Janssen Submits New Drug Application to U.S. FDA for Three-Month Paliperidone Palmitate

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TITUSVILLE, N.J., Nov. 19, 2014 /PRNewswire/ -- Janssen Research & Development, LLC (Janssen) today announced the submission of a New Drug Application (NDA) for three-month atypical antipsychotic paliperidone palmitate to the U.S. Food and Drug Administration (FDA). The NDA seeks approval for the medication as a treatment for schizophrenia in adults. If approved, it will be the first and only long-acting atypical antipsychotic that has a four times a year dosing schedule.

"This innovative three-month formulation has the potential to positively affect the care of many people with schizophrenia," said Husseini K. Manji, MD, Global Head, Neuroscience Therapeutic Area, Janssen Research & Development, LLC. "The option for this dosing schedule would offer a welcome new choice for patients and may provide benefits to society."

Schizophrenia is a complex and chronic brain disorder that can be severe and disabling. It affects approximately one percent of the population, often beginning in early adulthood. If left untreated, schizophrenia can greatly interfere with education, employment, and interpersonal functioning. The course of schizophrenia is varied, generally involving a series of relapses or the return of disease after partial recovery.

"Schizophrenia is often a devastating condition, and treatment interventions are needed early in the course of the disease," said Joseph A. Kwentus, MD, a psychiatrist at Hinds Behavioral Health Services, Jackson, Miss., who was a clinical investigator in the Phase 3 paliperidone palmitate three-month formulation study. "Psychotherapy, medication, and community support can help people with schizophrenia better manage their illness. It's important that medical professionals, policy makers, and patients' loved ones support comprehensive treatment."

The filing was based on a Phase 3, international, randomized, multicenter, double-blind, relapse prevention study of paliperidone palmitate three-month injection. The study, which included more than 500 patients, evaluated the efficacy of three-month paliperidone palmitate compared with placebo in delaying time to first occurrence of relapse symptoms of schizophrenia.

In March 2014, Janssen announced that following an Independent Data Monitoring Committee (IDMC) recommendation based on positive efficacy, it halted the Phase 3 clinical study of paliperidone palmitate three-month formulation early. The recommendation to stop and unblind the clinical study at the interim analysis was made by the IDMC based on pre-specified criteria, specifically achieving a statistically significant difference from placebo in delaying time to relapse. Based on this study, the safety profile of paliperidone palmitate three-month formulation is consistent with that of once-monthly INVEGA® SUSTENNA® (paliperidone palmitate). The full study results will be presented at future medical congresses and are being submitted for publication in a peer-reviewed journal.

While there is no cure for the illness, individuals with schizophrenia, working with their treatment teams, can lead meaningful lives with a treatment regimen that may include medication, psychotherapy, and other interventions. Patients with acute illness often do not have insight about schizophrenia, which contributes to their not taking medication or using treatment services. Medication, including daily pills or long-acting therapy, is the mainstay of treatment for symptoms. Relapses are often caused by not taking enough of or completely stopping prescribed antipsychotic medication.

INVEGA® SUSTENNA® (paliperidone palmitate) was approved by the U.S. FDA in July 2009 as the first once-monthly atypical long-acting injection to treat schizophrenia and is now approved in more than 80 countries. Efficacy was established in four short-term studies and one longer-term study in adults. Janssen Pharmaceuticals, Inc. markets INVEGA SUSTENNA in the United States.

INVEGA® SUSTENNA® and three-month paliperidone palmitate utilize Alkermes' proprietary NanoCrystal® technology, which enables solubility of poorly water-soluble compounds.

About Janssen Research & Development, LLC
Janssen Research & Development, LLC, is headquartered in Raritan, N.J. and has affiliated facilities in Europe, the United States and Asia. Driven by its commitment to patients, Janssen R&D works to bring innovative ideas, products, services and solutions to address serious unmet medical needs around the world. The company is leveraging a combination of internal and external innovation to discover and develop novel medicines and solutions in five distinct therapeutic areas: Neuroscience, Oncology, Immunology, Infectious Diseases and Vaccines, and Cardiovascular and Metabolism. For more information about Janssen Research & Development, LLC visit www.janssenrnd.com.

About Janssen Pharmaceuticals, Inc.
Janssen Pharmaceuticals, Inc. is dedicated to addressing and resolving the major unmet medical needs of our time. Driven by its commitment to patients, healthcare professionals, and caregivers, Janssen strives to develop sustainable and integrated healthcare solutions by working in partnership with all stakeholders on the basis of trust and transparency. The company's daily work is guided by meeting goals of excellence in quality, innovation, safety, and efficacy in order to advance patient care. Janssen provides medicines for an array of illnesses and disorders in several therapeutic areas. For more information on Janssen Pharmaceuticals, Inc., visit www.JanssenPharmaceuticalsInc.com or follow Janssen on Twitter at www.twitter.com/JanssenUS and on YouTube at www.YouTube.com/JanssenUS.

Janssen Pharmaceuticals, Inc. and Janssen Research & Development, LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

INVEGA® SUSTENNA® (paliperidone palmitate) is indicated for the treatment of schizophrenia.

IMPORTANT SAFETY INFORMATION FOR INVEGA® SUSTENNA® (paliperidone palmitate)

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS.

See full Prescribing Information for complete Boxed Warning

- Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death
- INVEGA® SUSTENNA® is not approved for the treatment of patients with dementia-related Psychosis

Contraindications: Paliperidone is contraindicated in patients with a known hypersensitivity to either paliperidone, risperidone, or to any excipients of the formulation.

Cerebrovascular Adverse Reactions: Cerebrovascular adverse reactions (e.g., stroke, transient ischemic attacks), including fatalities, were reported in placebo-controlled trials in elderly patients with dementia-related psychosis taking oral risperidone, aripiprazole, and olanzapine. The incidence of cerebrovascular adverse reactions was significantly higher than with placebo. INVEGA® SUSTENNA® is not approved for the treatment of patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome (NMS): NMS, a potentially fatal symptom complex, has been reported with the use of antipsychotic medications, including paliperidone. Clinical manifestations include muscle rigidity, fever, altered mental status, and evidence of autonomic instability (see full Prescribing Information). Management should include immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, intensive symptomatic treatment and close medical monitoring, and treatment of any concomitant serious medical problems.

QT Prolongation: Paliperidone causes a modest increase in the corrected QT (QTc) interval. Avoid the use of drugs that also increase QTc interval and in patients with risk factors for prolonged QTc interval. Paliperidone should also be avoided in patients with congenital long QT syndrome and in patients with a history of cardiac arrhythmias. Certain circumstances may increase the risk of the occurrence of torsades de pointes and/or sudden death in association with the use of drugs that prolong the QTc interval.

Tardive Dyskinesia (TD): TD is a syndrome of potentially irreversible, involuntary, dyskinetic movements that may develop in patients treated with antipsychotic medications. The risk of developing TD and the likelihood that dyskinetic movements will become irreversible are believed to increase with duration of treatment and total cumulative dose, but can develop after relatively brief treatment at low doses. Elderly female patients appeared to be at increased risk for TD, although it is impossible to predict which patients will develop the syndrome. Prescribing should be consistent with the need to minimize the risk of TD (see full Prescribing Information). Discontinue drug if clinically appropriate. The syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn.

Metabolic Changes: Atypical antipsychotic drugs have been associated with metabolic changes that may increase cardiovascular/cerebrovascular risk. These metabolic changes include hyperglycemia, dyslipidemia, and body weight gain. While all of the drugs in the class have been shown to produce some metabolic changes, each drug has its own specific risk profile.

Hyperglycemia and Diabetes Mellitus: Hyperglycemia and diabetes mellitus, in some cases extreme and associated with ketoacidosis, hyperosmolar coma or death, have been reported in patients treated with all atypical antipsychotics (APS). Patients starting treatment with APS who have or are at risk for diabetes mellitus should undergo fasting blood glucose testing at the beginning of and during treatment. Patients who develop symptoms of hyperglycemia during treatment should also undergo fasting blood glucose testing. All patients treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia. Some patients require continuation of antidiabetic treatment despite discontinuation of the suspect drug.

Dyslipidemia: Undesirable alterations have been observed in patients treated with atypical antipsychotics.

Weight Gain: Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended.

Orthostatic Hypotension and Syncope: INVEGA® SUSTENNA® may induce orthostatic hypotension in some patients due to its alpha-blocking activity. INVEGA® SUSTENNA® should be used with caution in patients with known cardiovascular disease, cerebrovascular disease or conditions that would predispose patients to hypotension (e.g., dehydration, hypovolemia, treatment with antihypertensive medications). Monitoring should be considered in patients for whom this may be of concern.

Leukopenia, Neutropenia and Agranulocytosis have been reported with antipsychotics, including paliperidone. Patients with a history of clinically significant low white blood cell count (WBC) or drug-induced leukopenia/neutropenia should have frequent complete blood cell counts during the first few months of therapy. At the first sign of a clinically significant decline in WBC, and in the absence of other causative factors, discontinuation of INVEGA® SUSTENNA® should be considered. Patients with clinically significant neutropenia should be carefully monitored for fever or other symptoms or signs of infection and treated promptly if such symptoms or signs occur. Patients with severe neutropenia (absolute neutrophil count &< 1000/mm3) should discontinue INVEGA® SUSTENNA® and have their WBC followed until recovery.

Hyperprolactinemia: As with other drugs that antagonize dopamine D2 receptors, INVEGA® SUSTENNA® elevates prolactin levels, and the elevation persists during chronic administration. Paliperidone has a prolactin-elevating effect similar to risperidone, which is associated with higher levels of prolactin elevation than other antipsychotic agents.

Potential for Cognitive and Motor Impairment: Somnolence, sedation, and dizziness were reported as adverse reactions in subjects treated with INVEGA® SUSTENNA®. INVEGA® SUSTENNA® has the potential to impair judgment, thinking, or motor skills. Patients should be cautioned about performing activities that require mental alertness such as operating hazardous machinery, including motor vehicles, until they are reasonably certain that INVEGA® SUSTENNA® does not adversely affect them.

Seizures: INVEGA® SUSTENNA® should be used cautiously in patients with a history of seizures or with conditions that potentially lower seizure threshold. Conditions that lower seizure threshold may be more prevalent in patients 65 years or older.

Administration: For intramuscular injection only by a healthcare professional. Care should be taken to avoid inadvertent injection into a blood vessel.

Drug Interactions: Strong CYP3A4/P-glycoprotein (P-gp) inducers: It may be necessary to increase the dose of INVEGA® SUSTENNA® when a strong inducer of both CYP3A4 and P-gp (e.g. carbamazepine, rifampin, St. John's wort) is co-administered. Conversely, on discontinuation of the strong inducer, it may be necessary to decrease the dose of INVEGA® SUSTENNA®.

Pregnancy/Nursing: Patients should be advised to notify their physician if they become pregnant/intend to become pregnant or intend to nurse during treatment with INVEGA® SUSTENNA®.

Commonly Observed Adverse Reactions for INVEGA® SUSTENNA®: The most common adverse reactions in clinical trials in patients with schizophrenia (&> 5% and twice placebo) were injection site reactions, somnolence/sedation, dizziness, akathisia and extrapyramidal disorder.
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(This press release contains "forward-looking statements," as defined in the Private Securities Litigation Reform Act of 1995 regarding product development. 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 or Johnson & Johnson. Risks and uncertainties include, but are not limited to, challenges and difficulties inherent in new product development, including obtaining regulatory approvals; competition, including technological advances, new products and patents attained by competitors; changes to regulations and domestic and foreign health care reforms; and trends toward health care cost containment. A further list and description of 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, 2013, including in Exhibit 99 thereto, and in its 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 or Johnson & Johnson undertakes to update any forward-looking statements as a result of new information or future events or developments.)

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