Tolebrutinib data refine the niche for BTK inhibitors in MS

Market Event Summary

Grant Nix, M.B.A. | September 2024

Tolebrutinib data refine the niche for BTK inhibitors in MS

The BTK inhibitor class may target a key mechanism of action driving the underlying progression of disability.

A breakthrough from the HERCULES trial…

- Sanofi's tolebrutinib is now poised to become the first therapy approved for nonrelapsing SP-MS (nrSPMS)—a landmark achievement. Data from HERCULES support the contention that BTK inhibitors can penetrate the blood-brain barrier and, through microglia, may counteract the local CNS inflammation that contributes to disability progression, known as "smoldering MS." Detailed data from ECTRIMS will clarify the magnitude of tolebrutinib's benefit in nrSPMS, but the topline results bode well for Sanofi's ongoing PERSEUS trial in PP-MS, as well as Roche's trial of rival BTK inhibitor fenebrutinib, FENtrepid, in PP-MS. The trials will read out in 2025 and 2026, respectively.

…is offset by failure on ARR in the GEMINI program.

- In GEMINI 1 and 2, tolebrutinib failed to separate from the active comparator teriflunomide on the primary annualized relapse rate (ARR) endpoint. Detailed data are pending but, as observed with Merck KGaA's evobrutinib, teriflunomide likely emerged again as a stronger comparator than expected. These results signal trouble for Novartis's and Roche's BTK inhibitors in their respective teriflunomide-controlled relapsing MS trials. Failure to attain a label for the large relapsing MS segment, which comprises more than two-thirds of MS patients, will significantly limit BTK inhibitors' commercial opportunity. Novartis is not currently testing remibrutinib in progressive MS.

Clarivate™

Clarivate's takeaways

The GEMINI outcome is disappointing but not surprising; the HERCULES data portend fulfillment of an unmet need.

Current therapies (e.g., anti-CD20 MAbs) control relapses and focal inflammation well, but relapsing MS patients still accumulate disability over time, a process that is often not temporally linked to relapses (i.e., progression independent of relapse activity [PIRA]). The HERCULES outcome and tolebrutinib's outperformance of teriflunomide on disability outcomes in GEMINI suggest it has the potential to deliver on this key clinical unmet need.

A relapsing MS label for tolebrutinib is unlikely, but physicians may want to prescribe it from the outset.

Given that PIRA is detectable from the earliest stages of MS, clinicians would likely want access to the drug early in the disease, if it is safe. However, the GEMINI data will not likely support a relapsing MS label for tolebrutinib. A label for PIRA could expand access to it, but this step would entail blazing a new regulatory pathway in MS.

The bar for entry into the MS market is high.

Given that tolebrutinib will likely vie within class with at least Roche's fenebrutinib in nonrelapsing MS and in view of the development risks / challenges of proving a differentiated impact on focal inflammation in relapsing patients, entry into the MS market is challenging. Neuroprotective or restorative treatments, or those that preclude or reduce chronic therapy—such as CAR T-cell therapies—are emerging as key foci of interest in the pipeline.

About the author

Grant Nix, M.B.A.

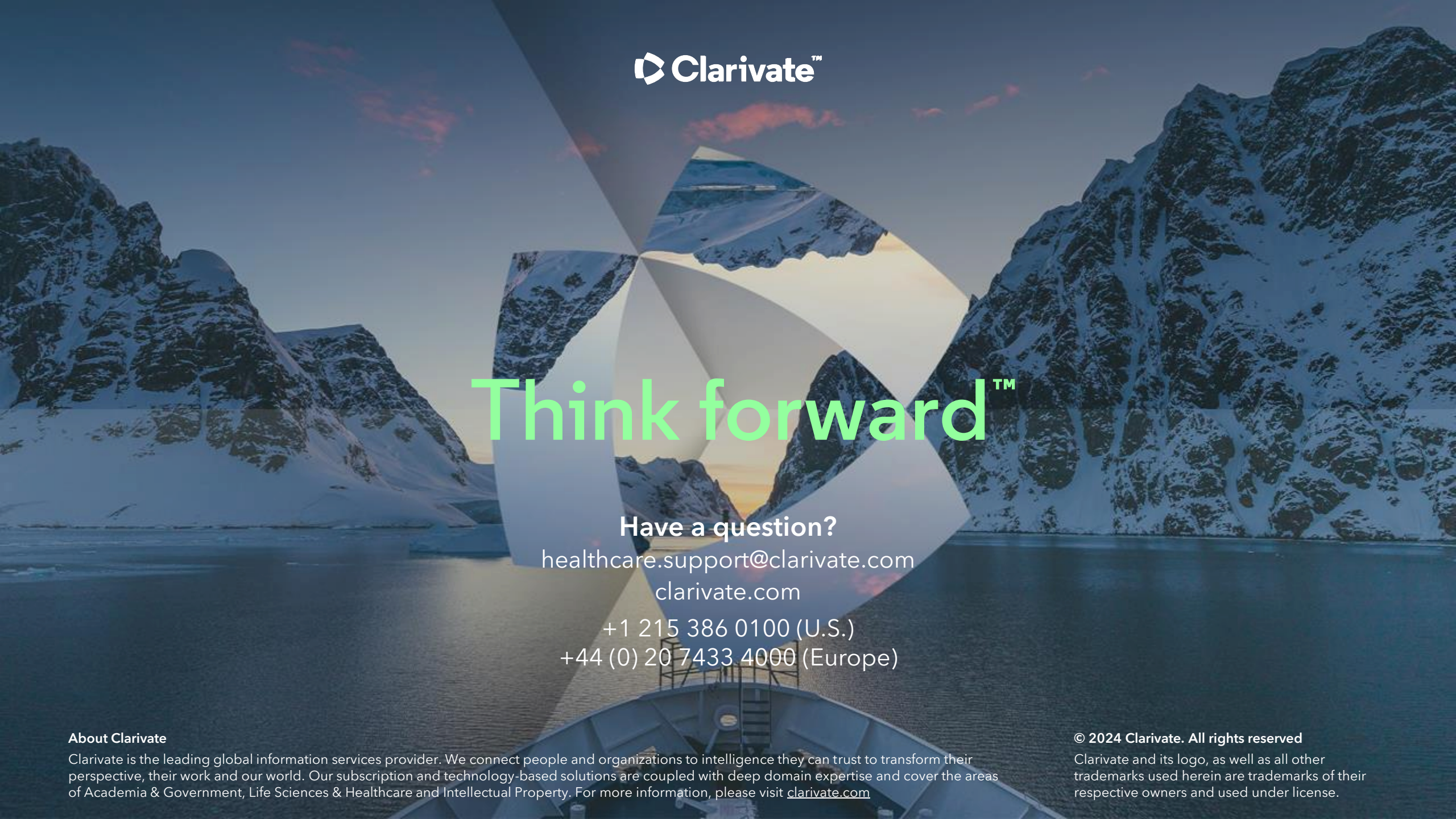
Healthcare Research & Data Analyst

Grant Nix focuses on the neurology market, particularly the treatment of multiple sclerosis. In this role, he conducts primary and secondary research. Prior to joining Clarivate, he was an operations analyst at UNC Health in the behavioral health unit. He earned his M.B.A. at North Carolina Central University, where he specialized in finance. He also holds a B.S. in chemistry from Campbell University.

grant.nix@clarivate.com

Clarivate coverage of multiple sclerosis

- Access & Reimbursement | Multiple Sclerosis (US), providing insights on the impact of payer policy on prescribing behavior in MS.
- Current Treatment: Physician Insights | Multiple Sclerosis (US), exploring the prescribing trends of ophthalmologists and retinal specialists.
- Disease Landscape & Forecast | Multiple Sclerosis (G7), providing comprehensive market intelligence insights and a patient- based forecast segmented by clinical subtype.
- Epidemiology (G7), diagnosed incidence and prevalence data for all subtypes of MS.
- Treatment Algorithms: Claims Data Analysis | Multiple Sclerosis (US), with details on the treatment journey and brand usage practices based on patient-level claims data.
- Unmet Need | Progression Independent of Relapse Activity (US & EU), which includes an Excel-based Target Product Profile Simulator.



Have a question?

healthcare.support@clarivate.com
clarivate.com
+1 215 386 0100 (U.S.)
+44 (0) 20 7433 4000 (Europe)

About Clarivate

Clarivate is the leading global information services provider. We connect people and organizations to intelligence they can trust to transform their perspective, their work and our world. Our subscription and technology-based solutions are coupled with deep domain expertise and cover the areas of Academia & Government, Life Sciences & Healthcare and Intellectual Property. For more information, please visit clarivate.com