Multiple Sclerosis: Large market with unmet need

BTKi as an emerging potential threat to the leading market of Ocrevus

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Multiple Sclerosis Overview

MS affects 2.8M people worldwide and around 1M in the US

MS is the leading cause of non-traumatic neurological disability in young adults

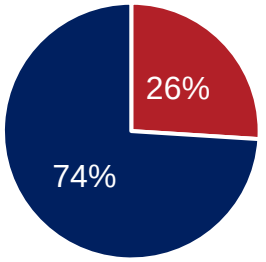
Worldwide

2.8 Million
People WW lives with MS

1 in 3,000
People WW are affected by MS

United States

~1 Million
People in the US are impacted by MS



3 in 4 MS patients
in the US are female. Hormones may play a role in MS susceptibility

There are 4 types of disease courses in MS; RRMS is the most frequent form of MS

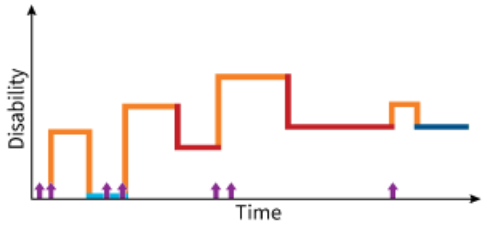
Clinically Isolated Syndrome

First episode of symptoms caused by inflammation and myelin loss

~63%
People experiencing a CIS episode would receive MS diagnosis

Relapsing-remitting MS

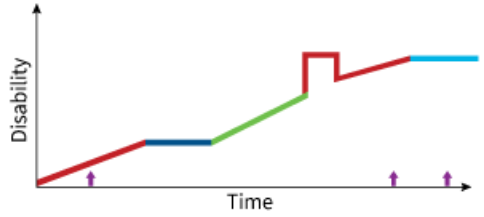
Relapses of symptoms followed by periods of symptom relief



~85%
People with MS are diagnosed with RRMS

Primary progressive MS

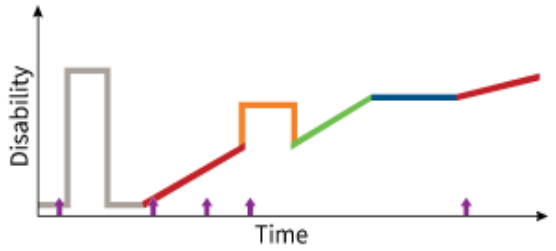
Symptom progression starts from disease onset with no relapses



~15%
People with MS are diagnosed with PPMS

Secondary progressive MS

~50%
People diagnosed with RRMS would transition to SPMS within 10 years



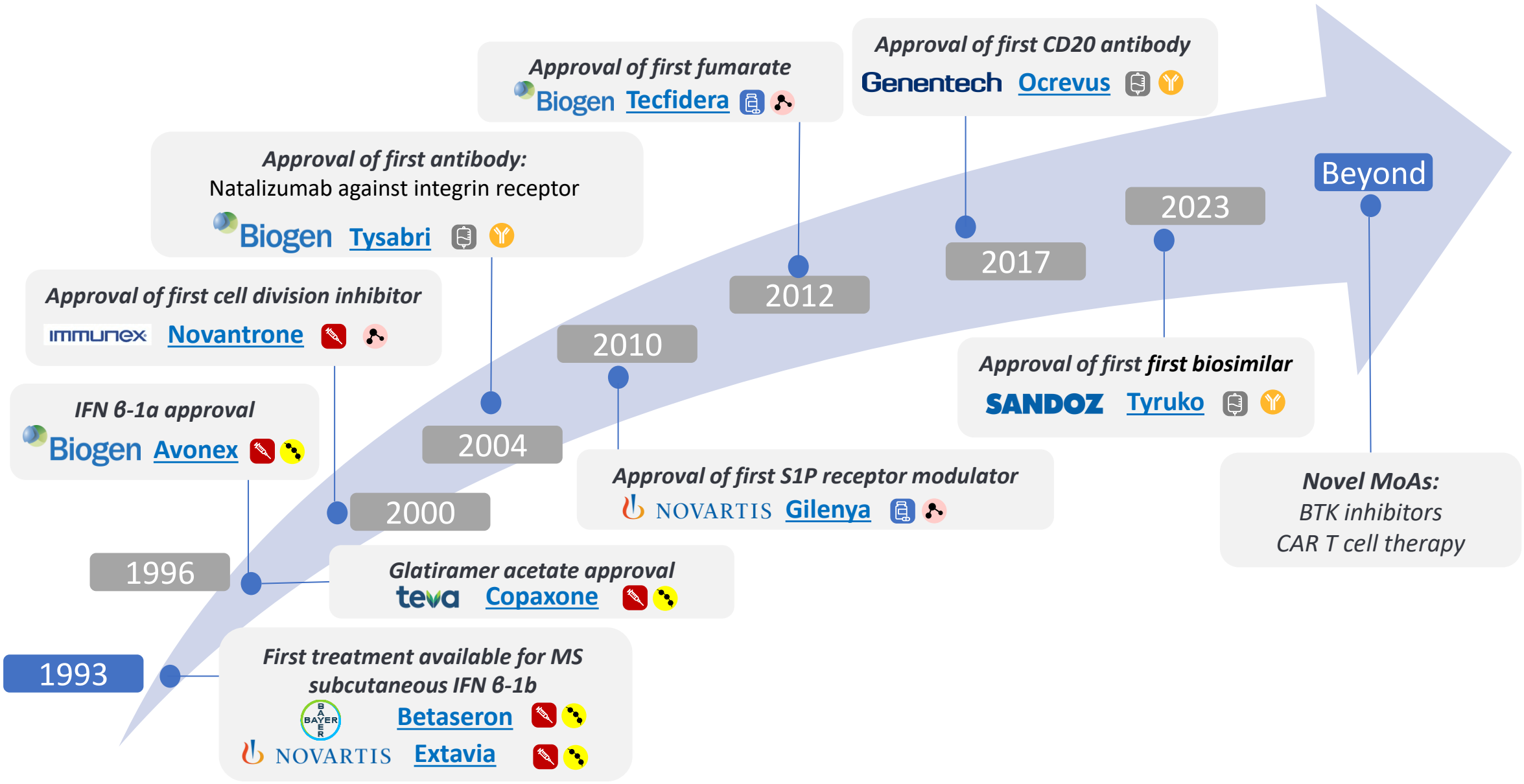
Developed from RRMS to progressive course where symptoms worsen

Sources: 1. Atlas of MS 3rd Edition; 2. National MS Society; 3. Lublin et al., (2014)

CIS: Clinically Isolated Syndrome; ***PPMS***: Primary progressive MS; ***RRMS***: Relapsing remitting MS; ***SPMS***: Secondary Progressive MS

Evolution of DMTs for MS treatment

The MS treatment landscape has expanded over the years, with an increase in high-efficacy therapies



Ocrevus is the only approved treatment for PPMS

Highlighting a major unmet need for therapies to address the disability progression in MS; Novel MoAs such as BTKIs has potential to treat PPMS

Roche to maintain market leadership

- Ocrevus is the top selling MS treatment and the only one approved for PPMS
- Roche expects to broaden Ocrevus's target market by developing SC formulation, with expected approval by 2H24; pediatric RRMS and high-dose formulation are also part of the LCM strategy for Ocrevus

Unmet needs

- Lack of treatment options for progressive forms of MS (Ocrevus only approved therapy for PPMS)
- Novel treatments with superior risk/benefit are needed as currently available DMTs are associated with AEs such as PML (Tysabri/Ocrevus), liver injury (Aubagio/Tecfidera), herpes infection (Kesimpta/Mavenclad), etc.

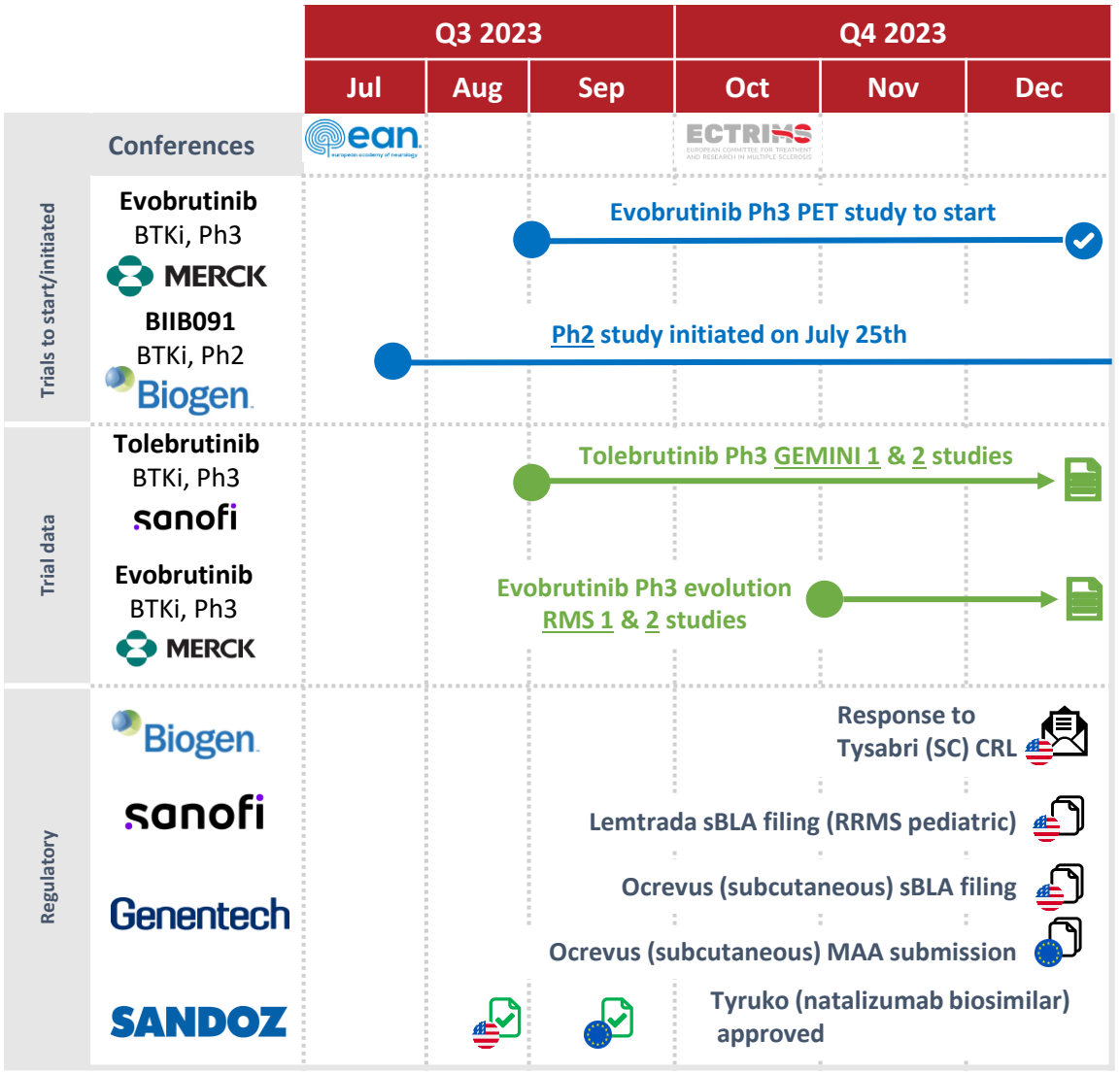
Novel MoAs in MS landscape

- Several BTKi assets under development for MS has potential to address unmet needs
- Preclinical studies have shown BTKi suppress key pathological features of MS: B cell activation, CNS lymphocyte infiltration, leptomeningeal inflammation, pro-inflammatory microglial activation, and demyelination
- BTKi under development such as Roche's **fenebrutinib** and Sanofi's **tolebrutinib** in Ph3 has the potential to treat all forms of MS competing with Ocrevus for PPMS

PPMS: Primary progressive MS; ***RRMS***: Relapsing remitting MS; ***SPMS***: Secondary Progressive MS; ***PML***: Progressive multifocal leukoencephalopathy; ***AEs***: Adverse events

Key Highlights for MS therapies in 2023

No new molecules entering MS space in 2023; Merck and Sanofi's late-stage BTKi data readout in near term



New assets targeting Burton's tyrosine kinase under development

- Initiation of Ph3 PET study for **Evobrutinib** in relapsing forms of MS
- Ph2 initiated for **BIIB091** in relapsing forms of MS

Upcoming topline results for 2 BTK inhibitors for relapsing forms of MS treatment

- Topline results for Ph3 GEMINI 1 and GEMINI 2 studies for **Tolebrutinib** (SAR442168) in relapsing forms of MS
- Topline results for Ph3 evolution RMS1 and RMS2 studies of **Evobrutinib** in relapsing forms of MS

Biogen and Genentech are evaluating new ROAs (SC vs. IV) for Tysabri and Ocrevus to grow share, while Sanofi is pursuing pediatric label expansion to broaden its target patient pool

- CRL response for a new subcutaneous form of **Tysabri** to treat RMS by Oct'23
- sBLA and MAA submission for SC **Ocrevus** for the treatment of RMS and PPMS.

Sandoz obtained the first and only biosimilar approval for MS

- European approval follows FDA approval for CIS, RRMS, and SPMS

Sources: 1. Biomedtracker

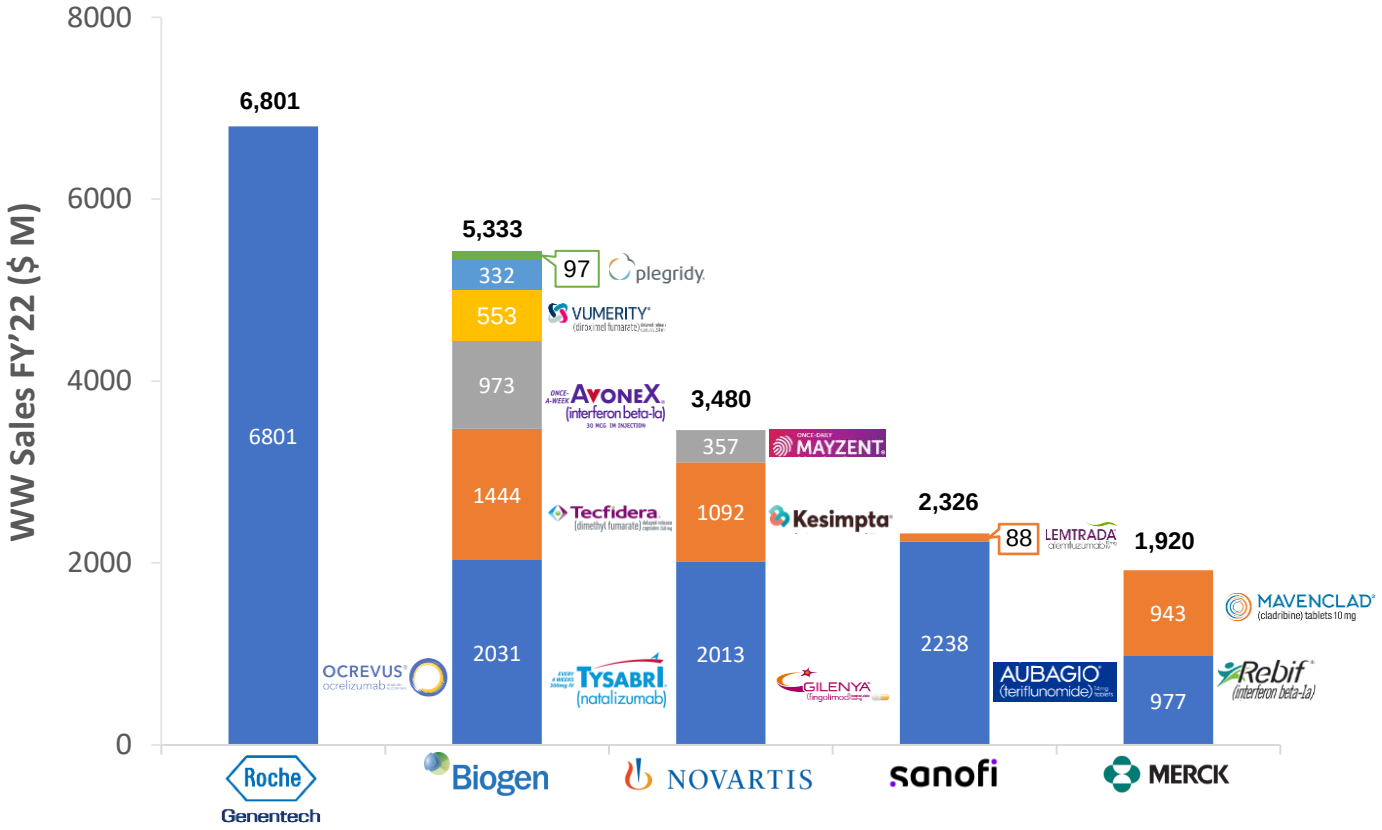
Filing | Approval | Expected Trial to start | Top-line results

BTKi: Bruton's tyrosine kinase inhibitor : ***PET***: positron emission tomography

MS market continue to be dominated by a few large players in 2024

Roche/Genentech accounts for over 28% of MS global sales

Today: Ocrevus MS dominance can be attributed to its broad label with strong efficacy and a strong long-term safety profile
2024+: A subcutaneous ROA approval for Ocrevus in 2024 could further advance its market penetration



Notes: Novartis did not disclose Extavia FY'22 sale revenues

Key Takeaways

- **Roche/Genentech** is the clear market leader, with Ocrevus as the sole approved drug for CIS, RRMS, PPMS, and SPMS
  - **Ocrevus SC** anticipated 2024 launch may boost sales and compete with **Kesimpta** in the self-injected formulation market
- **Biogen** has the broadest MS franchise with 5 approved drugs; Tysabri is the highest MS revenue generator, accounting for 37% of net product sales revenue
- **Sandoz's** Tyruko, is expected to launch as the first Tysabri biosimilar in the US – it is unlikely to significantly affect Biogen's MS franchise share in the near term

Sources: 1.Citeline; 2. Novartis 2022 annual report; 3. Biogen 2022 annual report; 4. Sanofi 2022 annual report; 5. Merck 2022 annual report; 6. Roche 2022 annual report; 7. FDA report; Note: Biogen gets royalty-based revenues on Ocrevus sales

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