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News Release

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Sunovion's Latuda® (lurasidone HCl) Receives Health Canada Approval to Treat Adolescents with Schizophrenia

– Health Canada has also accepted for review a Supplemental New Drug Submission (SNDS) for LATUDA for the treatment of bipolar depression in pediatric patients –

MARLBOROUGH, MA, July 21, 2017 – [Sunovion Pharmaceuticals Inc.](http://www.sunovion.com) (Sunovion) today announced that Health Canada approved the Supplemental New Drug Submission (SNDS) for Latuda® (lurasidone HCl) for the management of the manifestations of schizophrenia in adolescents aged 15 to 17 years. LATUDA is currently indicated in Canada for the management of the manifestations of schizophrenia and the acute management of depressive episodes associated with bipolar I disorder in adults.

“The expansion of LATUDA’s indication in Canada to include adolescents with schizophrenia marks an important milestone for patients and families in need of new treatment options for this difficult-to-manage condition,” said Antony Loebel, M.D., Executive Vice President and Chief Medical Officer at Sunovion, Head of Global Clinical Development for Sumitomo Dainippon Pharma Group. “We are pleased that LATUDA can now be considered for use in Canada for adolescent as well as adult patients with schizophrenia.”

The approval is based on results from a randomized, double-blind, placebo-controlled, six-week study in which adolescent patients with schizophrenia received fixed doses of LATUDA 40 mg/day, LATUDA 80 mg/day or placebo. At study endpoint, patients treated with LATUDA 40 mg/day and 80 mg/day demonstrated statistically significant and clinically meaningful improvement in symptoms of schizophrenia compared to placebo. LATUDA was also generally well tolerated with limited effects on weight and metabolic parameters.

In addition, Health Canada in June 2017 accepted for review, but has not yet approved, the SNDS for the expanded use of LATUDA in children and adolescents (10 to 17 years of age) with major depressive episodes associated with bipolar I disorder (bipolar depression) as monotherapy.

The bipolar depression SNDS is supported by data from a Phase 3 clinical study of children and adolescents (10 to 17 years of age), in which LATUDA was associated with statistically significant and clinically meaningful improvement in depressive symptoms compared to placebo and was generally well-tolerated with few effects on weight and metabolic parameters.

“Bipolar depression and schizophrenia are chronic and disabling conditions that can be particularly challenging to diagnose and treat in younger patients,” said Len Cortese, M.D., Medical Director of the Toldo Neurobehavioural Institute at Hotel Dieu Grace Hospital in Windsor, Ontario. “These milestones are important to the mental health community in addressing the need for additional effective and well-tolerated treatment options to manage pervasive psychiatric illnesses.”

About Schizophrenia

Schizophrenia is a chronic, serious and often severely disabling brain disorder. Symptoms such as hallucinations and delusions usually start between ages 16 and 30. Other symptoms may include unusual or dysfunctional ways of thinking, agitated body movements, reduced expression of emotions and cognitive symptoms such as poor focus, memory or executive functioning.¹

Although rare in young children, incidence of schizophrenia rises during adolescence and peaks in early adulthood. Adolescent schizophrenia is associated with poor functioning prior to the onset of illness and early developmental delays. Similar types of early developmental and social impairments have been reported in adult-onset schizophrenia, but appear to be more common and severe in adolescents.² A diagnosis of schizophrenia in adolescence may be a predictor of less independence, poorer educational achievement, lower likelihood of employment or access to further education, higher global disability scores and poor social relationships in adulthood.³

About Bipolar Disorder

Bipolar disorder is a mental health condition that is characterized by potentially debilitating mood swings, including periods of depression and mania.^{4,5} It affects approximately 12.6 million adults in the United States.^{6,7} Approximately 50 to 60 percent of adults with bipolar disorder experience their first symptoms during adolescence and it can be difficult to diagnose.^{8,9} Pediatric bipolar disorder affects approximately 1.7 percent of children and adolescents in the United States.¹⁰ 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.¹¹

Bipolar disorder is the fourth leading cause of disability among children and adolescents worldwide.¹² Bipolar I disorder is characterized by at least one lifetime manic or mixed episode; individuals often have one or more depressive episodes.¹³ 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.⁴ When symptomatic, depressive symptoms affect patients more commonly than manic symptoms.¹⁴ Depressive episodes associated with bipolar disorder have been shown to result in significant impairment in work, family and social function,^{15,16} and are associated with increased risk of suicide and direct and indirect health care costs.^{17,18}

About LATUDA

LATUDA is approved in the U.S. and Canada for the treatment of adult patients with schizophrenia and for the treatment of major depressive episodes associated with bipolar I disorder (bipolar

depression) as monotherapy or as adjunctive therapy with lithium or valproate. LATUDA is also approved in the U.S. for the treatment of adolescents ages 13 to 17 years with schizophrenia.

LATUDA is approved for the treatment of adult patients with schizophrenia in the EU, Switzerland, Australia, Taiwan, Russia, Singapore, Thailand and Hong Kong.

(U.S.) IMPORTANT SAFETY INFORMATION AND INDICATIONS FOR LATUDA

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

Elderly people 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 the treatment of patients with dementia-related psychosis.

Antidepressant medicines may increase suicidal thoughts or behaviors in some children, teenagers, and young adults within the first few months of treatment. Depression 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 change 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.

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 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.

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 health care provider should check your blood sugar before you start LATUDA and during therapy. Call 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 prolactin. 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 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 health care 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 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 <http://www.fda.gov/medwatch> or call 1-800-FDA-1088.

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

(CANADA) IMPORTANT SAFETY INFORMATION FOR LATUDA

LATUDA is used to treat patients with:

- Depressive episodes in bipolar I disorder (bipolar depression) when used alone or with lithium or valproate in adults
- Schizophrenia in adults and adolescents 15 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, or 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 antipsychotic efficacy of LATUDA was established in short-term (6-week) controlled trials [see CLINICAL TRIALS]. The efficacy of LATUDA in long-term use, that is, for more than 6 weeks, has not been systematically evaluated in controlled trials of patients with manifestations of schizophrenia.

The efficacy of LATUDA for long-term use, that is, for more than 6 weeks, in depressive episodes associated with bipolar I disorder, has not been systematically evaluated in controlled studies. 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 <http://www.sunovion.ca/monographs/latuda.pdf>

Indications and Clinical Use:

LATUDA is indicated for the management of the manifestations of schizophrenia in adolescents (15-17 years of age) and adults (17+).

The efficacy of LATUDA for long-term use, > 6 weeks, has not been systematically evaluated in controlled trials.

LATUDA is NOT indicated for the treatment of schizophrenia in adolescents < 15 years of age in Canada due to insufficient safety and efficacy data.

The physician who elects to use LATUDA for extended periods in adolescents 15-17 should periodically re-evaluate the long term usefulness of the drug for the individual patient.

When prescribing to adolescents (15-17 years of age), clinicians must take into account the safety concerns associated with all antipsychotic drugs which include: extrapyramidal effects, hyperglycemia, weight gain, and hyperlipidemia, which can be more frequent or more severe in this patient population than in adults. LATUDA should only be prescribed to adolescents with manifestations of schizophrenia by clinicians who are experienced in the diagnosis and treatment of adolescents with psychiatric illness and who are experienced in the early detection and management of the above-mentioned safety issues associated with this class of drugs.

LATUDA is not indicated in elderly patients with dementia. The safety and efficacy of LATUDA in patients > 65 years of age has not been established.

Most serious warnings and precautions:

Increased mortality in elderly patients with dementia: Elderly patients with dementia treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of thirteen placebo-controlled trials with various atypical antipsychotics in these patients showed a mean 1.6-fold increase in the death rate in the drug-treated patients. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular or infectious in nature.

Other relevant warnings and precautions:

- Body temperature disruption with antipsychotic use
- Orthostatic hypotension
- Angioedema
- Glucose abnormalities associated with atypical antipsychotics
- Hyperprolactinemia
- Weight gain
- Rare risk of priapism with antipsychotic use
- Antiemetic effect
- Leukopenia, neutropenia and agranulocytosis
- Venous thromboembolism
- Neuroleptic malignant syndrome
- Tardive dyskinesia associated with antipsychotic use
- Use in patients with a history of seizures
- Caution in patients with hepatic impairment
- Caution in patients with renal impairment
- Potential for cognitive and motor impairment
- Possibility of suicide inherent in psychiatric illness
- QT interval prolongation
- Dependence/tolerance¹

For more information:

Please consult the Product Monograph at <http://www.sunovion.ca/monographs/latuda.pdf> for important information relating to adverse reactions, interactions and dosing information which have not been discussed in this piece.

The Product Monograph is also available by calling 1-866-260-6291.

Sunovion Pharmaceuticals Canada Inc. contact information:

Medical Information or to Report an Adverse Drug Reaction

1-866-260-6291 Phone

1-866-933-6799 Fax

sunovionmedinfo@solutionsinhealth.com

1. LATUDA Product Monograph, July 19, 2017.
2. Goldman R, Loebel A, Cucchiari J, Deng L, Findling RL. Efficacy and Safety of Lurasidone in Adolescents with Schizophrenia: A 6-Week, Randomized Placebo-Controlled Study. J Child Adolesc Psychopharmacol. 2017 May 5. doi: 10.1089/cap.2016.0189. [Epub ahead of print]

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

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- Report online at <https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>
 - Call toll-free at 1-866-234-2345
 - Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: **Canada Vigilance Program
Health Canada
Postal Locator 0701D
Ottawa, Ontario
K1A 0K9**

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 an unwavering commitment to support people with psychiatric, neurological and respiratory conditions. Sunovion's track record of discovery, development and/or commercialization of important therapies has included Utibron™ Neohaler® (indacaterol/glycopyrrolate) inhalation powder, Brovana® (arformoterol tartrate) inhalation solution, Latuda® (lurasidone HCl) and Aptiom® (eslicarbazepine acetate).

Headquartered in Marlborough, Mass., Sunovion is an indirect, wholly-owned subsidiary of Sumitomo Dainippon Pharma Co., Ltd. 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.eu 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 operating globally in major pharmaceutical markets, including Japan, the United States, China and the European Union. Sumitomo Dainippon Pharma aims to create innovative pharmaceutical products in the Psychiatry & Neurology area and the Oncology area, which have been designated as the focus therapeutic areas. Sumitomo Dainippon Pharma is based on the merger in 2005 between Dainippon Pharmaceutical Co., Ltd., and Sumitomo Pharmaceuticals Co., Ltd. Today, Sumitomo Dainippon Pharma has about 6,500 employees worldwide. Additional information about Sumitomo Dainippon Pharma is available through 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

References

¹ National Institute of Mental Health. Schizophrenia. [Internet]. Available from:

<http://www.nimh.nih.gov/health/topics/schizophrenia/index.shtml>. Accessed January 2017.

² Hollis, C. BJPych Advances. 2015; 21:333-341.

³ Hollis, C. Am J Psychiatry. 2000; 157:1652-1659.

⁴ Swann, AC. Long-term treatment in bipolar disorder. *Journal of Clinical Psychiatry*. 2005; 66(1):7-12.

⁵ American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Fifth Edition. Washington, DC: American Psychiatric Association, 2013.

⁶ National Institute of Mental Health. Bipolar Disorder. [Internet]. Available from:

<http://www.nimh.nih.gov/health/topics/bipolar-disorder/index.shtml>. Accessed April 2017.

⁷ "Bipolar Disorder." Decision Resources. Table 2-2. Burlington, MA. December 2013.

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- ⁸ Chang K. *Dialogues Clin Neurosci*. 2009; 11(1):73-80.
- ⁹ National Institute of Mental Health. Bipolar disorder in adults. [Internet]. Available from: <http://www.nimh.nih.gov/health/publications/bipolar-disorder-tr-15-3679/index.shtml>. Accessed April 2017.
- ¹⁰ Van Meter AR, Moreira AL, Youngstrom EA. Meta-analysis of epidemiologic studies of pediatric bipolar disorder. *J Clin Psychiatry*. 2001; 72(9): 1250-1256.
- ¹¹ National Institute of Mental Health. Bipolar disorder in Children and Adolescents. [Internet]. Available from: <http://www.nimh.nih.gov/health/publications/bipolar-disorder-in-children-and-adolescents/index.shtml>. Accessed April 2017.
- ¹² Gore FM, et al. *Lancet* 2011; 377(9783):2093-2102.
- ¹³ American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Fifth Edition. Washington, DC: American Psychiatric Association, 2013.
- ¹⁴ The Depression and Bipolar Support Alliance. Bipolar Disorder. [Internet]. Available from: http://www.dbsalliance.org/site/PageServer?pagename=education_bipolar. Accessed April 2017.
- ¹⁵ Huxley N, Baldessarini RJ. Disability and Its Treatment in Bipolar Disorder Patients. *Bipolar Disorder*. 2007; 9(1-2):183-96.
- ¹⁶ Calabrese JR, Hirschfeld RM, Frye MA, Reed ML. Impact Of Depressive Symptoms Compared With Manic Symptoms In Bipolar Disorder: Results Of A U.S. Community-Based Sample. *Journal of Clinical Psychiatry*. 2004; 65(11):1499-504.
- ¹⁷ Parker G, McCraw S, Hadzi-Pavlovic D, Fletcher K. Costs Of The Principal Mood Disorders: A Study Of Comparative Direct And Indirect Costs Incurred By Those With Bipolar I, Bipolar II And Unipolar Disorders. *Journal of Affective Disorders*. 2012; 149(1-3):46-55. (ePub).
- ¹⁸ Leverich GS, Altshuler LL, Frye MA, et al. Factors Associated With Suicide Attempts In 648 Patients With Bipolar Disorder In The Stanley Foundation Bipolar Network. *Journal of Clinical Psychiatry*. 2003; 64(5):506-15.