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# News Release

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## Sunovion Pharmaceuticals Inc. Announces Positive Results for Latuda® (lurasidone HCl) in First Placebo-Controlled Trial of Patients with Major Depressive Disorder with Mixed (Subsyndromal Hypomanic) Features

*Phase 3 Study Meets Primary and Secondary Efficacy Endpoints*

**Marlborough, Mass., May 19, 2015** – Sunovion Pharmaceuticals Inc. (Sunovion) today announced results from the first placebo-controlled study in adults with major depressive disorder (MDD) who presented with a limited number of associated manic symptoms (mixed features). This study demonstrated that Latuda® (lurasidone HCl) significantly reduced depressive symptoms in adults with MDD with mixed features when compared to placebo. The study results were presented at the 168th Annual Meeting of the American Psychiatric Association (APA). LATUDA is an atypical antipsychotic agent indicated in the United States for the treatment of adult patients with major depressive episodes associated with bipolar I disorder (bipolar depression) both as monotherapy and as adjunctive therapy with lithium or valproate, and for the treatment of adult patients with schizophrenia.

"The presence of manic symptoms in patients with MDD is associated with greater levels of anxiety, increased risk for suicide attempt, substance abuse and functional disability," said Gary Sachs, M.D., Founding Director of the Bipolar Clinic and Research Program at Massachusetts General Hospital in Boston, Massachusetts. "This novel study provides the first placebo-controlled evidence of an effective treatment in this patient population."

In this randomized, double-blind, placebo-controlled, 6-week clinical trial, adults patients with MDD with a limited number of manic symptoms (mixed features) were randomized to receive 6 weeks of treatment with flexibly-dosed LATUDA 20 – 60 mg/day (N=109) or placebo (N=102). The primary efficacy endpoint in the study was change from baseline at Week 6 in Montgomery-Asberg Depression Rating Scale (MADRS) total score. The key secondary endpoint was change from baseline at Week 6 in the Clinical Global Impression, Severity (CGI-S) score, which assessed global severity of illness.

Results from the study showed that treatment with LATUDA was associated with a statistically significant reduction in MADRS total scores at the end of the study (Week 6) compared with placebo (-20.5 vs. -13.0; $p<0.0001$; Cohen's d effect size=0.80), with separation from placebo starting at the first post-baseline assessment (Week 1). In addition, patients treated with LATUDA experienced a statistically significant reduction in change from baseline at Week 6 in CGI-S scores compared with placebo (-1.83 vs. -1.18;

p<0.0001; Cohen's d effect size=0.60), with separation from placebo starting at Week 2, as well as significant differences from placebo on all other secondary efficacy endpoints, including manic symptoms (based on Young Mania Rating Scale assessment).

LATUDA was generally well-tolerated with low rates of change in weight and metabolic parameters and had an overall discontinuation rate that was lower than placebo (6.4% vs. 14.7%). The most common adverse events (AEs) reported with an incidence ≥ 5% and greater than placebo in patients receiving LATUDA vs. placebo were nausea (6.4% vs. 2.0%) and somnolence (including the combined terms hypersomnia, hypersomnolence, sedation and somnolence) (5.5% vs. 1.0%).

"These results demonstrate that LATUDA significantly reduced depressive symptoms in adult patients with an often severe form of depression, MDD with mixed features," said Antony Loebel, M.D., Executive Vice President and Chief Medical Officer, Sunovion Pharmaceuticals Inc., Head of Global Clinical Development for Sumitomo Dainippon Pharma Group. "We believe this is an important finding as patients with this condition may not respond adequately to standard antidepressant treatment."

**About Major Depressive Disorder with Mixed Features**

Research suggests that manic symptoms below the threshold criteria for hypomania (mixed features) occurs in at least 25% of individuals with MDD.[1,2] Patients with MDD with mixed features often have greater symptom severity and higher rates of depressive episode recurrence, inadequate treatment response to standard antidepressants, increased risk for suicide attempt, anxiety disorders and substance abuse, and greater overall associated disability.[1,2,3,4,5,6,7] Patients with MDD with mixed features have an increased risk for the development of a future bipolar disorder diagnosis.[8] Given increased understanding regarding this form of depression, the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders introduced a new "mixed features" specifier for patients who present with a limited set of manic symptoms during a major depressive episode.[9] To date, no controlled trials have been conducted for psychotropic agents in this patient population.[8]

**About LATUDA**

LATUDA is used to treat adult patients with:

- Depressive episodes associated with bipolar I disorder (bipolar depression) when used alone or with lithium or valproate
- Schizophrenia

The efficacy of LATUDA was established in a 6-week monotherapy study and a 6-week adjunctive therapy study with lithium or valproate in adult patients with bipolar depression. The efficacy of LATUDA in the treatment of adult patients with schizophrenia was established in five 6-week controlled studies. The effectiveness of LATUDA for longer-term use, that is, for more than 6 weeks, has not been established in controlled studies. Therefore, the physician who elects to use LATUDA for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient. The efficacy of LATUDA in the treatment of mania associated with bipolar disorder has not been established.

The most common side effects of LATUDA include sleepiness or drowsiness; restlessness or feeling like you need to move around (akathisia); difficulty moving, slow movements, muscle stiffness or tremor; and nausea.

LATUDA is available in five tablet strengths: 20 mg, 40 mg, 60 mg, 80 mg and 120 mg.

Please see Important Safety Information, including **Boxed Warnings,** below and full Prescribing Information at www.LATUDA.com.

**IMPORTANT SAFETY INFORMATION AND INDICATIONS FOR LATUDA**

**INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS; AND SUICIDAL THOUGHTS AND BEHAVIORS**

- **Elderly patients with dementia-related psychosis (having lost touch with reality due to confusion and memory loss) treated with this type of medicine are at an increased risk of death compared to patients receiving placebo (sugar pill). LATUDA is not approved for treating elderly patients with dementia-related psychosis.**
- **Antidepressants have increased the risk of suicidal thoughts and actions in some children, teenagers, and young adults. Patients of all ages starting treatment should be watched closely for worsening of depression, suicidal thoughts or actions, unusual changes in behavior, agitation, and irritability. Patients, families, and caregivers should pay close attention to any changes, especially sudden changes in mood, behaviors, thoughts, or feelings. This is very important when an antidepressant medicine is started or when the dose is changed. Report any change in these symptoms immediately to the doctor. LATUDA is not approved for patients under the age of 18 years.**

LATUDA can cause serious side effects, including stroke that can lead to death, which can happen in elderly people with dementia who take medicines like LATUDA.

Neuroleptic malignant syndrome (NMS) is a rare but very serious condition that can happen in people who take antipsychotic medicines, including LATUDA. NMS can cause death and must be treated in a hospital. Call your healthcare provider right away if you become severely ill and have some or all of these symptoms: high fever, excessive sweating, rigid muscles, confusion, or changes in your breathing, heartbeat, or blood pressure.

Tardive dyskinesia (TD) is a serious and sometimes permanent side effect reported with LATUDA and similar medicines. Tell your doctor about any movements you cannot control in your face, tongue, or other body parts, as they may be signs of TD. TD may not go away, even if you stop taking LATUDA. TD may also start after you stop taking LATUDA.

Increases in blood sugar can happen in some people who take LATUDA. Extremely high blood sugar can lead to coma or death. If you have diabetes or risk factors for diabetes (such as being overweight or a family history of diabetes), your healthcare provider should check your blood sugar before you start LATUDA and during therapy. Call your healthcare provider if you have any of these symptoms of high blood sugar (hyperglycemia) while taking LATUDA: feel very thirsty, need to urinate more than usual, feel very hungry, feel weak or tired, feel sick to your stomach, feel confused, or your breath smells fruity.

Increases in triglycerides and LDL (bad) cholesterol and decreases in HDL (good) cholesterol have been reported with LATUDA. You may not have any symptoms, so your healthcare provider may decide to check your cholesterol and triglycerides during your treatment with LATUDA.

Some patients may gain weight while taking LATUDA. Your doctor should check your weight regularly. Tell your doctor if you experience any of these:

- feeling dizzy or light-headed upon standing,
- decreases in white blood cells (which can be fatal),
- trouble swallowing.

LATUDA and medicines like it may raise the level of prolactin. Tell your healthcare provider if you experience a lack of menstrual periods, leaking or enlarged breasts, or impotence.

Tell your healthcare provider if you have a seizure disorder, have had seizures in the past, or have conditions that increase your risk for seizures.

Tell your healthcare provider if you experience prolonged, abnormal muscle spasms or contractions, which may be a sign of a condition called dystonia.

LATUDA can affect your judgment, thinking, and motor skills. You should not drive or operate hazardous machinery until you know how LATUDA affects you.

LATUDA may make you more sensitive to heat. You may have trouble cooling off. Be careful when exercising or when doing things likely to cause dehydration or make you warm.

Avoid eating grapefruit or drinking grapefruit juice while you take LATUDA since these can affect the amount of LATUDA in the blood.

Tell your healthcare provider about all prescription and over-the-counter medicines you are taking or plan to take, since there are some risks for drug interactions with LATUDA. Tell your healthcare provider if you are allergic to any of the ingredients of LATUDA or take certain medications called CYP3A4 inhibitors or inducers. Ask your healthcare provider if you are not sure if you are taking any of these medications.

Avoid drinking alcohol while taking LATUDA.

Tell your healthcare provider if you are pregnant or if you are planning to get pregnant. Avoid breastfeeding while taking LATUDA.

The most common side effects of LATUDA include sleepiness or drowsiness; restlessness or feeling like you need to move around (akathisia); difficulty moving, slow movements, muscle stiffness, or tremor; and nausea.

These are not all the possible side effects of LATUDA. For more information, ask your healthcare provider or pharmacist.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

**About Sunovion Pharmaceuticals Inc. (Sunovion)**
Sunovion is a leading pharmaceutical company dedicated to discovering, developing and commercializing therapeutic products that advance the science of medicine in the Psychiatry, Neurology and Respiratory disease areas to improve the lives of patients and their families.

Sunovion, an indirect, wholly-owned subsidiary of Sumitomo Dainippon Pharma Co., Ltd., is headquartered in Marlborough, Mass. More information about Sunovion Pharmaceuticals Inc. is available at www.sunovion.com.

**About Sumitomo Dainippon Pharma Co., Ltd.**
Located in Osaka, Japan, Sumitomo Dainippon Pharma defines its corporate mission as "to broadly contribute to society through value creation based on innovative research and development activities for the betterment of healthcare and fuller lives of people worldwide". By pouring all our efforts into the research and development of new drugs, we aim to provide innovative and effective pharmaceutical solutions to people not only in Japan but also around the world in order to realize our corporate mission. Additional information about Sumitomo Dainippon Pharma is available through its corporate website, www.ds-pharma.com.



For a copy of this release, visit Sunovion's web site at www.sunovion.com

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