News Release

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Janssen Showcases Recent Data in Relapsing Multiple Sclerosis at the 2021 European Committee for Treatment and Research in Multiple Sclerosis Congress

Titusville, N.J., September 29, 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that its latest data in multiple sclerosis (MS) will be presented at the 2021 European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) virtual congress from October 13 to 15, in Vienna, Austria. A total of 10 Janssen-sponsored data abstracts on MS research will be presented, including post-hoc analyses highlighting the benefit of PONVORY™ (ponesimod) compared with Aubagio® (teriflunomide) and an analysis of increased clinical benefits in early patient use. PONVORY™, a once-daily oral selective sphingosine-1-phosphate receptor 1 (S1P1) modulator, was approved to treat adults with relapsing forms of MS in both the United States and European Union earlier this year.

"We're pleased to present data from our ongoing clinical program in multiple sclerosis at the ECTRIMS congress, which further support the clinical benefits of PONVORY™, and underscore the unmet needs that continue to exist within the space," said Bill Martin, Ph.D., Global Therapeutic Area Head, Neuroscience, Janssen Research & Development, LLC. "The approval of PONVORY™ marks an important step in reinforcing our company commitment to the broader neurology field, and provides patients with a safe and efficacious new option to treat MS. Still, we know there is much more work to be done to address the needs of MS patients globally and we're continuing to enhance our postlaunch research and development programs as part of our endeavors to providing patients with the support they need to help navigate life with MS."

Janssen Data Presentations Include:

Ponesimod demonstrated increased clinical benefit over teriflunomide in early disease subgroup compared with overall population

A subgroup analysis of the pivotal OPTIMUM trial, a Phase 3, randomized, double-blind study, demonstrated increased clinical benefits of ponesimod over teriflunomide by evaluating whether a patient population with early disease has a differential benefit with ponesimod compared to teriflunomide. The study demonstrated increased clinical benefits in terms of Confirmed Disability Accumulation (CDA) in early disease subgroups compared with the overall

population and confirmed the advantage of using ponesimod as an early, high-efficacy treatment.

A short pause in ponesimod treatment completely restores the ability to mount post-vaccination antibody titers in mice
An open question is whether patients taking ponesimod can respond to a novel vaccine or would benefit from a drug holiday prior to vaccination. The antibody response after vaccination was blunted in mice that were maintained on ponesimod, but not when treatment is temporarily paused. These data suggest that briefly halting ponesimod treatment may help in achieving maximal vaccination effectiveness.

Effect of ponesimod compared to teriflunomide on concomitant corticosteroid treatment of relapse in patients with relapsing forms of multiple sclerosis
The objective of this analysis was to compare the use of corticosteroids for treatment of relapses between ponesimod and teriflunomide groups in OPTIMUM. In the OPTIMUM trial, patients with relapsing multiple sclerosis (RMS) treated with ponesimod achieved a lower rate of concomitant Systemic Corticosteroids (SCS) usage for the management of relapses compared with patients treated with teriflunomide.

Ponesimod shows improved effect on Brain Volume Loss (BVL) over other MS Disease Modifying Treatments, based on Model-Based Meta-Analysis (MBMA)
The MBMA included longitudinal BVL data from 21 eligible Randomized Clinical Trials (RCTs) that investigated 11 unique drugs and placebo. Ponesimod appears to lead to less BVL at 2 years than placebo and all 10 other comparators in the network, including other S1P receptor modulators, orals and anti-CD20 B cell depleting monoclonals.

Empowerment of multiple sclerosis patients in treatment decision-making
This study evaluated the degree to which MS patients are empowered in treatment decisions and attitudes regarding their role in MS treatment choice. The study was conducted using data from the Adelphi MS Disease Specific Programme, a cross-sectional survey of neurologists and their MS patients in the US and several European countries between December 2020 and May 2021. It was found in this study that many MS patients play an active role in treatment decision-making, and patients in the US reported a higher engagement and greater likelihood to receive medication they request.

Understanding symptoms and their impact on patients with multiple sclerosis: what we can learn from social media
This study evaluated real-world evidence from social media, including patient forums, to understand the prevalence and impact of symptoms among patients with MS by collecting data-set keywords and overall sentiment toward fatigue burden. The data collected show that fatigue was reported as the most prevalent symptom. The consistency of these findings, with previous research using other methods of analysis, suggests that social media data can be a valuable source of insight into patients' experience of MS symptoms.

A complete listing of Janssen-sponsored abstracts is provided below. Abstracts can also be viewed on the ECTRIMS virtual congress 2021 website.

Presentation #	Title

P712	**Ponesimod in CNS modulates astrocytic genes to protect against limbic fiber demyelination via S1P1-selective modulation**
P646	**A short pause in ponesimod treatment completely restores the ability to mount post-vaccination antibody titers in mice**
P359	**Ponesimod demonstrated increased clinical benefit over teriflunomide in early disease subgroup compared with overall population**
P595	**Ponesimod shows improved effect on Brain Volume than other DMTs, a model-based meta-analysis**
P883	**Relationships between Brain Volume and disability, cognition, motor function, and MS-fatigue in RMS: MS-fatigue and ambulation move at their own pace**
P910	**Analysis and evaluation of ponesimod hepatic safety data**
P703	**Effect of ponesimod compared to teriflunomide on concomitant corticosteroid treatment of relapse in patients with relapsing forms of multiple sclerosis**
P902	**Empowerment of multiple sclerosis patients in treatment decision making**
P872	**Differences in expected number of clinical management events before and during treatment with sphingosine-1-phosphate receptor modulators for multiple sclerosis**
P313	**Understanding symptoms and their impact on patients with multiple sclerosis: what we can learn from social media**

About PONVORY™ (Ponesimod)

PONVORY™ (ponesimod) is a daily oral selective sphingosine-1-phosphate receptor 1 (S1P1) modulator, indicated to treat adults with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease and active secondary progressive disease.[1,2,3] PONVORY™ is believed to work by keeping immune cells called lymphocytes out of the blood by trapping them in the lymph nodes.[3] The way PONVORY™ exerts therapeutic effects in MS is unknown, but may help keep the lymphocytes out of the central nervous system, where they could cause damage.[3]

PONVORY™ does not require genetic testing or first-dose cardiac monitoring for most patients. Because initiation of PONVORY™ treatment results in a decrease in heart rate, first-dose monitoring is recommended in patients with certain preexisting cardiac conditions.[3]

It is not known if PONVORY™ is safe and effective in children.

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

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.

IMPORTANT SAFETY INFORMATION

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT

PONVORY™?

PONVORY™ may cause serious side effects, including:

Infections - PONVORY™ can increase your risk of serious infections that can be life-threatening and cause death. PONVORY™ lowers the number of white blood cells (lymphocytes) in your blood. This will usually go back to normal within 1 to 2 weeks of stopping treatment. Your healthcare provider should review a recent blood test of your white blood cells before you start taking PONVORY™. Call your healthcare provider right away if you have any of these symptoms of an infection during treatment and for 1 to 2 weeks after your last dose of PONVORY™:

- fever
- tiredness
- body aches
- chills
- nausea
- vomiting
- headache with fever, neck stiffness, sensitivity to light, nausea, or confusion (these may be symptoms of meningitis, an infection of the lining around your brain and spine)

Your healthcare provider may delay starting or may stop your PONVORY™ treatment if you have an infection.

- Slow heart rate (bradycardia or bradyarrhythmia) when you start taking PONVORY™.

PONVORY™ can cause your heart rate to slow down, especially after you take your first dose. You should have a test to check the electrical activity of your heart called an electrocardiogram (ECG) before you take your first dose.

Only Start your treatment with PONVORY™ using the Starter Pack. You must use the PONVORY™ Starter Pack by slowly increasing the dose over a 14-day period to help reduce the effect of slowing of your heart rate. It is important to follow the recommended dosing instructions.

Call your healthcare provider if you experience the following symptoms of slow heart rate:

- dizziness
- lightheadedness
- feeling like your heart is beating slowly or skipping beats
- shortness of breath
- confusion
- chest pain
- tiredness

Do not take PONVORY™ if you:

- have had a heart attack, chest pain called unstable angina, stroke or mini-stroke (transient ischemic attack or TIA), or certain types of heart failure in the last 6 months.
- have certain types of heart block or irregular or abnormal heartbeat (arrhythmia) unless you have a pacemaker.
- Talk to your healthcare provider if you have any of these conditions, or do not

know if you have any of these conditions.

Before you take PONVORY™, tell your healthcare provider about all your medical conditions, including if you:

- have a fever or infection, or you are unable to fight infections due to a disease or taking medicines that lower your immune system.
- have had chicken pox or have received the vaccine for chicken pox. Your healthcare provider may do a blood test for chicken pox virus. You may need to get the full course of vaccine for chicken pox and then wait 1 month before you start taking PONVORY™.
- have slow heart rate.
- have an irregular or abnormal heartbeat (arrhythmia).
- have a history of stroke.
- have heart problems, including a heart attack or chest pain.
- have high blood pressure.
- have breathing problems, including during your sleep (sleep apnea).
- have liver problems.
- had or now have a type of skin cancer called basal cell carcinoma (BCC), melanoma, or squamous cell carcinoma
- have eye problems, especially an inflammation of the eye called uveitis.
- have diabetes.
- are pregnant or plan to become pregnant. PONVORY™ may harm your unborn baby. Talk with your healthcare provider if you are pregnant or plan to become pregnant. If you are a woman who can become pregnant, you should use effective birth control during your treatment with PONVORY™ and for 1 week after you stop taking PONVORY™. Talk to your healthcare provider about what method of birth control is right for you during this time. Tell your healthcare provider right away if you do become pregnant while taking PONVORY™ or within 1 week after you stop taking PONVORY™.
- are breastfeeding or plan to breastfeed. It is not known if PONVORY™ passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take PONVORY™.

Tell your healthcare provider about all the medicines you take, including prescription medicines, over-the-counter medicines, vitamins, and herbal supplements.

Using PONVORY™ and other medicines together may affect each other causing serious side effects. Especially tell your healthcare provider if you take or have taken: Medicines to control your heart rhythm (antiarrhythmics), or blood pressure (antihypertensives), or heart-beat (such as calcium channel blockers or beta-blockers); medicines that affect your immune system, such as alemtuzumab; and medicines such as rifampin, phenytoin, or carbamazepine.

You should not receive live vaccines during treatment with PONVORY™, for at least 1 month before taking PONVORY™, and for 1 to 2 weeks after you stop taking PONVORY™. If you receive a live vaccine, you may get the infection the vaccine was meant to prevent. Vaccines may not work as well when given during treatment with PONVORY™.

Talk with your healthcare provider if you are not sure if you take any of these medicines.

HOW SHOULD I TAKE PONVORY™?

- Take PONVORY™ exactly as your healthcare provider tells you to take it.
- Take PONVORY™ 1 time each day.
- Swallow PONVORY™ tablets whole.
- Take PONVORY™ with or without food.
- Do not stop taking PONVORY™ without talking with your healthcare provider first.
- Do not skip a dose.
- Start taking PONVORY™ with a 14-day starter pack.
- If you miss taking 1, 2, or 3 tablets in a row of PONVORY™ in the 14-day starter pack, continue treatment by taking the first dose you missed. Take 1 tablet as soon as you remember. Then, take 1 tablet a day to continue with the starter pack dose as planned.
- If you miss taking 1, 2, or 3 tablets in a row of PONVORY™ while taking the 20 mg maintenance dose, continue treatment with the 20 mg maintenance dose.
- If you miss taking 4 or more tablets in a row of PONVORY™, while taking the 14-day starter pack or the 20 mg maintenance dose, you need to restart treatment with a new 14-day starter pack. Call your healthcare provider if you miss 4 or more doses of PONVORY™. Do not restart PONVORY™ after stopping it for 4 or more days in a row without talking to your healthcare provider. If you have certain heart conditions, you may need to be monitored by your healthcare provider for at least 4 hours when you take your next dose.

What are the possible side effects of PONVORY™?

PONVORY™ may cause serious side effects, including:

- breathing problems. Some people who take PONVORY™ have shortness of breath. Call your healthcare provider right away if you have new or worsening breathing problems.
- liver problems. PONVORY™ may cause liver problems. Your healthcare provider should do blood tests to check your liver before you start taking PONVORY™. Call your healthcare provider right away if you have any of the following symptoms of liver problems:
    - unexplained nausea
    - vomiting
    - stomach (abdominal) pain
    - tiredness
    - loss of appetite
    - yellowing of the whites of your eyes or skin
    - dark urine
- increased blood pressure. Your healthcare provider should check your blood pressure during treatment.
- types of skin cancer called basal cell carcinoma (BCC), melanoma, and squamous cell carcinoma. Certain types of skin cancer have happened with drugs in the same class. Tell your healthcare provider if you have any changes in the appearance of your skin, including changes in a mole, a new darkened area on your skin, a sore that does not heal, or growths on your skin, such as a bump that may be shiny, pearly white, skin-colored, or pink. Your doctor should check your skin for any changes during treatment with PONVORY™. Limit the amount of time you spend in sunlight and ultraviolet (UV) light. Wear protective clothing and use a sunscreen with a high sun

protection factor.
- a problem with your vision called macular edema. Tell your healthcare provider about any changes in your vision. Your healthcare provider should test your vision before you start taking PONVORY™ and any time you notice vision changes during treatment with PONVORY™. Your risk of macular edema is higher if you have diabetes or have had an inflammation of your eye called uveitis.

Call your healthcare provider right away if you have any of the following symptoms:

- blurriness or shadows in the center of your vision
- a blind spot in the center of your vision
- sensitivity to light
- unusually colored (tinted) vision
- swelling and narrowing of the blood vessels in your brain. A condition called Posterior Reversible Encephalopathy Syndrome (PRES) has happened with drugs in the same class. Symptoms of PRES usually get better when you stop taking PONVORY™. However, if left untreated, it may lead to a stroke. Call your healthcare provider right away if you have any of the following symptoms:
- sudden severe headache
- sudden confusion
- sudden loss of vision or other changes in vision
- seizure
- severe worsening of multiple sclerosis (MS) after stopping PONVORY™.

When PONVORY™ is stopped, symptoms of MS may return and become worse compared to before or during treatment. Always talk to your healthcare provider before you stop taking PONVORY™ for any reason. Tell your healthcare provider if you have worsening symptoms of MS after stopping PONVORY™.

The most common side effects of PONVORY™ include:

- upper respiratory tract infections
- elevated liver enzymes (abnormal liver tests)
- high blood pressure (hypertension)

These are not all the possible side effects of PONVORY™. For more information, ask your healthcare provider or pharmacist. See "What is the most important information I should know about PONVORY™?"

Tell your doctor if you have any side effect that bothers you or that does not go away.

Call your doctor for medical advice about side effects. You are also encouraged to report side effects to the FDA: visit http://www.fda.gov/medwatch or call 1-800-FDA-1088. You may also report side effects to Janssen Pharmaceuticals, Inc., at 1-800-JANSSEN (1-800-526-7736).

Please see full Prescribing Information and Medication Guide.

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About Multiple Sclerosis (MS)
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.[4] This affects how the CNS processes information and communicates with the rest of the body, causing the neurologic signs and symptoms of MS.[5] 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.[6,7,8]

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. Follow us at www.twitter.com/JanssenGlobal. Janssen Research & Development, LLC and Actelion Pharmaceuticals Ltd are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Aubagio® (teriflunomide) is a trademark of Sanofi.

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 materialize, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, 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; changes in behavior and spending patterns of purchasers of healthcare products and services; changes to applicable laws and regulations, including global healthcare reforms; and trends toward healthcare 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," 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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