

Tolebrutinib

The anatomy of a Drug to Watch

Key evaluation criteria in neurodegenerative diseases and how tolebrutinib was selected as a Drug to Watch 2026

Clarivate analysts rely on actionable data and market intelligence from our suite of products to identify each year's Drugs to Watch — the blockbusters and treatment paradigm-shifters.

Identifying the next breakthroughs for neurodegenerative diseases

The multi-faceted landscape of neurodegenerative diseases encompasses heterogeneous patient populations, intersecting therapeutic classes and complexities related to treatment adherence and accessibility, presenting challenges for forecasting which interventions will effectively transform standard treatment. The first step is translating the evidence base into a clear view of which drugs are

likely to launch and succeed within the Drugs to Watch target timeframe.

Mapping the therapeutic landscape: Cortellis Competitive Intelligence

Our analysts gain a broad view of the status and potential success of drugs for neurodegenerative diseases using Cortellis Competitive Intelligence, which:

- Covers the entire development lifecycle
- Provides clinical, deals, regulatory and patent intelligence for each drug and company
- Predicts the likelihood and timing of drug launches with the Drug Timeline & Success Rates statistical modeling methodology and ML-based predictive analytics

By reviewing the therapeutic landscape, Clarivate analysts narrow the field to a short list of assets, including tolebrutinib (Sanofi) for multiple sclerosis (MS), that warrant deeper investigation as Drugs to Watch.

Figure 1: Assets in development for neurodegenerative diseases in Cortellis Competitive Intelligence

Drug name	Highest status	Other drug name	Active indication	Target-based action	Technology	Regulatory designation
elcubragistat	Phase 2 Clinical	ABX-1431 ABX-1431.HCl more	Epilepsy Fibromyalgia more	Monoglyceride lipase inhibitor	Capsule formulation Once daily formulation more	N/A
valdemstat	Phase 2 Clinical	LSD-1 inhibitor (Alzheimer's d... LSD1/MAOI8 (Alzheimer's disea... more	Acute respiratory distress syn... Aggression more	Lysine specific histone demethylase 1... MAO B inhibitor	Capsule formulation Oral formulation Small molecule	N/A
zirconium #9 crelmirumab berdoxam	Phase 2 Clinical	89Zr-Df-IAB 22M2C 89Zr-Df-crelmirumab more	Advanced solid tumor Cancer more	T-cell surface glycoprotein CD8 inhibitor	Antibody Antibody fragment more	N/A
BAV-85-8102	Phase 2 Clinical	18F-DPA-714 BAV-85-8102 more	Carotid stenosis Chronic fatigue syndrome more	Benzodiazepine receptor agonist Translocator protein modulator	Injection Intravenous formulation more	N/A
mastinib	Pre-registration	AB-1210 Abilek more	Alzheimer disease Amyotrophic lateral sclerosis more	CSF-1 antagonist FGF3 receptor antagonist more	Film coating Oral formulation more	Orphan Drug
debamastrocel	Phase 3 Clinical	GDNF/BDNF-producing glial a... MSC-NTF more	Acute respiratory distress syn... Alzheimer disease more	Brain derived neurotrophic factor ligand Glial cell neurotrophic factor ligand	Autologous stem cell therapy Biological more	Fast Track Orphan Drug
ibudilast (oral, neurodegenerative disease/substance dependence/COVID-19), Medicinova	Phase 3 Clinical	AV-411 Ketas more	Acute respiratory distress syn... Alcoholism more	Interleukin-1 beta ligand inhibitor Macrophage migration inhibitory fact... more	Capsule formulation Essences more	Fast Track Orphan Drug Rare Pediatric Disease
EQ-8	Discovery	EQ-8	Multiple sclerosis Neurodegenerative disease Parkinsons disease	N/A	Oral formulation Small molecule	N/A

Tolebrutinib

Next-generation BTK inhibitor for underserved progressive MS

Cortellis Competitive Intelligence

Tracks three pivotal phase 3 programs.

- HERCULES (1,131 non-relapsing secondary progressive MS [nrSP-MS] patients): 31% reduction in 6-month confirmed disability progression (CDP) vs placebo; 10% confirmed disability improvement vs 5% placebo; liver enzyme elevations an issue (4.1% vs placebo) but overall tolerability acceptable
- GEMINI 1 and 2 (1,873 relapsing MS): annualized relapse rate (ARR; 0.12 vs 0.12) similar to AUBAGIO® (teriflunomide; Sanofi) but 29% reduction in 6-month CDP vs AUBAGIO and balanced safety profile, supporting use for disability progression despite neutral relapse effect
- PERSEUS (primary progressive MS [PP-MS]): failure to significantly reduce 6-month composite CDP vs placebo, leading Sanofi to halt PP-MS registration plans and narrow focus to nrSP-MS

Disease Landscape & Forecast

Shows how tolebrutinib could provide therapeutic value in a high-growth progressive MS market with unmet needs and substantial commercial upside.

- ~229,000 diagnosed prevalent SP-MS cases in the G7 markets in 2025, with a substantial subset classified as nrSP-MS, which is underserved compared with other MS populations
- MS therapy market expected to see rising treatment rates in progressive disease driven by BTK inhibitors (tolebrutinib, fenebrutinib, orelabrutinib) and novel antibodies like frexalimab
- BTK inhibitor class forecast to reach multi-billion-dollar sales in the G7 markets by 2034, with a sizable footprint in progressive MS segments

Epidemiology Intelligence

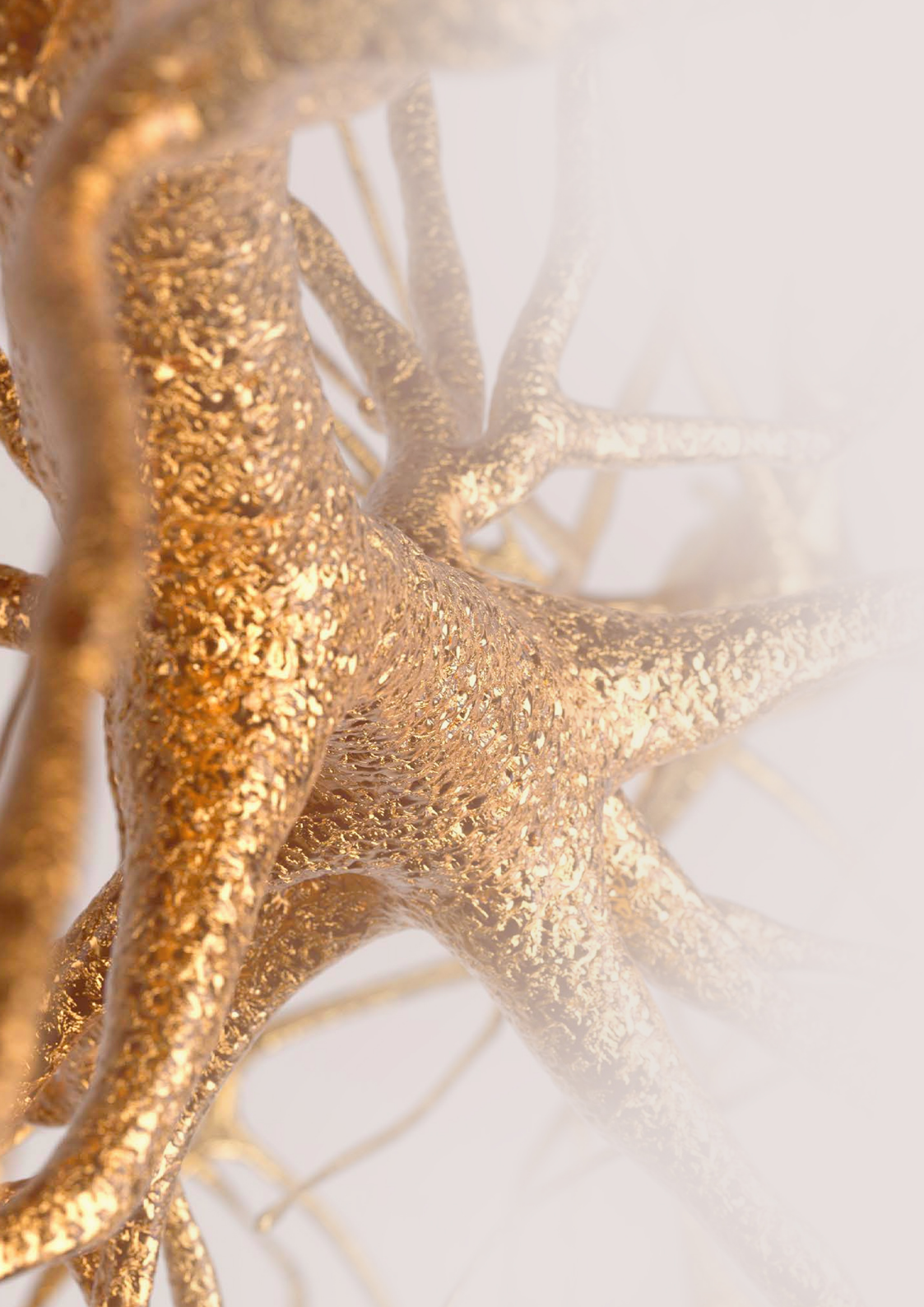
Identifies how BTK inhibitors could address a critical unmet need in progressive MS and provide a differentiated maintenance option where current therapies fall short.

- NrSP-MS representing high burden subset where disability accumulates despite absence of relapses, manifesting as fatigue, cognitive decline, gait/balance issues and sphincter dysfunction
- Existing therapies primarily targeting peripheral B and T cells, leaving smoldering CNS microglial inflammation unaddressed, a key driver of progression independent of relapse activity
- KOLs highlighting BTK inhibitors as attractive maintenance options post-OCREVUS® (ocrelizumab; Genentech) or when patients on OCREVUS progress without relapses, creating a clear clinical niche for BTK inhibitors

Cortellis Deals Intelligence

Highlights tolebrutinib's position as a strategic neurology priority within a validated and competitive BTK inhibitor landscape, supporting lifecycle growth.

- Sanofi internal development of tolebrutinib as a cornerstone asset in its neurology portfolio, positioning it alongside frexalimab in the company's MS strategy
- Competitive BTK programs (fenebrutinib, remibrutinib, orelabrutinib) from Roche, Novartis and Zenas/InnoCare, respectively, highlighting intense interest in CNS-penetrant BTK inhibition and validating the mechanism



Summary of impact

Tolebrutinib

Tolebrutinib demonstrates how CNS penetration and microglial targeting could redefine progressive MS treatment standards, transforming a high-burden, underserved segment into a defensible commercial niche. It also highlights the delicate balance between efficacy and safety needed for regulatory approval, as evidenced by the US FDA Complete Response Letters issued in late 2025.

Ready to see if your drug is one to watch?

Contact us to learn how integrating intelligence from multiple Clarivate products, powered by AI, drives confident predictions of the potential competitive impact of your drug on the market and patients' lives.

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