News Release

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Janssen Demonstrates Its Commitment to Advancing Transformative Solutions for Multiple Sclerosis at ACTRIMS Forum 2022

An analysis identifies physician and patient perspectives on multiple sclerosis symptoms and management with an emphasis on hidden symptoms of the disease

Janssen presents the use of a novel patient recruitment strategy in real-world evidence study to seek enhanced credibility of results and the potential for significant cost efficiencies

Titusville, N.J., February 22, 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that 13 company-sponsored data presentations from its multiple sclerosis (MS) research program will be presented at the 2022 Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Forum. ACTRIMS will take place from February 24-26, West Palm Beach, Florida.

"We're pleased to present data that highlight our scientific progress of the PONVORY® (ponesimod) program, which underscores our responsibility to address unmet needs in MS. Post-launch trials are critical to continuing to evaluate the benefits and risks of the treatment and to broaden our understanding to help address the complexities of the disease," said Bill Martin, Ph.D., Global Therapeutic Area Head, Neuroscience, Janssen Research & Development, LLC. "Our work in MS is just one part of our ongoing commitment to advancing the science across a wide array of nervous system disorders. We are building a pipeline in neurology driven by innovation that we hope will lead to transformative therapies for patients with neurological disorders."

Janssen Data Presentations Include:

Differences in Physician and Patient Perspectives on Patients' Burden Related to Hidden Symptoms of Multiple Sclerosis

This analysis aimed to identify areas of alignment and differences between patients and their physicians in reporting MS severity and hidden symptoms, such as depression, anxiety, and cognitive problems, which can be difficult to communicate, recognize, detect, and monitor.

The Use of a Novel Patient Recruitment Strategy, Up-Front Matching to Mimic Randomization: Phase IV PONVO Study

The real-world evidence PONVO study, a prospective observational study, was

designed to demonstrate that in early stage of disease, S1P1 monoselective receptor modulator ponesimod is superior on MS-fatigue compared with anti-CD20 agent ocrelizumab, and non-inferior with respect to relapse-free rates. For prospective observational studies, like PONVO, that are designed to compare treatments, a recruitment method, called "up-front matching," will result in balance for selected baseline covariates that mimics what one would see with randomization.

The Selective Sphingosine-1-Phosphate Receptor 1 (S1P1) Modulator Ponesimod Enhances Murine Oligodendrocyte Precursor Cell (OPC) Differentiation and Retains OPC Migration
The effect of functional antagonism by the S1P1 monoselective modulator ponesimod on OPC migration and differentiation relative to S1P5 monoselective modulator and S1P1/S1P5 dual modulation was evaluated. The study showed promise for further research into the remyelinating capacity of S1P1 monoselective modulations.

A complete listing of Janssen-sponsored abstracts is provided below. Abstracts can also be viewed on the ACTRIMS Forum 2022 website.

Presentation #	Title
P080	**Fetal Exposure With Ponesimod Treatment Across Clinical Development Studies**
P084	**Ponesimod in Relapsing Forms of Multiple Sclerosis—Long-Term Pooled Safety Results From the Clinical Development Program**
P085	**Prognostic Value of the MAGNIMS Score and Its Application in Clinical Outcome Assessment of Disease-Modifying Therapy in Patients With Relapsing Multiple Sclerosis: Results From the OPTIMUM Study of Ponesimod**
P088	**Results of the Phase 3 OPTIMUM Study of Ponesimod Compared With Teriflunomide in Female Patients With Relapsing Multiple Sclerosis**
P104	**Optimum Trial Patients Treated With Ponesimod Show Less Ventricular Enlargement Over Time Compared to Patients Treated With Teriflunomide**
P111	**The Use of a Novel Patient Recruitment Strategy, Up-Front Matching to Mimic Randomization: Phase IV PONVO Study**
P168	**Preventative Effects of Ponesimod on Cingulum Demyelination: Implications for MS Fatigue**
P198	**The Selective Sphingosine-1-Phosphate Receptor 1 (S1P1) Modulator Ponesimod Enhances Murine Oligodendrocyte Precursor Cell (OPC) Differentiation and Retains OPC Migration**
P334	**Estimated Prevalence of First-Dose Cardiac Observation in Patients Taking Ponesimod**
P386	**A Real-World Study Characterizing Impact of Fatigue and Patient Symptom Recall in Adults With Relapsing Multiple Sclerosis**
P387	**A Systematic Literature Review of the Measurement of Patient-Reported Fatigue in Studies of Disease-Modifying Therapies for Multiple Sclerosis**
P395	**The Benefit of MS Patient Involvement in Treatment Decision Making**
P415	**Differences in Physician and Patient Perspectives on Patients' Burden Related to Hidden Symptoms of Multiple Sclerosis**

For more information about our work in neuroscience, please visit the Janssen Neuroscience R&D Newsroom.

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 it 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. As seen in PK-PD assessments, the effects of PONVORY® on lymphocyte counts are reversible in about seven days in 90% of 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.

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

Do not take PONVORY® if you:

- have had a heart attack, chest pain called unstable angina, stroke or ministroke (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.
- have liver problems.
- have 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 week before taking and for 1 month 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.

Ocrevus® (ocrelizumab) is a trademark of Genentech.

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 2, 2022, 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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