About the Phase III PARADIGMS study
Media Fact Sheet

Background

- Approximately 2.3 million people worldwide are affected by multiple sclerosis (MS), of which **3-5% are estimated to be children** (pediatric MS).[1,2]
- Pediatric MS is the appearance of MS symptoms in young people **aged up to 18 years old**.[3]
- Pediatric MS is associated with **more frequent relapses than adults with MS**[4], resulting in **physical and cognitive (e.g. memory) disabilities** which severely limit patients' ability to go about daily activities, like going to school.[5]

In May 2018 the US Food and Drug Administration (FDA) approved Gilenya® (fingolimod) for the treatment of children and adolescents, ages 10 to less than 18, with relapsing forms of MS (RMS).[6] This approval makes Gilenya the first disease-modifying therapy (DMT) indicated for these patients in the US. Gilenya is has been approved for the treatment of adults in the US since 2010, with the new approval expanding the indication to include patients from ages 10 to less than 18.[6]

The approval was based on data from the Phase III PARADIGMS study of **Gilenya in children and adolescents with MS**. PARADIGMS was the **first ever controlled, randomized trial specifically designed for pediatric MS**.[7]

PARADIGMS study design

- Initiated in 2013, PARADIGMS (**NCT01892722**) was conducted in **87 sites over 26 countries**.[8]
- PARADIGMS was designed in partnership with the **FDA**, **European Medicines Agency** and the **International Pediatric Multiple Sclerosis Study Group**.

PARADIGMS study design: key information[8]

Aim:	Evaluate the safety and efficacy of daily oral Gilenya versus weekly interferon beta-1a intramuscular injections in children and adolescents with MS
Design:	Flexible duration (up to two years), double-blind, randomized, multi-center study, followed by a five-year open label extension phase
Enrollment:	Two hundred and fifteen children and adolescents with MS, ages 10 to less than 18. Patients had an Expanded Disability Status Scale (EDSS) score between 0 and 5.5
Randomization:	Oral Gilenya once daily (0.5 mg or 0.25 mg, dependent on body weight) versus intramuscular interferon beta-1a, once weekly
Primary endpoint:	Frequency of relapses (annualized relapse rate) over the course of up to two years
Secondary endpoints:	• Number of new or newly enlarged T2 lesions and Gd-enhancing T1 lesions in the brain, per year (annualized rate) • Safety • Pharmacokinetic properties of Gilenya

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PARADIGMS results

- Full results from the Phase III PARADIGMS study **showed the study met its primary and secondary endpoints**, showing that Gilenya treatment resulted in:
    - **An 82% reduction in the rate of relapses** (annualized relapse rate) over a period of up to two years versus interferon beta-1a ($p<0.001$).[7]
    - A **significant reduction in the number of new / newly enlarging T2 and Gd-enhancing T1 lesions in the brain**, as measured by magnetic resonance imaging (MRI). The number and volume of lesions are associated with increased relapses and disability progression.[7]
    - Individuals treated with Gilenya had **significantly less brain shrinkage** (measured by MRI as brain volume loss), compared to those treated with interferon beta-1a.[7] Brain shrinkage in adults is associated with the loss of physical and cognitive function.[9]
    - The **safety profile** of Gilenya was overall **consistent with that seen in previous clinical trials, with more adverse events reported in the interferon group**.[7]
    - In an additional analysis, Gilenya **significantly delayed disability progression**, defined as Confirmed Disability Progression (CDP), compared to interferon beta-1a.[7]
- Full positive results from the Phase III PARADIGMS study were presented at the 7th Joint European and Americas Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS-ACTRIMS) meeting in Paris, France, in October 2017.

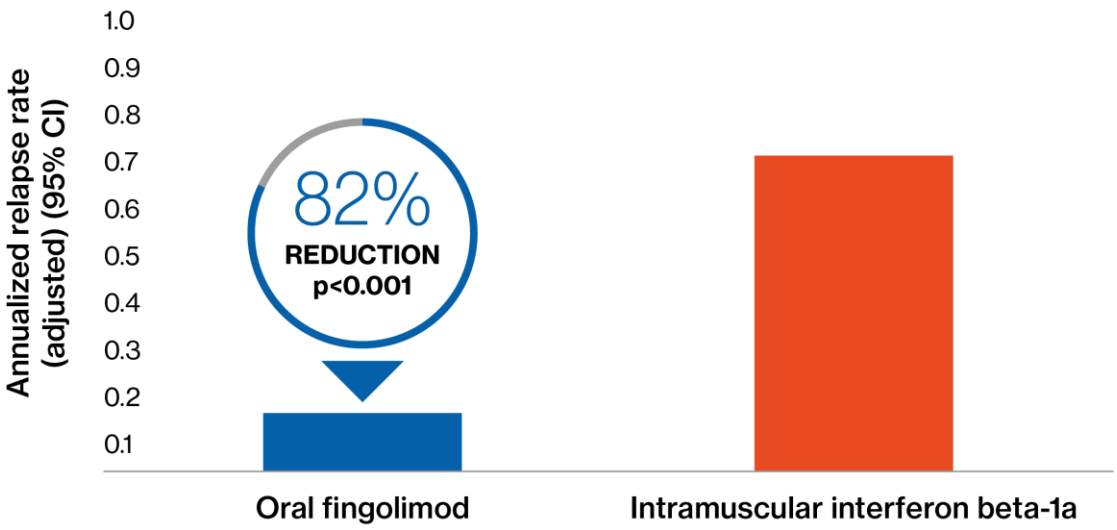

Figure 1: PARADIGMS study results (primary endpoint data)

About Gilenya® (fingolimod)

- Gilenya is approved in the US and Switzerland for the first-line treatment of relapsing forms of MS in adults and in the EU for adult patients with highly-active relapsing-remitting MS (RRMS) defined as either high disease activity despite treatment with at least one DMT, or rapidly-evolving severe RRMS.[10,11]
- In the US, Gilenya is now also approved for the treatment of children and adolescents, ages 10 to less than 18, with RMS.[6]

References

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