Sunovion Presents Data from Phase 3 Studies of Latuda® (Ilarasdone HCl) in Children and Adolescents with Bipolar Depression

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- Full Phase 3 study results have been published in the Journal of the American Academy of Child and Adolescent Psychiatry-

- Post-hoc analysis of positive Phase 3 placebo-controlled study showed six weeks of treatment with LATUDA was associated with significant improvement in a wide range of depressive symptoms in children and adolescents with bipolar depression -

- Interim data from a long-term open-label extension study showed safety and continued efficacy of LATUDA treatment for up to 28 weeks -

MARLBOROUGH, Mass.--BUSINESS WIRE--(Sunovion Pharmaceuticals Inc.) today announced post-hoc analysis results of a positive Phase 3 placebo-controlled clinical study, as well as interim data from a long-term open-label extension study evaluating Latuda® (Ilarasdone HCl in children and adolescents (10 to 17 years of age) with major depressive episodes associated with bipolar disorder (bipolar depression).

The results showed that six weeks of treatment with LATUDA was associated with statistically significant and clinically meaningful improvement in a wide range of depressive symptoms compared to placebo and that long-term treatment with LATUDA for 28 weeks was well-tolerated and continued to improve depressive symptoms with minimal effect on weight and metabolic parameters in children and adolescents with bipolar depression. Results were presented at a scientific meeting in Washington, D.C., being held October 23-28, 2017.

LATUDA is atypical antipsychotic agent approved in the United States for the treatment of bipolar depression as monotherapy and as an adjunctive therapy with lithium or valproate in adults and for the treatment of schizophrenia in adults and adolescents (10 to 17 years of age).

"Depressive symptoms can be severely debilitating to schoolwork and social activities in children and adolescents living with bipolar disorder, which is recognized as the fourth leading cause of disability among children and adolescents around the world," said Kiki Chang, M.D., clinical study investigator. "The findings presented today are encouraging, as we need additional treatment options that are well tolerated and can be used on an ongoing basis by children and adolescents who live with bipolar disorder."

"Sunovion is committed to advancing the understanding of serious psychiatric conditions," said Antony Loebel, M.D., Executive Vice President and Chief Medical Officer at Sunovion, Head of Global Clinical Development for Sumitomo Dainippon Pharma Group. "Given the significant impact bipolar depression can have on children and adolescents, it is encouraging to see results that support the potential for LATUDA to be an effective and well-tolerated treatment for this population."

Sunovion submitted a supplemental New Drug Application (sNDA) for the use of LATUDA in children and adolescents (10 to 17 years of age) with bipolar depression that was accepted for review by the U.S. Food and Drug Administration (FDA) on June 30, 2017.

Phase 3 Study Results

Full Phase 3 study results were recently published in the Journal of the American Academy of Child and Adolescent Psychiatry. In the six-week, randomized, double-blind, placebo-controlled study, 347 children and adolescents 10 to 17 years of age with bipolar depression received once-daily LATUDA, flexibly dosed (20-80 mg/day), or placebo. LATUDA was associated with statistically significant and clinically meaningful improvement in bipolar depression symptoms compared to placebo, based on the primary endpoint of change from baseline to Week 6 on the Children’s Depression Rating Scale, Revised (CDRS-R) total score (-21.0 vs. -15.3; effect size = 0.45, p<0.0001).

A post-hoc item analysis of the CDRS-R endpoint presented today showed that LATUDA effectively treated a wide range of depressive symptoms. Compared to placebo, patients randomized to LATUDA demonstrated significantly greater improvement on 13 of the 17 CDRS-R items including social withdrawal, sleep disturbance, listless speech, depressed facial affect, excessive guilt, difficulty having fun, depressed feelings, low self-esteem, excessive weeping, hypomanic, impaired schoolwork, irritability, and appetite disturbance. Changes were not significant between the LATUDA group and placebo group in four CDRS-R items, including excessive fatigue, physical complaints, morbid ideation and social isolation.

LATUDA was generally well-tolerated with minor effects on weight, metabolic parameters and prolactin levels. Most common adverse events (AEs) with an incidence greater than five percent of LATUDA-treated patients included nausea, somnolence, weight increase, vomiting, dizziness and insomnia.

Long-term Open Label Extension Study Interim Results

A total of 263 participants who completed the six-week trial enrolled in a two-year, open-label, flexible dose extension study (NCT01914393). Results from an interim analysis showed that among the 155 people who completed 28 weeks of treatment, LATUDA was generally well-tolerated with similar adverse events to those reported during the six-week pivotal study. The most common AEs with an incidence greater than 10 percent were headache (19.7 percent), somnolence (18.5 percent) and nausea (14.3 percent).

Minimal effects were observed on weight, metabolic parameters and prolactin levels. The mean change in weight from double-blind baseline to Week 28 of the open-label extension study was +3.0 kg (as compared to an expected weight gain of +2.3 kg based on normative CDC data). The median change in prolactin from baseline to Week 28 was +2.0 ng/mL for females and +1.6 ng/mL for males. Median change in metabolic parameters from baseline to Week 28 was -4.5 mg/dL in total cholesterol, -3.0 mg/dL in LDL cholesterol, -2.0 mg/dL in triglycerides and +1.0 mg/dL in glucose. No participants in the study had a QTcF >460 or an increase in QTcF of >60 milliseconds.

At 28 weeks, participants who were treated with LATUDA throughout the initial six-week trial had continued improvement in the CDRS-R total score in the open-label long-term extension phase (-7.3). Continued improvement in the open-label phase was similarly observed on the Clinical Global Impressions- Bipolar Version, Severity of Illness (CGI-BP-S) depression score (-1.0).

About LATUDA

LATUDA is used to treat patients who:

- Depressive episodes in bipolar I disorder (bipolar depression) when used alone or with lithium or valproate in adults
- Schizophrenia in adults and adolescents 13 to 17 years of age

The efficacy of LATUDA was established in a 6-week placebo-controlled monotherapy study and a 6-week placebo-controlled adjunctive therapy study with lithium or valproate in adult patients with bipolar depression. The efficacy of LATUDA in schizophrenia was established in five 6-week placebo-controlled studies in adult patients and one 6-week placebo-controlled study in adolescents (13 to 17 years).

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, tremor; runny nose/nasal inflammation, and nausea.

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

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.

Please see important Safety Information, including BOXED WARNINGS, below and full Prescribing Information at www.LATUDA.com.

Important Safety Information and Indications for LATUDA
In elderly people with dementia-related psychosis (having lost touch with reality due to confusion and memory loss) treated with this type of medication, there is an increased risk of death compared to patients receiving placebo (sugar pill). LATUDA is not approved for the treatment of patients with dementia-related psychosis.

Antidepressant medications may increase suicidal thoughts or behaviors in some children, teenagers, and young adults within the first few months of treatment. Bipolar disorder and other serious mental illnesses are themselves associated with an increase in the risk of suicide. Patients on antidepressants and their families or caregivers should watch for new or worsening depression symptoms, 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 changes in these symptoms immediately to the doctor. LATUDA is not approved for use in pediatric patients with depression.

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.

Use usual precautions when handling LATUDA, as the tablets can contain high levels of sugar. LATUDA may cause unusual excitement or decrease your need for sleep, confusion, or changes in your breathing. It is also possible that LATUDA may cause high blood pressure, or high blood sugar, especially if you are taking medicine that raises these levels.

Neuroleptic malignant syndrome (NMS) is a rare but very serious condition that can happen in people who take atypical psychiatric medicines, including LATUDA. NMS can cause death and must be treated in a hospital. Call your health care 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.

Tell your healthcare provider if you are pregnant or if you are breastfeeding. Tell your health care 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 health care 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 prolatin. Tell your health care provider if you experience a lack of menstrual periods, leaking or enlarged breasts, or impotence.

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

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

Avoid drinking alcohol while taking LATUDA.

Tell your health care 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; runny nose/nasal inflammation, and nausea.

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

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

About Bipolar Disorder

Bipolar disorder is a mental health condition that is characterized by potentially debilitating mood swings, including periods of depression and mania. It affects approximately 12.6 million adults in the United States.

Approximately 50 to 60 percent of adults with bipolar disorder experience their first symptoms during adolescence and it can be difficult to diagnose.  Pediatric bipolar disorder affects approximately 1.7 percent of children and adolescents in the United States.

Symptoms of bipolar disorder in children and adolescents can be severe and may cause young people to think about death or suicide during depressive episodes.

Bipolar disorder is the fourth leading cause of disability among children and adolescents worldwide. Bipolar disorder is characterized by at least one lifetime manic or mixed episode; individuals often have one or more depressive episodes. Bipolar depression refers to the depressive phase of bipolar disorder; its symptoms include: depressed mood, loss of interest or pleasure in activities, significant weight loss, insomnia, fatigue, feelings of worthlessness, diminished ability to concentrate and recurrent thoughts of death or suicide attempt. When symptomatic, depressive symptoms affect patients more commonly than manic symptoms. Depressive episodes associated with bipolar disorder have been shown to result in significant impairment in work, family and social function, and are associated with increased risk of suicide and direct and indirect health care costs.

About Sunovion Pharmaceuticals Inc. (Sunovion)

Sunovion is a global biopharmaceutical company focused on the innovative application of science and medicine to help people with serious medical conditions. Sunovion's vision is to lead the way to a healthier world. The company's spirit of innovation is driven by the conviction that scientific excellence paired with meaningful advocacy and relevant education can improve lives. With patients at the center of everything it does, Sunovion has charted new paths to life-transforming treatments that reflect ongoing investments in research and development and a unwavering commitment to supporting people with psychiatric, neurological and respiratory conditions. Sunovion's track record of discovery, development and/or commercialization of important therapies includes Lestoral® Neoral® (eslicarbazepine acetate). Sunovion has multiple ongoing programs in target therapeutic areas. Sunovion Pharmaceuticals Europe Ltd., based in London, England, and Sunovion Pharmaceuticals Canada Inc., based in Mississauga, Ontario, are wholly-owned direct subsidiaries of Sunovion Pharmaceuticals Inc. Additional information can be found on the company's web sites: www.sunovion.com, www.sunovion-europe.com, and www.sunovion.ca. Connect with Sunovion on Twitter, LinkedIn, Facebook, and YouTube.

About Sumitomo Dainippon Pharma Co., Ltd.

Sumitomo Dainippon Pharma is among the top-ten listed pharmaceutical companies in Japan and the United States, China and the European Union. Sumitomo Dainippon Pharma aims to create innovative pharmaceutical products in the Psychiatry & Neurology and the Oncology area, which have been designated as important areas. Sumitomo Dainippon Pharma is headquartered in Tokyo, Japan. In addition, Sumitomo Dainippon Pharma Co., Ltd. Today, Sunumitomo Dainippon Pharma has about 6,500 employees worldwide. Additional information about Sumitomo Dainippon Pharma is available at its corporate website at www.ds-pharma.com.

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For a copy of this release, visit Sunovion's web site at www.sunovion.com (1).


5 Bipolar Disorder. Decision Resources. Table 2-2, Burlington, MA. December 2013.