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.\(^5\)
  - An earlier accumulation of physical disability, compared to those diagnosed as adults.\(^1\,^6\)
- Progression to secondary progressive MS (SPMS), a highly disabling form of MS, occurs on average 10 years earlier in pediatric MS patients than in those diagnosed as adults.\(^4\)
- There is currently no treatment indicated for children and adolescents living with MS, based on randomized, controlled, clinical study data; there is a significant unmet need for new, safe and effective treatments for these patients.
- Sponsored by Novartis, the Phase III PARADIGMS study was initiated to investigate whether Gilenya® (fingolimod) is a safe and effective treatment option for children and adolescents with MS.

PARADIGMS study design
- PARADIGMS (NCT01892722) is the first ever controlled, randomized trial specifically designed for pediatric MS.
- Initiated in 2013, PARADIGMS was conducted in 87 sites over 25 countries.
- PARADIGMS was designed in partnership with the US Food and Drug Administration, European Medicines Agency and the International Pediatric Multiple Sclerosis Study Group.

PARADIGMS study design: key information\(^7\)

| Aim: | Evaluate the safety and efficacy of daily oral fingolimod 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, aged between 10 and 17 years. Patients had an Expanded Disability Status Scale (EDSS) score between 0 and 5.5 |
| Randomization: | Oral fingolimod 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 fingolimod

PARADIGMS results
- In October 2017, Novartis announced positive full results from the Phase III PARADIGMS study, also presented at the 7th Joint European and Americas Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS-ACTRIMS) meeting in Paris, France.
- 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).  
  - 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.
  - Individuals treated with fingolimod had significantly less brain shrinkage (measured by MRI as brain volume loss), compared to those treated with interferon beta-1a. Brain shrinkage in adults is associated with the loss of physical and cognitive function.
  - The safety profile of Gilenya was overall consistent with that seen in previous clinical trials, with more adverse events reported in the interferon group.
  - In an additional analysis, Gilenya significantly delayed disability progression, defined as Confirmed Disability Progression (CDP), compared to interferon beta-1a.

Figure 1: PARADIGMS study results (primary endpoint data)
Next steps
Based on these data, Novartis is working with health authorities to discuss regulatory submissions for fingolimod in pediatric patients.

About Gilenya® (fingolimod)
- Gilenya is not currently approved for the treatment of pediatric MS.
- 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

References