneous. Patients with the same clinical diagnosis can have different biological mechanisms, rates of progression and treatment responses. This makes target validation, patient selection and endpoint design particularly difficult.

"A central challenge is the heterogeneity of neurological disease. A promising target may be relevant only to particular cell types, patient groups or disease stages," explained **Associate Professor Zeng Li, Deputy Director, Basic Science and Translational Research, Department of Research & Innovation, National Neuroscience Institute (NNI), Singapore.**

"Successful translation therefore depends on identifying the right target, the right patient and the right time for intervention, supported by models and biomarkers that accurately reflect human disease."

The development statistics remain sobering. According to a BIO and Informa Pharma Intelligence analysis, the overall Phase I-to-likelihood-of-approval (LOA) success rate for CNS therapies is 5.9 per cent, compared with 23.9 per cent for haematology.

The challenge is therefore not simply discovering a promising molecule. Developers must demonstrate that the therapy reaches the relevant tissue, affects the intended biological pathway, produces a clinically meaningful outcome and does so in the right patient population.

The measurement challenge

One of the most important constraints on future CNS development may be the ability to measure disease progression accurately.

Neurological diseases can evolve slowly, with subtle changes in cognition, movement or function occurring over years. This makes it difficult to distinguish treatment effects from natural disease variability. "The field urgently needs validated biomarkers, patient-reported outcomes, digital endpoints, and functional measures that better reflect disease burden, progression, and real-world impact," said Mistry.

The problem is particularly acute in rare diseases, where patient populations are small and natural-history data are often limited. "Future success will depend not only on novel therapies, but on parallel investment in outcome development, natural history studies, registries, and real-world evidence generation to support regulatory, clinical, and payer decision-making," Mistry added.

From scientific promise to clinical reality

Neurology is therefore entering a new development cycle. The combination of improved disease biology, new modalities, stronger investment and advances in drug delivery has created possibilities that were difficult to imagine when CNS research

was characterised primarily by high attrition. But the current wave of innovation still has to clear several hurdles.

Phase III trials must establish durable clinical benefit. Biomarkers must become sufficiently reliable to support earlier intervention and patient selection. BBB technologies must demonstrate that they can be applied safely and consistently across different modalities. Genetic medicines will require long-term safety monitoring, while healthcare systems will need new approaches to assessing the value of potentially high-cost, highly targeted therapies.

The opportunity is consequently larger than a new generation of drugs. The industry is beginning to build an entirely new CNS development model—one that combines precision biology, advanced modalities, delivery technologies, biomarkers and real-world evidence.

The question is no longer whether neurology can produce breakthroughs. Recent approvals demonstrate that it can. The bigger question is whether the industry can convert these individual breakthroughs into a repeatable development model capable of slowing, stopping or fundamentally altering the course of neurological disease.

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