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Media Enquiries:
Chandni Kerai
Phone: +44 (0) 792 020 5356
Email: CKerai@ITS.JNJ.com

PONVORY® ▼ (ponesimod), a Once Daily, Oral Therapy Authorised in Great Britain for the Treatment of Adults with Relapsing Forms of Multiple Sclerosis (RMS) with Active Disease Defined by Clinical or Imaging Features

- *The pivotal Phase 3 OPTIMUM trial showed treatment with ponesimod (n=567) led to a 30.5 percent relative reduction in annual relapse rate (p=0.0003) vs. treatment with teriflunomide (n=566), an active comparator and established first-line oral treatment in adult patients with relapsing multiple sclerosis (RMS)*[1–4]
- *The OPTIMUM trial is the first head-to-head comparison of two oral disease modifying treatments (DMT) for RMS*[1]
- *Authorisation follows more than 10 years of cumulative data from Phase 2 and Phase 3 studies (plus their open label extensions) showing ponesimod's efficacy and safety profile*[1,5,6]

High Wycombe, UK, 10 August 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the Medicines and Healthcare Products Regulatory Agency (MHRA) has granted Marketing Authorisation in Great Britain for PONVORY® (ponesimod) for the treatment of adult patients with relapsing multiple sclerosis (RMS) with active disease defined by clinical or imaging features.[2–4]

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"We are delighted to receive MHRA authorisation for ponesimod, Janssen's first treatment for relapsing multiple sclerosis," said Tito Roccia, Therapeutic Area Medical Affairs Director, Neuroscience and Immunology, Janssen-Cilag Ltd. *"We are committed to helping people living with MS and this milestone is a positive step forward in providing a new therapeutic solution which can help to address some of the life-long and life-limiting symptoms of MS."*

"Unfortunately, there is no cure for multiple sclerosis and a high unmet medical need remains," said Gavin Giovannoni, Professor of Neurology, Blizzard Institute, Barts and The London School of Medicine and Dentistry.* *"Most people are diagnosed with multiple sclerosis in their younger years, between the ages of twenty to forty. As such, people living with multiple sclerosis are often looking for treatment solutions which help to minimise the burden and impact the condition has on their daily lives. Disease modifying treatments for relapsing multiple sclerosis are designed to reduce the number and severity of relapses, as well as slow disease and disability progression. Having a new oral therapy will provide patients with greater choice."*

The MHRA authorisation of ponesimod is based on data from the Phase 3 OPTIMUM trial, a multicentre, randomised, double-blind, parallel-group, active-controlled superiority study of 1,133 adult patients (aged 18-55 years) with RMS in 28 countries. The trial was designed to evaluate the efficacy and safety of once-daily oral ponesimod (20 mg) vs. once-daily teriflunomide (14 mg), an approved and established first-line oral treatment, in adult patients with RMS.[1]

The Phase 3 study showed the mean annualised relapse rate (ARR) (defined as confirmed relapses per year up to end of study) for ponesimod 20 mg (n=567) and teriflunomide (n=566) were 0.202 and 0.290, respectively. The study showed superior efficacy of ponesimod (n=567) on the primary endpoint, ARR, with a relative rate reduction of 30.5 percent (p=0.0003) compared with teriflunomide (n=566). Ponesimod (n=539) showed statistically significant superiority on one of the secondary endpoints, combined unique active lesions (CUALs), with relative reduction of new or enlarging inflammatory lesions on brain MRI by 56 percent (p<0.0001) at week 108, in comparison to teriflunomide (n=536). Another

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secondary endpoint was time to 12-week and 24-week confirmed disability accumulation (CDA). The risk of 12-week and 24-week CDA was not different in the two groups of ponesimod (n=567) and teriflunomide (n=566) (10.8 percent and 13.2 percent; 8.7 percent and 10.5 percent, respectively). The relative rate reduction of 12-week CDA was 17 percent (p=0.2939) in comparison to teriflunomide (n=566), and the relative rate reduction of 24-week CDA between ponesimod (n=567) and teriflunomide (n=566) was 16 percent (p=0.3720).[1–4]

"The unpredictable and fluctuating nature of multiple sclerosis makes it a challenge to manage day-to-day. Disease modifying treatment options that can reduce the rate of relapse, mean that people living with the condition can minimise some of the life-limiting symptoms of multiple sclerosis," said Dr Ruth Dobson, Clinical Senior Lecturer and Consultant Neurologist at Barts Health.* *"This authorisation marks a significant step forward for people living with relapsing multiple sclerosis, providing them an additional treatment option to manage their condition."*

Within the OPTIMUM study, 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 result in treatment discontinuation.[1] The most commonly reported adverse events in either the ponesimod 20 mg group versus the teriflunomide 14 mg group were Alanine Aminotransferase (ALT) enzyme elevations (19.5 vs. 9.4 percent), nasopharyngitis (19.3 vs. 16.8 percent), headache (11.5 vs. 12.7 percent), upper respiratory tract infection (10.6 vs. 10.4 percent) and alopecia (3.2 vs. 12.7 percent).[1–4] The current/currently known safety profile of ponesimod is consistent with the known safety profile of other S1P receptor modulators, although no other head-to-head comparisons have been conducted to date.[1] The ponesimod clinical development programme showed patients could take ponesimod with or without food.[+2-4,7] The programme also showed rapid elimination and reversibility of lymphocyte levels within 7-15 days after discontinuation.[2–4]

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*Professor Gavin Giovannoni and Dr Ruth Dobson have received consultancy honoraria from Janssen. They have not been compensated for any media work.

[+]Ponesimod contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.[2-4]

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.[8] This affects how the CNS processes information and communicates with the rest of the body, causing the neurologic signs and symptoms of MS.[9] 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.[9–11]

About PONVORY® (ponesimod)

Ponesimod is an oral, highly selective S1P1 modulator that functionally inhibits S1P1 receptor activity and, in doing so, it is believed to reduce the number of circulating lymphocytes.[12] In patients with multiple sclerosis (MS), inflammatory immune cells, including lymphocytes, can cross the blood brain barrier into the brain and damage myelin, the protective sheath that insulates nerve cells. Damage to myelin slows or halts nerve conduction, producing the neurologic signs and symptoms of MS.[13]

One 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.

▼ 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. Reporting forms and

information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Janssen-Cilag Ltd on 01494 567447.

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.

Janssen-Cilag Limited is a Janssen Pharmaceutical Company of Johnson & Johnson. Learn more at www.janssen.com/uk. Follow us at www.twitter.com/JanssenUK.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding PONVORY® (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 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

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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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