10-year observational study shows benefit of fingolimod (Gilenya®) on patient disability progression

- ACROSS study shows that patients with relapsing remitting multiple sclerosis (RRMS) continuously treated with fingolimod (Gilenya®) had significantly lower disability progression compared to those whose treatment was interrupted

- Almost 60% of patients enrolled in ACROSS remained on fingolimod at 10 years, demonstrating long-term persistence¹

- Fewer patients who stayed on fingolimod for eight to 10 years had developed secondary progressive MS compared to those who discontinued it

Frimley, UK, September 16, 2016 – Novartis today announced new data from the ACROSS study, which assessed 10-year disability outcomes in people with relapsing remitting multiple sclerosis (RRMS) treated with fingolimod (Gilenya®). These results provide supportive evidence of the long-term effectiveness of continuous fingolimod treatment on controlling disability progression. Full results were presented at 32nd Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), in London, UK.

According to the MS Trust and the MS Society: 107,000 people in the UK have MS. MS is a chronic neurological disease, associated with worsening physical and cognitive (e.g. memory) disability over time that limits sufferers’ abilities to go about everyday tasks.² Limiting disability progression as early on in the disease process as possible is an important treatment goal in MS and can help improve the long-term outcomes of people with the condition, as well as delaying progression to secondary progressive MS.³,⁴

ACROSS is a single visit observational study of 175 individuals previously enrolled in the Phase II study of fingolimod in RRMS.¹ The study met its primary endpoint of a significantly lower change from baseline at 10 years in patients’ Expanded Disability Status Scale (EDSS) score with continuous versus non-continuous fingolimod treatment (0.55 versus 1.21, respectively; p=0.0155).¹ Analyses of key secondary endpoints showed that after 10 years, the risk of progression to secondary progressive MS (SPMS) was reduced by 66.2% in patients who remained on fingolimod for at least eight years, compared to those who did not.¹ There was also a significant four-fold delay in the time to use of a wheelchair.¹ Almost 60% (59.4%) of patients in ACROSS stayed on fingolimod at 10 years, demonstrating persistence of treatment over the long term.¹

“Multiple sclerosis is a debilitating, life-long disease, and greatly impacts how individuals are able to go about their daily lives,” said Vasant Narasimhan, Global Head of Drug Development and Chief Medical Officer for Novartis. “The ACROSS data add to our understanding of the long-term use of fingolimod as a highly-effective treatment option for people with relapsing remitting MS.”

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See www.mhra.gov.uk/yellowcard for how to report side effects.

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About the ACROSS study
The ACROSS study is a multi-centre, single visit, 10-year observational study evaluating the long-term efficacy of fingolimod in relapsing remitting MS (RRMS) over a 10-year follow-up period. The study included 175 people with RRMS who were previously enrolled in the Phase II D2201 study, evaluating the efficacy, safety and tolerability of fingolimod in RRMS. Patients enrolled in ACROSS were divided into the continuous fingolimod treatment group (defined as fingolimod treatment for at least eight years) and the non-continuous fingolimod treatment group (defined as fingolimod treatment for less than eight years).\(^1\)

The primary objective was to evaluate whether continuous use of fingolimod over 10 years reduces the progression of disability, as measured by the mean Expanded Disability Status Scale (EDSS) score, compared to shorter treatment duration.\(^1\) Key secondary objectives included the proportion of people with disability progression, the time to first use of a wheelchair, and the proportion of people who developed SPMS with continuous versus non-continuous fingolimod treatment at 10 years.\(^1\)

As in any study without parallel control, biases related to the design of the study need to be considered.

About fingolimod (Gilenya)
Fingolimod is an oral disease-modifying therapy (DMT) which has demonstrated efficacy in controlling disease activity in relapsing MS (RMS).\(^5\) Long-term experience has shown fingolimod treatment to be convenient for individuals to incorporate into everyday life, leading to high treatment satisfaction, long-term persistence, and ultimately, improved long-term outcomes for people with RMS.\(^5,10\)

Fingolimod impacts four key measures of disease activity: relapses, MRI lesions, brain shrinkage (brain volume loss) and disability progression.\(^5,6\) Its effectiveness on all of these measures has been shown in multiple controlled clinical studies and in the real-world setting.\(^5,11,12,13,14\) Studies have shown its efficacy to be sustained over the long term, demonstrating that switching to fingolimod treatment as early in the disease course as possible can be beneficial in helping to preserve individuals’ function.\(^13,15\)

Fingolimod is approved in the US 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.\(^15\)

Fingolimod has been used to treat approximately 155,000 patients in both clinical trials and the post-marketing setting, with approximately 343,000 years of patient experience.\(^16\)

About Multiple Sclerosis
Multiple sclerosis (MS) is a chronic disorder of the central nervous system (CNS) that disrupts the normal functioning of the brain, optic nerves and spinal cord through inflammation and tissue loss.\(^17\) There are three main types of MS: relapsing remitting MS (RRMS), secondary progressive MS (SPMS) and primary progressive MS (PPMS).\(^18\) The evolution of MS results in an increasing loss of both physical and cognitive (e.g. memory) function. This has a substantial negative impact on the lives of the approximately 2.3 million people worldwide affected by MS.\(^19\)

About Novartis in Multiple Sclerosis
The Novartis multiple sclerosis (MS) portfolio includes fingolimod (Gilenya), which is indicated for relapsing remitting MS and also in development for paediatric MS. Extavia\(^\circledast\) (interferon beta-1b for subcutaneous injection) is approved in the US for the treatment of relapsing forms of MS. In Europe, Extavia is approved to treat people with relapsing remitting MS, secondary
progressive MS (SPMS) with active disease and people who have had a single clinical event suggestive of MS.

Investigational compounds include BAF312 (siponimod) in development in SPMS, and ofatumumab (OMB157), a fully human monoclonal antibody in development for relapsing MS. Ofatumumab targets CD20, and is currently being investigated in two Phase III pivotal studies. In the US, the Sandoz Division of Novartis markets Glatopa® (glatiramer acetate injection) 20mg/mL, the first generic version of Teva's Copaxone™ 20mg.

About Novartis
Novartis provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. In 2015, the Group achieved net sales of USD 49.4 billion, while R&D throughout the Group amounted to approximately USD 8.9 billion (USD 8.7 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 118,000 full-time equivalent associates. Novartis products are available in more than 180 countries around the world.

In the UK, Novartis develops, manufactures and markets innovative medicines, devices and diagnostic tests which help improve patient outcomes. Based on four sites across the north and south of England, we employ approximately 1,500 people to serve healthcare needs across the whole of the UK, as well as supporting the global operations of Novartis by manufacturing the active pharmaceutical ingredients used worldwide in many medicines. The company is the largest commercial sponsor of clinical trials in the UK with over £16million spent on R&D in the UK in 2015. For more information, please visit www.novartis.co.uk.

“Copaxone® is a registered trademark of Teva Pharmaceutical Industries Ltd.

References
1. Derfuss T et al. The ACROSS Study: Long-term efficacy of fingolimod in patients with RRMS (follow-up at 10 years). Poster presented at: 32nd Congress of the European Committee for Treatment and Research in Multiple Sclerosis; September 14-17, 2016; London, UK. Poster 1215
11. Fox E et al, on behalf of EPOC study investigators, Outcomes of switching directly to oral fingolimod from injectable therapies: Results of the randomized, open-label, multicenter, Evaluate Patient Out Comes (EPOC) study in relapsing multiple sclerosis, 607-619.
14. Cascione, M. et al. Randomized, open-label study to evaluate patient-reported outcomes with fingolimod after changing from prior disease-modifying therapy for relapsing multiple sclerosis: EPOC study rationale and design. Journal of Medical Economics. 2013; 16(7);859-865
15. He, A. et al. Comparison of switch to fingolimod or interferon beta/ glatiramer acetate in active multiple sclerosis. JAMA Neurol. 2015; 72(4):405-413

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