NEWS RELEASE

New Study Published in JAMA Psychiatry Found Three-Month Paliperidone Palmitate Significantly Delayed Time to Relapse in Patients with Schizophrenia

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TITUSVILLE, N.J., March 29, 2015 /PRNewswire/ -- Three-month paliperidone palmitate, an investigational atypical antipsychotic, significantly delayed time to relapse compared to placebo in patients with schizophrenia, according to a new Phase 3 clinical study published this week in the **Journal of the American Medical Association (JAMA) Psychiatry**. Results of the study served as the basis for the recent New Drug Application (NDA) filing for three-month paliperidone palmitate injection to treat schizophrenia in adults with the U.S. Food and Drug Administration ("FDA") by Janssen Research & Development, LLC, ("Janssen"), the study sponsor. The FDA granted the filing Priority Review status in January, with a regulatory action date of May 18, 2015.

If approved, the treatment would enable patients to receive injections once every three months, compared to currently available formulations that are administered monthly, or oral medicines that must be taken daily. It would be the first and only long-acting atypical antipsychotic with a dosing schedule of four times a year. Janssen plans filings for three-month paliperidone palmitate in many markets outside of the U.S. later this year.

The final published analysis results are consistent with previously announced **interim analysis results** which showed a statistically significant benefit of three-month paliperidone palmitate compared to placebo. In March 2014, following an Independent Data Monitoring Committee (IDMC) recommendation based on positive efficacy, Janssen halted this study early.

The study data also are being presented this week at the 23rd annual European Congress of Psychiatry in Vienna, Austria, and at the 15th annual International Congress on Schizophrenia Research in Colorado Springs, Colorado.

"There remains significant unmet need for the approximately 2.4 million people in the United States who live with schizophrenia. The results of this study reinforce the need for this unprecedented treatment option for patients with schizophrenia who may benefit from a new, less frequently dosed treatment choice," said Husseini K. Manji, MD, Global Head, Neuroscience Therapeutic Area, Janssen. "We look forward to continuing to work with the FDA and other regulatory authorities to bring this innovative three-month formulation to patients as soon as possible."

"Physicians need a broad range of treatments to help patients with schizophrenia early in the course of their disease," said David Hough, MD, Schizophrenia Disease Area Leader, Janssen, a study author. "This clinical trial showed three-month paliperidone palmitate demonstrated a statistically significant difference from placebo in delaying time to relapse, validating its potential as a new treatment option which could positively affect the care of people with schizophrenia."

This Phase 3, international, randomized, multicenter, double-blind, placebo-controlled, relapse prevention study evaluated 305 adults in the double-blind phase. There were 160 study patients in the three-month paliperidone palmitate treatment group and 145 patients in the placebo group. All of the patients enrolled in the study met the DSM-IV diagnosis of schizophrenia and had a Positive and Negative Syndrome Scale (PANSS) total score of less than 120 at screening and baseline. Prior to randomization, individuals were first stabilized with INVEGA SUSTENNA® (paliperidone palmitate) one-month formulation during a 17-week, open-label transition period. Patients who met criteria for clinical stability then received a single three-month paliperidone palmitate injection during a 12-week, open-label maintenance phase. Stable patients were then randomized to treatment with either three-month paliperidone palmitate or placebo. Patients remained in the double-blind phase until they relapsed, withdrew from the study, or the study terminated.

Relapse was defined as worsening schizophrenia symptoms as determined by PANSS assessment criteria, hospitalization for schizophrenia symptoms, clinically significant self-injury, suicidal or homicidal ideation or violent behavior.

After the first 42 relapse events occurred in the double-blind phase, a pre-specified interim analysis overseen by an IDMC showed that three-month paliperidone palmitate significantly delayed time to relapse compared to placebo (hazard ratio [HR] 3.45; 95% CI: 1.73-6.88; p=0.0002; median time to relapse for placebo group: 274 days). While there were 11 relapses in the three-month paliperidone palmitate treatment group, these were too few to provide a reliable estimate of the duration of time until relapse for that group of patients. Final analysis results were consistent with that of the interim analysis, confirming three-month paliperidone palmitate's superiority over placebo for delaying time to relapse of schizophrenia symptoms (HR 3.81; 95% CI: 2.08-6.99; p<0.0001; median time

to relapse for placebo group: 395 days, and three-month paliperidone palmitate group: not estimable).

In this study, the most common treatment-emergent adverse events (TEAEs), which occurred in at least 3% of patients in the double-blind phase of the study and that occurred more frequently in the three-month paliperidone palmitate group than placebo group, were headache (9% vs. 4%), increased weight (9% vs. 3%), nasopharyngitis (6% vs. 1%) and akathisia, a movement disorder (4% vs. 1%). During the double-blind phase, a total of 6 patients (4%) in the three-month paliperidone palmitate group reported injection site-related TEAEs; of which, injection site pain (2 patients [1%]) was most frequently reported. Prolactin-related TEAEs occurred in 1 of 42 female patients in the three-month paliperidone palmitate group (2%). Serious TEAEs occurred 4 times more often in the placebo group than in the three-month paliperidone palmitate group (10% vs. 3%), and were mostly related to an increase in psychiatric symptoms reflecting the course of the underlying disease.

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. Late last year the FDA approved INVEGA SUSTENNA® for the treatment of schizoaffective disorder, making it the first and only once-monthly medication to treat this condition. INVEGA SUSTENNA® and three-month paliperidone palmitate utilize Alkermes' proprietary NanoCrystal® technology, which enables solubility of poorly water-soluble compounds.

For additional study information, visit **ClinicalTrials.gov**.

About INVEGA SUSTENNA®

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About Schizophrenia

Schizophrenia is a complex and chronic brain disorder that can be severe and disabling. It affects approximately 2.4 million U.S. adults, often beginning in the late teens or early 20s. The disease typically manifests as hallucinations, delusions, and disorganized thoughts and behavior. Because there are currently no physical or laboratory tests that diagnose this condition, schizophrenia is diagnosed by the presence of symptoms. Researchers have identified various risk factors for this disease, including heredity and certain genetic risk factors, and environmental factors, such as social stress, isolation and drug use. 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.

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 Research & Development 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. Also 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 **https://www.youtube.com/user/JanssenUS**.

Janssen Pharmaceuticals, Inc. and Janssen Research & Development, LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson. Janssen Pharmaceuticals, Inc. markets INVEGA SUSTENNA® in the United States.

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

- Schizophrenia.
- Schizoaffective disorder as monotherapy and as an adjunct to mood stabilizers or antidepressants.

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. No adverse events occurred at a rate of =5% and twice placebo during the long-term double-blind, placebo-controlled study in patients with schizoaffective disorder. The following adverse reactions occurred more frequently (a =2% difference vs. placebo) in the long-term study in patients with schizoaffective disorder: weight increased, nasopharyngitis, headache, hyperprolactinemia, and pyrexia.

Please see full Prescribing Information including Boxed Warning for INVEGA SUSTENNA® (paliperidone palmitate) and INVEGA® (paliperidone) at **www.JanssenCNS.com/InvegaSustenna** and **www.JanssenCNS.com/Invega**.

(This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development. 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 and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges inherent in new product development, including obtaining regulatory approvals; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes to applicable laws and regulations, including global health care reforms; and trends

toward health care cost containment. A further list and description 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 28, 2014, including in Exhibit 99 thereto, 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 or Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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