Lumanity

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A New Era of Neuroscience series

# Drill Down & Catch Up: Autoimmune Neuroinflammatory Disorders

# Advances in Autoimmune Neuroinflammatory Disorders

Welcome to our third installment of our “Drill Down & Catch Up” series, part of the broader “A New Era of Neuroscience” initiative.

In our initial post, we expressed cautious optimism about transformational changes in various areas of neuroscience over the next 1-5 years. Here we continue with a deeper dive into Autoimmune Neuroinflammatory Disorders.

**Other installments in the series:**

- A New Era in Neuroscience: Untapped Potential, Unprecedented Progress in 2025 and beyond
- Bridging the Gap: Can AI Improve Patient-Clinician Connection in Psychiatry?
- Drill Down & Catch Up: The Role of Biomarkers in Neurodegenerative Disease
- Drill Down & Catch Up: Advances in Psychiatric Disorders
- 2025 Neuroscience: A Look into Key Events
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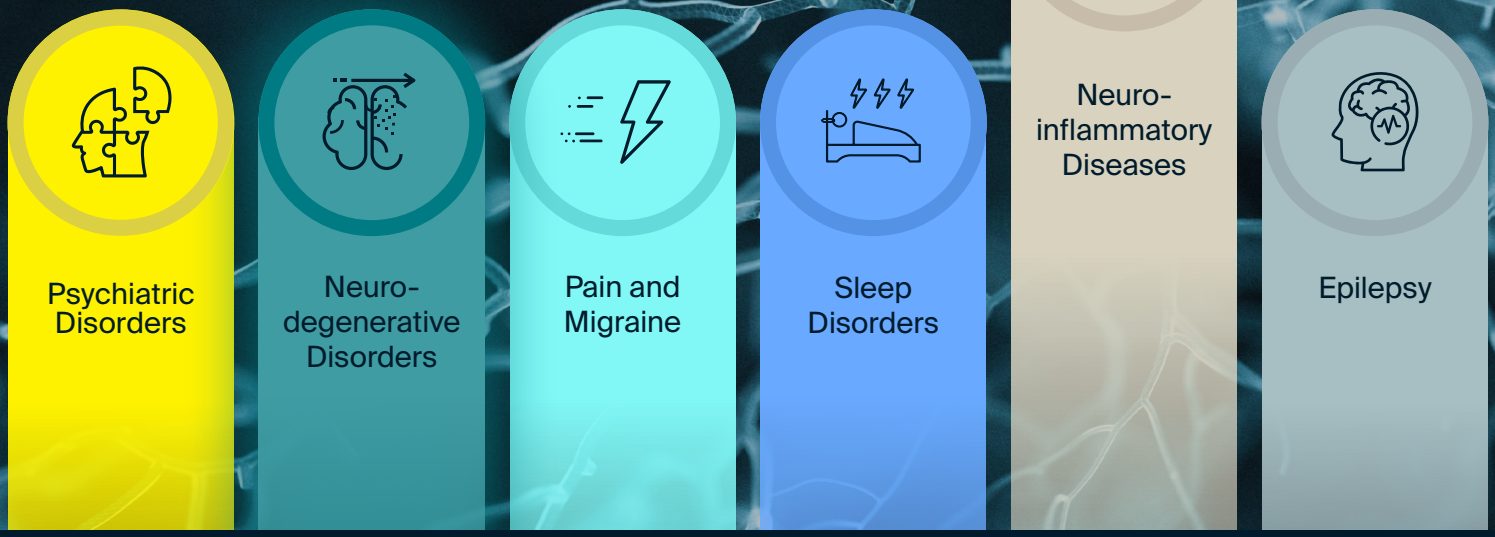


# Autoimmune Neuroinflammatory Diseases

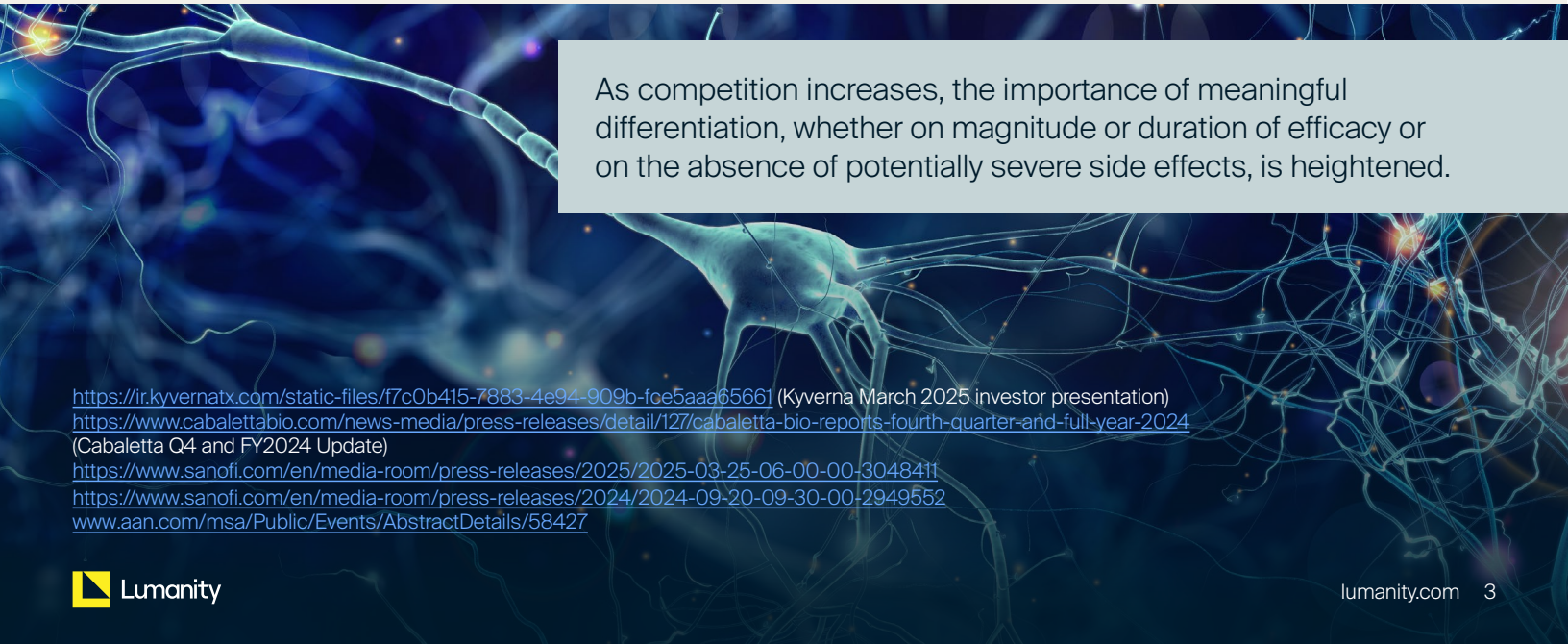
While they have received most of the attention, cell therapy's shift from oncology to autoimmune diseases has not been limited to lupus, systemic sclerosis, and inflammatory myopathies. Recently, companies have initiated proof-of-concept trials for cell therapies in B-cell driven neuroinflammatory diseases, led by **Kyverna Therapeutics, whose CD19-targeting CAR-T (KYV-101) is now in Phase II** trials for stiff person syndrome (SPS), myasthenia gravis (MG), and multiple sclerosis (MS), and **Cabaletta Bio, whose CD19-targeting CAR-T** (rese-cel) is in Phase I/II trials for antibody positive and negative MG and relapsing and progressive MS.

Depletion of disease-driving B-cells in patients with these autoimmune neuroinflammatory conditions will have the goal of achieving "immune reset," or at least durable drug free remissions. Those with severe, refractory disease who have tried multiple lines of therapy to no avail will be the first patients considered for these advanced modalities.

**Kyverna** has presented early-stage data from their trials – two patients with SPS showed a **marked reduction of autoantibody titers, improvement in mobility, and neither remains on immunosuppressive therapies**; of three patients with MG, two showed reductions in antibody titers, **all showed improvement in muscle function, and none remain on their prior immunosuppressive regimens**. The company has also recently shown that treatment was well-tolerated and led to cellular expansion in four patients with MS. In January 2025, Cabaletta announced that the first patient has been enrolled in their RESET-MG trial, and that their RESET-MS trial has been initiated and the FDA has granted them a Fast Track Designation for treatment of both relapsing and progressing MS.

Additional data from both companies is expected over the coming year, with the potential for KYV-101's topline data in 1H 2026 yielding a potential BLA filing. Other companies in the space, particularly those with off-the-shelf approaches (e.g., allogeneic CAR-T and T-cell engagers [TCEs]) are expected to develop in neuroinflammatory diseases as well, setting up a competitive environment in which companies will be looking to see who can deliver the longest drug-free remissions with the fewest side effects. These approaches have the potential to deliver truly transformative outcomes for patients who have faced such significant difficulties over many years.

Outside of the cell therapy realm, other B-cell-targeting approaches show significant promise, highlighted by **Sanofi's brain-penetrant BTK inhibitor tolebrutinib, which is currently under priority review from the FDA** for the treatment of non-relapsing secondary progressive MS (nrSPMS), with a decision expected by September 28, 2025. In its Phase 3 trials, tolebrutinib showed a 31% delay in time to onset of confirmed disability vs. placebo.



As competition increases, the importance of meaningful differentiation, whether on magnitude or duration of efficacy or on the absence of potentially severe side effects, is heightened.

https://ir.kyvernatx.com/static-files/f7c0b415-7883-4e94-909b-fce5aaa65661 (Kyverna March 2025 investor presentation)
https://www.cabalettabio.com/news-media/press-releases/detail/127/cabaletta-bio-reports-fourth-quarter-and-full-year-2024 (Cabaletta Q4 and FY2024 Update)
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