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New Subgroup Analysis of the Phase 3 OPTIMUM Study Demonstrates the Benefits of PONVORY™ ▼ (ponesimod) Over teriflunomide in Early Disease Multiple Sclerosis

Early treatment in multiple sclerosis (MS) with higher-potency therapies can improve long-term patient outcomes[1,2]

New subgroup analysis of the pivotal Phase 3 OPTIMUM trial shows that MS patients with early disease achieved increased clinical benefit when treated with ponesimod compared with teriflunomide[1,2]

BEERSE, BELGIUM, 13 October 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced results from a new subgroup analysis of the pivotal Phase 3 OPTIMUM trial. Featured as an e-poster at the 37th Congress of the European Committee for Treatment Research in Multiple Sclerosis (ECTRIMS) from October 13-15, the subgroup analysis showed that in the expanded disability status scale (EDSS) ≤ 3 subgroup, ponesimod significantly reduced annualised relapse rate (ARR) by 47 percent (rate ratio [RR] = 0.53; 99 percent confidence levels [CLs]: 0.372, 0.755; p<0.0001) and MS-fatigue was statistically significantly lower in the ponesimod group compared with the teriflunomide group at week 108, with a mean difference (MD) of -4.31 (95 percent CLs: -6.99, -1.63; p=0.0017).[1,2]

"Multiple sclerosis is a debilitating and degenerative disease for which there is no cure, so our current focus is on preventing progression and minimising

relapses," said Allitia DiBernardo, M.D., lead author of the e-poster and Global Medical Affairs Head, Neurology, Janssen Global Services, LLC. "The OPTIMUM subgroup analysis supports the principle of early treatment intervention with high potency therapies such as ponesimod, which aims to reduce relapse rates, improve patient outcomes and ultimately contribute to a better quality of life for people living with MS."

The OPTIMUM study subgroup analysis randomised 1,133 patients (ponesimod, n = 567; teriflunomide, n = 566) and examined those with EDSS ≤ 3 (up to moderate disability in one function, or mild disability in 3 or 4 functions; no impairment to walking) and/or who were treatment naïve.[1]

The analysis showed that in treatment-naïve patients, ponesimod significantly reduced ARR (RR = 0.714; 99 percent CLs: 0.486, 1.049; p=0.0241) and MS-fatigue was significantly lower in the ponesimod group compared with the teriflunomide group at week 108, MD = -5.30 (95 percent CLs: -8.25, -2.35; p=0.0004).[1,2]

Results from this subgroup analysis for combined unique active lesions (CUALs) were consistent with the overall population. Patients significantly benefited from ponesimod compared with teriflunomide in both the EDSS ≤3 (RR = 0.424; 95 percent CLs: 0.329, 0.546; p<0.0001) and treatment-naïve (RR = 0.411; 95 percent CLs: 0.310, 0.545; p<0.0001) groups.[1,2]

"These data represent a significant contribution towards our goal of making a positive impact for people living with MS," said Tamara Werner-Kiechle, M.D., Therapeutic Area Lead Neuroscience & Pulmonary Hypertension, Europe, Middle East and Africa (EMEA), Janssen Cilag GmBH. "The further research on ponesimod is testimony to our commitment to support people living with MS, with a particular focus on improving the treatment landscape in relapsing MS, where medical unmet needs among the MS community remain."

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About Multiple Sclerosis

MS is a chronic autoimmune inflammatory disease of the central nervous system (CNS) in which immune cells attack myelin (the protective casing that insulates nerve cells), damaging or destroying it and causing inflammation.[3] This affects how the CNS processes information and communicates with the rest of the body, causing the neurologic signs and symptoms of MS.[4] Symptoms vary by person, but common symptoms include fatigue, balance and walking problems, numbness or tingling, dizziness and vertigo, vision problems, bladder and bowel problems and weakness.[4,5,6]

About PONVORY™ ▼ (ponesimod)

Ponesimod is a daily oral selective sphingosine-1-phosphate receptor 1 (S1P1) modulator, indicated for the treatment of adult patients with relapsing multiple sclerosis (RMS) with active disease defined by clinical or imaging features.[7,8] Ponesimod is believed to work by keeping immune cells called lymphocytes out of the blood by trapping them in the lymph nodes and out of the central nervous system, where they could cause damage.[8]

Ponesimod does not require genetic testing or first-dose cardiac monitoring for most patients. Because initiation of ponesimod treatment results in a decrease in heart rate, first-dose monitoring is recommended in patients with certain pre-existing cardiac conditions.[8]

It is not known if ponesimod is safe and effective in children.

On 19 May 2021, the European Commission approved ponesimod for the treatment of adult patients with relapsing forms of multiple sclerosis (RMS) with active disease defined by clinical or imaging features.[8,9]

A member of the Janssen Pharmaceutical Companies of Johnson & Johnson, Actelion Pharmaceuticals Ltd is party to a revenue sharing agreement with Idorsia Pharmaceuticals Ltd, which provides for certain payments to Idorsia related to the sales of ponesimod.

About the OPTIMUM trial

The Phase 3 OPTIMUM (NCT02425644) trial – a large pivotal trial and the first to compare an oral disease-modifying therapy (DMT) vs. another oral DMT – was a multicentre, randomised, double-blind, parallel-group, active-controlled superiority study. The trial was designed to evaluate the efficacy and safety of once daily oral ponesimod 20mg vs. once per day teriflunomide 14mg, an approved and widely-used first-line oral treatment, in adult patients with RMS. In total, 1,133 adult patients were randomised at 162 sites in 28 countries.[10]

The primary endpoint of the 108-week study was the ARR (ponesimod showed a statistically significant rate reduction of 30.5 percent. The ARR for ponesimod 20mg was 0.202 vs. 0.290 for teriflunomide 14mg [p=0.0003]). Secondary endpoints included CUAL per year on magnetic resonance imaging (MRI) to week 108 (ponesimod significantly reduced the number of new inflammatory lesions on brain MRI by 56 percent [p<0.0001] at week 108 when compared to teriflunomide) and time to 12- and 24-week confirmed disability accumulation to end of study (ponesimod-treated patients also showed a numerical benefit in delaying disability progression compared to teriflunomide-treated patients, and had small improvements in the risk of new 3- and 6-month disability [17 percent and 16 percent lower risk, respectively, compared to teriflunomide], although the between-group difference was not statistically significant in either instance).[10]

The safety profile of ponesimod is consistent with the known safety profile of other S1P receptor modulators, although a head-to-head comparison, other than with teriflunomide, is not available. Overall, the number of treatment-emergent adverse events reported was similar between the ponesimod and teriflunomide treated groups, and the majority were mild/moderate and did not warrant treatment discontinuation. The most frequently reported adverse events in the ponesimod 20mg group vs. the teriflunomide 14mg group were Alanine Aminotransferase (ALT) enzyme elevations (19.5 percent vs. 9.4 percent), nasopharyngitis (19.3 percent vs. 16.8 percent), headache (11.5 percent vs. 12.7 percent), upper respiratory tract infection (10.6 percent vs. 10.4 percent) and alopecia (3.2 percent vs. 12.7 percent).[10]

▼ Adverse events should be reported. This medicinal product is subject to additional monitoring and it is therefore important to report any suspected adverse events related to this medicinal product.

About the Janssen Pharmaceutical Companies of Johnson & Johnson
At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

Learn more at www.janssen.com/emea. Follow us at www.twitter.com/janssenEMEA for our latest news.

Janssen-Cilag International NV, the marketing authorisation holder for PONVORY™ (ponesimod) in the EU, Janssen Global Services, LLC, and Janssen Cilag GmBH are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Cautions Concerning Forward-Looking Statements
This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding ponesimod. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialise, actual results could vary materially from the expectations and projections of Janssen-Cilag International NV, Actelion Pharmaceuticals Ltd, Janssen Pharmaceutica NV and/or any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining

regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behaviour and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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