**Advancements in Neuroscience Inspire New Pharma Partnerships & Support Investment Conviction**

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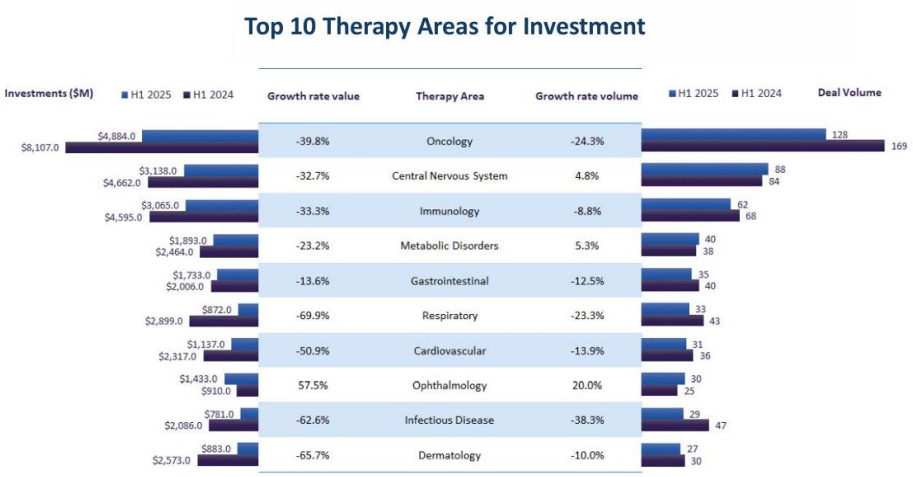
- The CNS market is projected to exceed $80B in sales in 2025, marking a substantial resumption in growth after a decade-long slump in biopharma revenue generation
- Extensive focus on neuroimmunology and neurodegeneration has reshaped the CNS pipeline industry landscape, overtaking historical dominance of dopamine and serotonin pathways in CNS drug development
- Psychiatric drug innovation has taken a leading role in the sector's commercial recovery, with renewed interest in N-methyl-D-aspartate (NMDA) receptor modulators for depression and clinical success with psychedelic regimens
- These mechanistic approaches clearly shift away from the conventional, rather exhausted serotonin and dopamine targeted approaches
- Potential breakthroughs for treatment-resistant depression and post-traumatic stress disorder appear in late-stage pipelines or have recently launched

- Robust sales of anti-CD20 mAbs for treatment of multiple sclerosis are also contributing substantially to the CNS sector's consistent commercial sales recovery

## CNS investment volume grew 4.8% in H1, 2025



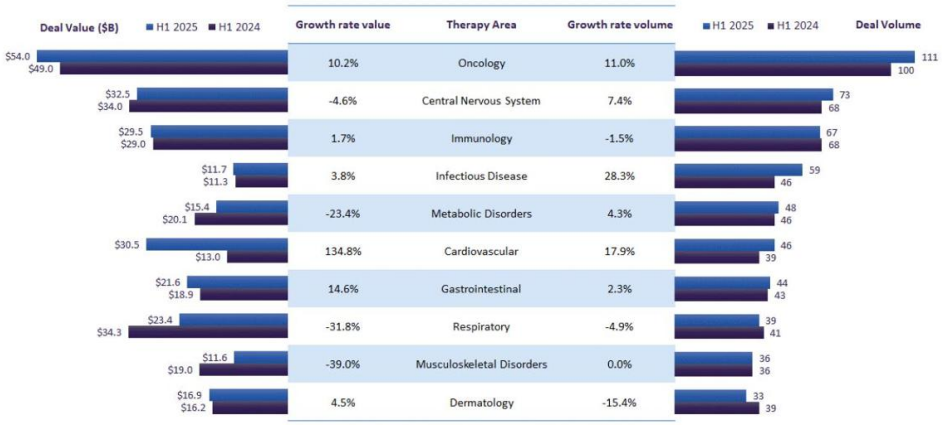

- CNS investment value declined by ~ 33% in H1, 2025 versus H1, 2024 however volume increased by ~5%
- While the drop in average investment value was more pronounced in CNS versus oncology, a similar trend was noted for both therapeutic area categories

➢ CNS: average deal value ~ -36%

➢ Oncology: average deal value ~ -20%

## CNS M&A Volume Grew ~ 7.5% in H1, 2025 vs. H1, 2024

### Top 10 Therapy Areas for Mergers & Acquisitions




▪ Cumulative M&A value for CNS-focused deals declined slightly in H1, 2025 versus H1, 2024 (- 4.6%)

▪ Neuroscience M&A edged out immunology both in overall category value as well as volume in H1, 2025

Global Data Pharma Intelligence Center, Investment Trends in Pharma Q2, 2025; Global Data M&A Trends, Q2, 2025 – July 2025

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**Influential factors catalyzing change & prompting more expansive CNS drug development**

**Key Themes in 2025:**

➢ **Greater emphasis on biology and disease pathology -**
**Less emphasis on which modality is hottest**

▪ The CNS field is evolving to a 'post-platform' era, with less competitive emphasis on which modality is best, be it gene therapy, RNA interference (RNAi), antisense oligonucleotides (ASOs), or neuroplasticity agents

▪ Emphasis has shifted to which biology is worth pursuing and how best to do it with precision and durability

▪ As examples:

o Numerous ALS programs have converged on TDP-43 and UNC13A

o An extensive number of Alzheimer's disease (AD) programs feature tau as the key target, with firms deploying the gamut of modalities including gene therapy, RNAi, antibodies and small molecules

o In Parkinson's and Schizophrenia, GBA1 and SPTLC1 targets have gained traction as next generation stratifiers

**Precision approaches are no longer just for rare CNS diseases**

▪ A shift is occurring around CNS trial design, endpoints, and patient segmentation with companies such as Alto Neurosciences, Denovo Biopharma and Switch Therapeutics exploring biomarker-driven endpoints

o EEG, genotyping, molecular biomarkers and digital behavior profiling are central to these large indication trial designs, which aim to stratify patients and improve trial outcomes

▪ These large indication trial strategies enrich for efficacy but also lay the foundation for translatability, enhanced targeted labeling and streamlined reimbursement reviews

**Delivery innovation overcomes blood-brain barrier challenges**

▪ Drug delivery to the CNS requires crossing the blood-brain barrier (BBB), a longstanding impediment for effective delivery of CNS therapeutics

▪ Development innovation features a new wave of systemically delivered, BBB-penetrant strategies designed to reach deep, disease-relevant structures in the CNS with reduced risk and greater control

▪ Notable examples include:

o Voyager Therapeutics TRACER capsids

o Sangamo Therapeutics' STACBBB capsids

o Arrowhead Pharma’s transferrin receptor shuttles

▪ From an industry-wide view, it’s increasingly clear that delivery

innovation is redefining not only translational success, but also speed to late-stage clinical development and commercialization

**Real-world factors and tools are becoming hallmarks of CNS drug development**

▪ Biomarker-driven strategies are streamlining and optimizing trial implementation, scalability and providing greater incentive for treatment adoption

▪ Tomorrow's innovative therapies that can be incorporated into standard clinical practice and align with payers' reimbursement structures will have out-sized appeal and commercial success

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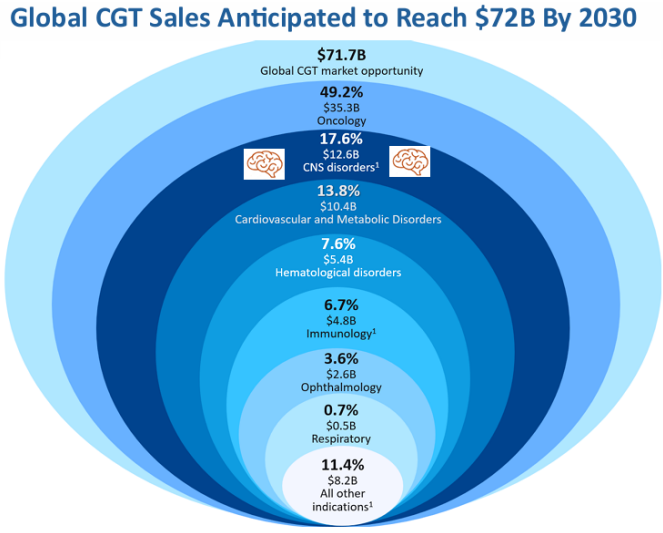
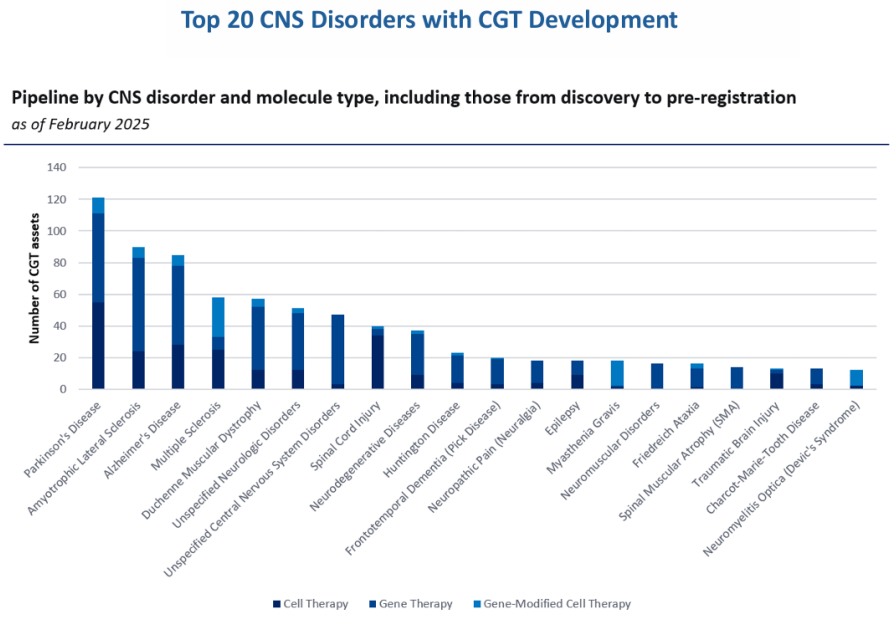
## Cell & Gene Therapy in CNS Disorders: Projected ~ 28% CAGR in commercial sales to 2030


- There are currently 9 commercialized cell and gene therapies for CNS disorders: 3 gene therapies, 3 gene-modified cell therapies & 3 conditionally approved cell therapies

- The Cell and Gene Therapy industry pipeline encompasses ~120 distinct CNS disorders, with the advancement of >800 assets from discovery through pre-registration phases

- CGT for CNS disorders will comprise 18% of commercialized CGT sales in 2030, with in vivo, targeted LNP delivery comprising a growing proportion of approved therapies




- Of the top 20 CNS disorders with the most CGT pipeline assets:

60% are gene therapies, 29% are cell therapies, and 11% are gene-modified cell therapies

▪ The top 5 CNS disorders targeted by CGT techniques are

Parkinson's, ALS, Alzheimer's, Multiple Sclerosis & DMD

▪ 18% of CGT pipeline assets are in clinical development (Phase I to pre-registration)

▪ Among the top 5 CNS disorders targeted by CGT, there are 44 products in Phase II through Pre-registration:

o 64% are cell therapies
o 27% are gene therapies
o 9% are gene-modified cell therapies

Global Data, Cell & Gene Therapies in CNS Disorders, Therapeutic Analysis Update – March 2025

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**Progress in Oligonucleotide-Based Drug Development Inspires New CNS-Focused Licensing Deals**

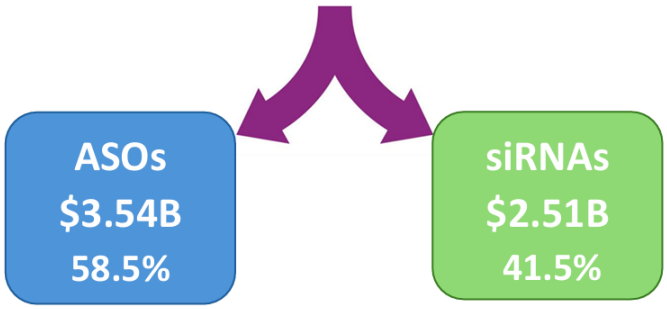
▪ Antisense oligonucleotides (ASOs) work by binding to messenger RNA (mRNA) to disrupt the production of disease-associated proteins

▪ Small interfering oligonucleotides (siRNAs) block protein production by triggering the degradation of specific mRNA molecules, effectively silencing the genes to which they correspond

▪ Recent advancements in oligonucleotide synthesis technologies, including liquid-phase and biocatalytic synthesis methods, have accelerated progress in the field by overcoming longstanding challenges, including issues with scalability, purity, and yield

▪ Development progress has paved the way for oligonucleotide therapy to serve as a cornerstone of precision medicine for complex conditions such as genetic and neurodegenerative disorders as well as cancer

▪ Licensing agreements for innovator oligonucleotides targeting CNS indications secured a cumulative total deal value of $6.05B from 2021 to 2025 YTD




**Leading Companies Developing or Partnering in Oligonucleotide Development**

Ionis is at the forefront of the growing field of oligonucleotide therapeutics, having out-licensed assets for a total of $13.4B over the past decade

▪ Ionis currently has 135 oligonucleotide-based drugs in its pipeline—32 of which target CNS disorders (~24%)

▪ Two Ionis developed therapies have reached the market: Spinraza (nusinersen) for SMA and Qalsody (tofersen sodium), co-developed and licensed by Biogen for ALS

**~ 63%**

▪ Four (4) large pharma accounted for 63% of licensing deals in the oligonucleotide space between 2021 and 2025 YTD

**Notable CNS Deals in 2025 involving ASOs, siRNAs**

▪ License and Collaboration agreement grants Sarepta rights to four clinical stage programs, three preclinical programs and up to six new targets for Arrowhead to perform discovery & preclinical work within the 5-year period

▪ Deal value exceeds $2B in biobucks, when accounting for all potential development and commercial milestones, plus tiered royalties



▪ Biogen acquired exclusive rights outside North America to develop and commercialize Zorevunersens, an RNA-based therapy targeting the SCN1A gene for Dravet syndrome

▪ Signed at Phase II, the deal includes a $165 million upfront payment and up to $385 million in development and commercial milestones. Biogen will fund 30% of global clinical development, while Stoke retains U.S., Canada, and Mexico rights and leads development

▪ Biogen also holds an option to license future SCN1A-targeting antisense therapies for markets beyond North America



▪ Sanofi partnered with Alloy to develop RNA-based therapies for CNS disorders using Alloy's AntiClastic antisense platform

▪ The discovery-stage collaboration grants Sanofi rights to advance undisclosed CNS candidates

▪ Alloy will receive up to $28 million upfront, including near-term preclinical milestones, and is eligible for over $400M in additional milestones tied to discovery, development, and commercialization progress, with tiered royalties on any approved products



▪ Eli Lilly acquired exclusive rights to develop and commercialize five antibody candidates for ALS, leveraging Alchemab's AI/MLenabled discovery platform and antibody technologies

▪ Alchemab may receive up to $415M in total payments across upfront, milestone, and commercial stages, plus royalties

▪ On May 5th, 2025, the companies nominated ATLX-1282, targeting UNC5C, as the lead candidate for development in ALS and frontotemporal dementia (FTD)

▪ Alchemab will oversee early Phase I trials, after which Lilly will lead further development and commercialization

DealForma, Neurology R&D Partnerships, M&A and Venture Funding – Q1, 2025 Review, June, 2025