



Phase 3 Data Demonstrate Efficacy and Tolerability of Paliperidone Palmitate, an Investigational Long-Acting Therapy for the Treatment of Schizophrenia

Results of Two Trials Identify Potential Initiation Dosing Regimen

Titusville, NJ, December 9, 2008 - Paliperidone palmitate, an investigational long-acting therapy (LAT) demonstrated statistically significant symptom control compared with placebo according to the results of a 13-week study presented today.¹ Statistical significance was evidenced at all doses tested (25, 100, and 150 mg equivalent [eq.^a]), when given every 4 weeks with a 150 mg eq. initiation dose. A separate 53-week non-inferiority trial^b evaluating paliperidone palmitate using only a 50 mg eq. initiation dose, and subsequent doses of 25, 50, 75, and 100 mg eq., showed that while paliperidone palmitate reduced symptoms, non-inferiority relative to risperidone LAT was not demonstrated. Safety findings in both trials were similar to those from previously published studies of paliperidone extended-release (ER) tablets in the treatment of schizophrenia.^{2,3} Based on these results, an additional phase III study is being conducted to further assess the higher initiation dosing regimen of paliperidone palmitate 150 mg eq. followed by a second injection of 100 mg eq. with subsequent injections every four weeks.

Paliperidone palmitate, an investigational LAT, is a formulation of the oral antipsychotic paliperidone ER, used for the acute and maintenance treatment of schizophrenia. Because of the delivery systems used, LAT formulations may produce more consistent levels of the drug in the blood and provide healthcare professionals with reassurance that patients are receiving their medication as scheduled. The two studies add more information to the body of evidence for paliperidone palmitate in the treatment of schizophrenia.

In the 13-week trial, patients were randomly assigned to receive either paliperidone palmitate 25, 100 or 150 mg eq. injection or placebo. On day 1, all patients randomly assigned to any of the paliperidone palmitate treatment groups received a 150 mg eq. injection in the deltoid muscle. On day 8 and every 4 weeks for the duration of the trial they received the randomly assigned fixed dose (25, 100 or 150 mg eq.) in the deltoid or gluteal muscle. The primary endpoint of the trial was change in PANSS^c total score from baseline to endpoint.

The results showed that with the 150 mg eq. initiation dose, patients taking paliperidone palmitate at any of the three doses (25, 100, or 150 mg eq.) had significantly improved symptoms, based on the primary outcome parameter of change in PANSS total scores, compared to patients on placebo ($p \leq 0.034$). Symptoms improved with increased dosage, with those taking the 150 mg eq. dose showing the greatest improvement. Overall treatment-emergent adverse events (TEAEs) occurred at similar rates among the paliperidone palmitate (60-63%) and placebo (65%) groups. The number of patients who reported serious TEAEs was higher in the placebo group (14%) than in any of the paliperidone palmitate groups (25 mg eq. 9.4%; 100 mg eq. 13.3%; 150 mg eq. 8.0%). Common TEAEs occurring $\geq 2\%$ more frequently in the total paliperidone palmitate group compared to the placebo group were injection site pain (placebo, 3.7% vs 7.6% with paliperidone palmitate), dizziness (placebo 1.2% vs 2.5% with paliperidone palmitate), sedation (placebo 0.6% vs 2.3% with paliperidone palmitate), pain in extremity (placebo 0% vs 1.6% with paliperidone palmitate) and myalgia (placebo 0% vs 1.0% with paliperidone palmitate). The overall safety profile was similar to previously published studies of paliperidone ER in the treatment of schizophrenia.^{1,2}

The authors concluded that using a 150 mg eq. deltoid initiation dose followed by subsequent injections every 4 weeks of 25-150 mg eq. of paliperidone palmitate produced statistically significant symptom control as measured by the PANSS total score.

In the 53-week non-inferiority trial, patients were randomly assigned to receive flexible dose paliperidone palmitate plus orally supplemented placebo (PP+Pbo) or flexible dose risperidone LAT plus orally supplemented risperidone (LAT RIS+RIS). All injections were administered in the gluteal muscle. Patients in the PP+Pbo group received two 50 mg eq. injections one week apart, followed by injections of 25, 50, 75 or 100 mg eq. every 4 weeks. Patients in the LAT RIS+RIS group received a placebo injection on day 1, 25 mg risperidone LAT on days 8 and 22 and injections every 2 weeks of 25, 37.5 or 50 mg. The primary endpoint was the change in PANSS total score from baseline to endpoint. Non-inferiority was planned to be demonstrated if paliperidone palmitate was no worse than risperidone LAT, as measured by a 95% confidence interval of more than -5 points in the change in PANSS total score.

Although patients receiving both paliperidone palmitate and risperidone LAT had similar improvements in PANSS scores at the end of the 53 week trial, the difference between paliperidone palmitate and risperidone LAT in the least square adjusted mean change in PANSS score was -2.6 points, with a 95% confidence interval (CI) of (-5.84, 0.61). As the lower limit (-5.84) of the CI was less than -5, non-inferiority of paliperidone palmitate versus risperidone LAT was not demonstrated using this dosing regimen. Comparative plasma concentrations of paliperidone in the PP+Pbo group were consistently lower than concentrations of active moiety in the LAT RIS+RIS group until day 260. Although non-inferiority was not demonstrated using this dosing regimen, it is not possible to conclude superiority of LAT RIS+RIS over PP+Pbo using the results from this study. Overall rates of adverse events were similar in both groups: 76% for paliperidone palmitate and 79% for risperidone LAT. The most common

(>10% in either group) TEAEs among the reported psychiatric disorders were insomnia (both groups 15%), psychotic disorder (PP+Pbo 14%; RIS+RIS 12%) schizophrenia (PP+Pbo 12%; RIS+RIS 9%) and anxiety (PP+Pbo 10%; RIS+RIS 15%). Adverse events leading to discontinuation occurred in 7% of PP+Pbo patients and 6% of LAT RIS+RIS patients. Based on these results, an additional phase III study is being conducted to further assess the dosing regimen of paliperidone palmitate 150 mg eq. followed by a second injection of 100 mg eq. with subsequent injections every four weeks, compared with risperidone LAT.

"These findings will help us determine the best dosing strategy for paliperidone palmitate in the treatment of schizophrenia," said lead author, Professor Wolfgang Fleischhacker, Dept of Psychiatry and Psychotherapy, Medical University Innsbruck*. "This could provide a valuable option for healthcare professionals to help people who are struggling with this illness."

INVEGA® (paliperidone) Extended-Release Tablets, the oral formulation of paliperidone, was first approved in 2006 in the U.S. for the acute treatment of schizophrenia. In March 2007, INVEGA was approved for the maintenance treatment of schizophrenia in the U.S. It was also approved for the treatment of schizophrenia in the European Union in June 2007.

Worldwide, it is estimated that one person in every 100 develops schizophrenia, one of the most serious types of mental illness.⁴ An estimated 2.4 million Americans have schizophrenia, with men and women affected equally.⁴ The disease is marked by positive symptoms (hallucinations and delusions) and negative symptoms (depression, blunted emotions, and social withdrawal), as well by disorganized thinking, speech and behavior.

The study was sponsored by Johnson & Johnson Pharmaceutical Research and Development, L.L.C. (J&JPRD). Once approved, Janssen, Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc. will market paliperidone palmitate in the U.S.

* Professor Wolfgang Fleischhacker has been a consultant, served on advisory boards and received research grants from J&JPRD and Janssen, Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc.

About Johnson & Johnson Pharmaceutical Research & Development, L.L.C.

Johnson & Johnson Pharmaceutical Research & Development, L.L.C. (J&JPRD) is headquartered in Raritan, New Jersey (USA), and has nine sites throughout Europe and the United States. J&JPRD employs approximately 3,500 people and is leveraging drug discovery, drug evaluation and drug development in a variety of therapeutic areas to address unmet medical needs worldwide. The company's major therapeutic areas of focus include hematology, oncology, infectious disease, obesity and metabolic disorders, neurology and psychiatry, pain and women's health.

About Janssen

Janssen, Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc., based in Titusville, N.J., is the only large pharmaceutical company in the U.S. dedicated solely to mental health. As the company celebrates its 50th year in mental health, it currently markets prescription medications for the treatment of schizophrenia, bipolar mania and the treatment of symptoms associated with autistic disorder. For more information about Janssen, visit www.janssen.com.

J&JPRD and Janssen are subsidiaries of Johnson & Johnson.

(This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or unknown risks or uncertainties materialize, actual results could vary materially from the Company's expectations and projections. Risks and uncertainties include general industry conditions and competition; economic conditions, such as interest rate and currency exchange rate fluctuations; technological advances and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approvals; domestic and foreign health care reforms and governmental laws and regulations; and trends toward health care cost containment. A further list and description of these risks, uncertainties and other factors can be found in Exhibit 99 of Johnson & Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended December 30, 2007. Copies of this Form 10-K, as well as subsequent filings, are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. The Company does not undertake to update any forward-looking statements as a result of new information or future events or developments.)

IMPORTANT SAFETY INFORMATION FOR INVEGA® (PALIPERIDONE)

Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Paliperidone is not approved for the treatment of patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome (NMS) is a rare and potentially fatal side effect reported with paliperidone and similar medicines. Call your doctor immediately if the person being treated develops symptoms such as high fever; stiff muscles; shaking; confusion; sweating; changes in pulse, heart rate, or blood pressure; or muscle pain and weakness. Treatment should be stopped if the person being treated has NMS.

One risk of paliperidone is that it may change your heart rhythm. This effect is potentially serious, and you should talk to your doctor about any current or past heart problems. Some medications interact with paliperidone. Please inform your healthcare professional of any medications or supplements that you are taking.

Tardive Dyskinesia (TD) is a serious, sometimes permanent side effect reported with paliperidone and similar medications. TD includes uncontrollable movements of the face, tongue, and other parts of the body. The risk of developing TD and the chance that it will become permanent is thought to increase with the length of therapy and the overall dose taken by the patient. This condition can develop after a brief period of therapy at low doses, although this is much less common. There is no known treatment for TD, but it may go away partially or completely if therapy is stopped.

High blood sugar and diabetes have been reported with paliperidone and similar medications. If the person being treated has diabetes or risk factors such as being overweight or a family history of diabetes, blood sugar testing should be performed at the beginning and throughout treatment with paliperidone. Complications of diabetes can be serious and even life threatening. If signs of high blood sugar or diabetes develop, such as being thirsty all the time, going to the bathroom a lot, or feeling weak or hungry, contact your doctor.

Paliperidone and similar medications can raise the blood levels of a hormone known as prolactin, causing a condition known as hyperprolactinemia. Blood levels of prolactin remain elevated with continued use. Some side effects seen with these medications include the absence of a menstrual period; breasts producing milk; the development of breasts by males; and the inability to achieve an erection. The connection between prolactin levels and side effects is unknown.

People with narrowing or blockage of the gastrointestinal tract (esophagus, stomach or small or large intestine) should talk to their healthcare professional before taking paliperidone.

Some people taking paliperidone may feel faint or lightheaded when they stand up or sit up too quickly. By standing up or sitting up slowly and following your healthcare professional's dosing instructions, this side effect may be reduced or it may go away over time.

Paliperidone may affect your driving ability; therefore, do not drive or operate machinery before talking to your healthcare professional. Avoid alcohol while on paliperidone.

Paliperidone should be used cautiously in people with a seizure disorder, who have had seizures in the past, or who have conditions that increase their risk for seizures.

Extrapyramidal Symptoms (EPS) are usually persistent movement disorders or muscle disturbances, such as restlessness, tremors, and muscle stiffness. If you observe any of these symptoms, talk to your healthcare professional.

Inform your healthcare professional if you are pregnant or if you are planning to get pregnant while taking paliperidone. Caution should be exercised when paliperidone is administered to a nursing woman.

Paliperidone may affect alertness and motor skills; use caution until the effect of paliperidone is known.

Paliperidone may make you more sensitive to heat. You may have trouble cooling off, or be more likely to become dehydrated, so take care when exercising or when doing things that make you warm.

Paliperidone should be swallowed whole. Tablets should not be chewed, divided, or crushed. Do not be worried if you see something that looks like a tablet in your stool. This is what is left of the tablet after all the medicine has been released.

The most common side effects that occurred with paliperidone were restlessness and extrapyramidal disorder (for example, involuntary movements, tremors and muscle stiffness).

References

¹Marder SR, Kramer M, Ford L, Eerdekens E, Lim P, Eerdekens M, Lowy A. Efficacy and safety of paliperidone extended-release tablets: results of a 6-week, randomized, placebo-controlled study. *Biol Psychiatry*. 2007 Dec 15;62(12):1363-70

²Davidson M, et al. *Schizophr Res*. 2007; 93(1-3): 117-130

³Kane J, et al. *Schizophr Res* 2007; 90 (1-3):147-161

⁴Royal College of Psychiatrists website: <http://www.rcpsych.ac.uk/default.aspx?page=1643> Accessed April 14, 2008

⁵American Psychiatric Association. Let's talk facts about schizophrenia. Available at: <http://healthyminds.org/factsheets/LTF-Schizophrenia.pdf> Accessed April 1, 2008.

^aPaliperidone palmitate doses are expressed as mg equivalent (eq.) of paliperidone, where 156 mg of paliperidone palmitate is equivalent to 100 mg of paliperidone.

^bNon-inferiority trials aim to show that a new treatment is not clinically less effective than a standard treatment by more than a pre-specified margin.

^cPositive and Negative Syndrome Scale (PANSS) is a standard rating scale used in trials to assess the severity of symptoms. The scale consists of 30 items, which are assessed from absent to extreme, and these are divided into both positive and negative symptoms

Contacts:

Media

Kara Russell:
(609) 730-3592

Investors

Louise Mehrotra:
(732) 524-6491
Johnson & Johnson

Lesley Fishman:
(732) 524-3922
Johnson & Johnson