News Release

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Janssen Submits Paliperidone Palmitate 6-Month (PP6M) Supplemental New Drug Application to U.S. FDA for Treatment of Schizophrenia in Adults

If approved, PP6M will be the first and only long-acting injectable schizophrenia treatment with a twice-yearly dosing regimen

TITUSVILLE, N.J., November 2, 2020 – The Janssen Pharmaceutical Companies of Johnson & Johnson (Janssen) today announced the submission of a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) for paliperidone palmitate 6-month (PP6M) for the treatment of adults diagnosed with schizophrenia. If approved, PP6M will be the first and only long-acting injectable (LAI) schizophrenia medication with a twice-yearly dosing regimen.

"Janssen's roots in neuroscience began with research and development of novel therapeutic options for schizophrenia, and this filing builds on that 60-year commitment," said Bill Martin, Ph.D., Global Therapeutic Area Head, Neuroscience, Janssen Research & Development, LLC. "We designed this unique dosing regimen so people with schizophrenia and their healthcare teams can focus less on medication intervals and more on other aspects of their treatment plans, such as psychosocial interventions. We look forward to working with the FDA to add a 6-month formulation to our family of paliperidone palmitate products."

The submission is based on the Route 6 Study, a randomized, double-blind, non-inferiority Phase 3 global study that enrolled 702 adults living with schizophrenia from 20 countries. Data showed non-inferior efficacy of PP6M compared to paliperidone palmitate 3-month (PP3M) on the primary endpoint of time to relapse at the end of the 12-month period in both intent-to-treat and per-protocol analysis sets.[1] The safety profile observed for PP6M was consistent with previous studies of paliperidone palmitate 1-month (PP1M) and 3-month (PP3M) formulations with no new safety signals emerging.

"Antipsychotic medication plays an important role in schizophrenia symptom control; however, nonadherence to prescribed medicines has been recognized as a problem worldwide," said Mathai Mammen, M.D., Ph.D., Global Head of Janssen Research & Development, LLC. "Addressing this challenging aspect of treatment has been the catalyst for our research and development of long-acting injectable medications for people living with schizophrenia."

PP6M is intended to be used only after patients have been stabilized on a shorter

acting formulation of paliperidone palmitate (PP1M or PP3M), with the goal of administering fewer injections. The Janssen U.S. portfolio of LAI medicines currently approved to treat adults with schizophrenia includes RISPERDAL CONSTA® (risperidone 2-weekly)[2], INVEGA SUSTENNA®[3] and INVEGA TRINZA®[4] (PP1M and PP3M formulations, respectively), all of which are administered in a clinical setting by a medical professional.

Janssen plans to submit a Marketing Authorization Application extension to the European Medicines Agency (EMA) for PP6M in the coming months.

INDICATIONS

INVEGA TRINZA® (3-month paliperidone palmitate) is a prescription medicine given by injection every 3 months by a healthcare professional and used to treat schizophrenia. INVEGA TRINZA® is used in people who have been treated with INVEGA SUSTENNA® (1-month paliperidone palmitate) for at least 4 months. INVEGA SUSTENNA® (In-VEY-guh Suss-TEN-uh) (paliperidone palmitate) is a prescription medicine given by injection by a healthcare professional. INVEGA SUSTENNA® is used to treat schizophrenia in adults.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about INVEGA TRINZA® and INVEGA SUSTENNA®?

INVEGA TRINZA® and INVEGA SUSTENNA® can cause serious side effects, including an increased risk of death in elderly people who are confused, have memory loss, and have lost touch with reality (dementia-related psychosis). INVEGA TRINZA® and INVEGA SUSTENNA® are not for treating dementia-related psychosis.

Do not receive INVEGA TRINZA® or INVEGA SUSTENNA® if you are allergic to paliperidone, paliperidone palmitate, risperidone, or any of the ingredients in INVEGA TRINZA® or INVEGA SUSTENNA®. See the end of the Patient Information leaflet in the full Prescribing Information for a complete list of INVEGA TRINZA® and INVEGA SUSTENNA® ingredients.

Before you receive INVEGA TRINZA® or INVEGA SUSTENNA®, tell your healthcare professional about all your medical conditions, including if you:

- have had Neuroleptic Malignant Syndrome (NMS)
- have or have had heart problems, including a heart attack, heart failure, abnormal heart rhythm, or long QT syndrome
- have or have had low levels of potassium or magnesium in your blood
- have or have had uncontrolled movements of your tongue, face, mouth, or jaw (tardive dyskinesia)
- have or have had kidney or liver problems
- have diabetes or have a family history of diabetes
- have had a low white blood cell count
- have had problems with dizziness or fainting or are being treated for high blood pressure
- have or have had seizures or epilepsy
- have any other medical conditions
- are pregnant or plan to become pregnant. It is not known if INVEGA TRINZA® SUSTENNA® will harm your unborn baby.
    - If you become pregnant while taking INVEGA TRINZA® or INVEGA SUSTENNA®, talk to your healthcare professional

about registering with the National Pregnancy Registry for Atypical Antipsychotics. You can register by calling 1-866-961-2388 or visit http://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry.

- Infants born to women who are treated with INVEGA TRINZA® or INVEGA SUSTENNA® may experience symptoms such as tremors, irritability, excessive sleepiness, eye twitching, muscle spasms, decreased appetite, difficulty breathing, or abnormal movement of arms and legs. Let your healthcare professional know if these symptoms occur.

- are breastfeeding or plan to breastfeed. INVEGA TRINZA or INVEGA SUSTENNA can pass into your breast milk. Talk to your healthcare professional about the best way to feed your baby if you receive INVEGA TRINZA® or INVEGA SUSTENNA®.

Tell your healthcare professional about all the medicines you take, including prescription and over-the- counter medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show to your healthcare professional or pharmacist when you get a new medicine.

Patients (particularly the elderly) taking antipsychotics with certain health conditions or those on long-term therapy should be evaluated by their healthcare professional for the potential risk of falls.

What should I avoid while receiving INVEGA TRINZA® or INVEGA SUSTENNA®?

- INVEGA TRINZA and INVEGA SUSTENNA may affect your ability to make decisions, think clearly, or react quickly. Do not drive, operate heavy machinery, or do other dangerous activities until you know how INVEGA TRINZA® or INVEGA SUSTENNA® affects you.
- Avoid getting overheated or dehydrated.

INVEGA TRINZA® and INVEGA SUSTENNA® may cause serious side effects, including:

- **See "What is the most important information I should know about INVEGA TRINZA® INVEGA SUSTENNA®?"**
- **stroke in elderly people (cerebrovascular problems) that can lead to death**
- **Neuroleptic Malignant Syndrome (NMS).** NMS is a rare but very serious problem that can happen in people who receive INVEGA TRINZA® or INVEGA SUSTENNA®. NMS can cause death and must be treated in a hospital. Call your healthcare professional right away if you become severely ill and have any of these symptoms: high fever; severe muscle stiffness; confusion; loss of consciousness; changes in your breathing, heartbeat, and blood pressure.
- **problems with your heartbeat.** These heart problems can cause death. Call your healthcare professional right away if you

have any of these symptoms: passing out or feeling like you will pass out, dizziness, or feeling as if your heart is pounding or missing beats.

- **uncontrolled movements of your tongue, face, mouth, or jaw (tardive dyskinesia)**
- **metabolic changes.** Metabolic changes may include high blood sugar (hyperglycemia), diabetes mellitus and changes in the fat levels in your blood (dyslipidemia), and weight gain.
- **low blood pressure and fainting**
- **changes in your blood cell counts**
- **high level of prolactin in your blood (hyperprolactinemia).** INVEGA TRINZA® or INVEGA SUSTENNA® may cause a rise in the blood levels of a hormone called prolactin (hyperprolactinemia) that may cause side effects including missed menstrual periods, leakage of milk from the breasts, development of breasts in men, or problems with erection.
- **problems thinking clearly and moving your body**
- **seizures**
- **difficulty swallowing that can cause food or liquid to get into your lungs**
- **prolonged or painful erection lasting more than 4 hours.** Call your healthcare professional or go to your nearest emergency room right away if you have an erection that lasts more than 4 hours.

- **problems with control of your body temperature, especially when you exercise a lot or spend time doing things that make you warm. It is important for you to drink water to avoid dehydration.**

The most common side effects of INVEGA TRINZA® include: injection site reactions, weight gain, headache, upper respiratory tract infections, feeling restlessness or difficulty sitting still, slow movements, tremors, stiffness and shuffling walk.

The most common side effects of INVEGA SUSTENNA® include: injection site reactions; sleepiness or drowsiness; dizziness; feeling of inner restlessness or needing to be constantly moving; abnormal muscle movements, including tremor (shaking), shuffling, uncontrolled involuntary movements, and abnormal movements of your eyes.

Tell your healthcare professional if you have any side effect that bothers you or does not go away. These are not all the possible side effects of INVEGA TRINZA® or INVEGA SUSTENNA®. For more information, ask your healthcare professional or pharmacist.

Call your healthcare professional for medical advice about side effects. You may report side effects of prescription drugs to the FDA at 1-800-FDA-1088.

General information about the safe and effective use of INVEGA TRINZA® or INVEGA SUSTENNA®

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use INVEGA TRINZA® or INVEGA SUSTENNA® for a condition for which it was not prescribed. Do not give INVEGA TRINZA® or INVEGA SUSTENNA® to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare professional for information about INVEGA TRINZA® or INVEGA SUSTENNA® that is written for healthcare professionals.

This Patient Information leaflet summarizes the most important information about INVEGA TRINZA® and INVEGA SUSTENNA®. If you would like more information, talk with your healthcare professional.

You can ask your healthcare professional or pharmacist for more information that is written for healthcare professionals. For more information, go to www.invegatrinza.com or www.invegasustenna.com or call 1-800-526-7736.

Please click to read the full Prescribing Information, including Boxed WARNING, for INVEGA TRINZA® and INVEGA SUSTENNA® and discuss any questions you have with your healthcare professional.

About the Route 6 Trial

The Route 6 Study was a randomized, double-blind, non-inferiority global Phase 3 study of 702 adults with schizophrenia, designed to demonstrate that injection of PP6M is not less effective than PP3M for the prevention of relapse in participants previously stabilized on corresponding doses of PP1M or PP3M.

The study consisted of three phases: a screening phase (up to 28 days), a maintenance phase (of 1 or 3 months), and a double-blind phase (of 12 months). Additional/conditional phases included a transition phase and maintenance phase. The maintenance phase was used to stabilize patients on PP1M or PP3M prior to the double-blind phase. Study evaluations included efficacy, pharmacokinetics, pharmacodynamics, and safety. The study's duration varied from approximately 13 months to 19 months.

About Long-Acting Injectables

Long-acting injectables (LAIs) allow for the slow release of medicine into the blood and have been available for more than 50 years.[5] LAI antipsychotics offer a number of advantages compared with oral medication, including not having to remember to take drugs daily, improved patient outcomes, improved patient and physician satisfaction, and lower relapse rates.[6] Based on clinical guidance developed by the American Association of Community Psychiatrists and research evidence from the National Institute for Mental Health and others, the National Council of Behavioral Health recommends LAIs as a first-line treatment to eligible patients.[7]

About Schizophrenia

Schizophrenia is a chronic and severe brain disorder affecting approximately 20 million people worldwide[8] and an estimated 2.8 million people in the U.S.[9,10] The disease is characterized by distortions in thinking, perception, emotions, language, sense of self and behavior leading to neurological impairment and severe disability.[8]

Antipsychotic medication is recognized as an essential component in the treatment of schizophrenia, and adherence to medication plays a critical role in

preventing symptoms and costly relapses.[11] However, nearly 75 percent of patients with schizophrenia experience a relapse, often driven by non-adherence to prescribed medication.[12,13]

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 is 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 paliperidone palmitate 6-month (PP6M) for the treatment of adults diagnosed with schizophrenia. 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; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior 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 December 29, 2019, 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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[1] Two analyses were conducted, per noninferiority study protocol: the first was conducted with all patients who were randomized (intent-to-treat), and the second population included only patients who followed the protocol.
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[5] National Alliance on Mental Illness. Long-Acting Injectables. Available at: https://www.nami.org/Learn-More/Treatment/Mental-Health-Medications/Long-Acting-Injectables. Accessed August 2020.
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