OTSUKA AND LUNDBECK TO SHOWCASE SAFETY AND EFFICACY DATA IN TREATMENTS FOR CHALLENGING MENTAL HEALTH CONDITIONS

Eight data presentations supporting treatments for major depressive disorder, bipolar I disorder and schizophrenia to be presented at the upcoming annual Psych Congress

(PRINCETON, N.J., & DEERFIELD, Ill., September 13, 2017) – Otsuka Pharmaceutical Development & Commercialization, Inc. and Lundbeck U.S. today announced upcoming data presentations reinforcing the long-term safety and efficacy of brexpiprazole for the adjunctive treatment of major depressive disorder (MDD) and treatment of schizophrenia as well as presentations regarding additional analyses of the long-term efficacy and safety of aripiprazole once-monthly injection as maintenance monotherapy treatment of bipolar I disorder in adult patients. The Otsuka and Lundbeck alliance will showcase eight data presentations, including two long-term studies, at the upcoming Psych Congress, which will be held in New Orleans from September 16-19, 2017.

The results include long-term analyses in open-label extension trials of the efficacy of brexpiprazole in adults with schizophrenia and as an adjunctive treatment for adults with MDD, as well as long-term analyses (both open-label and controlled trials) of the efficacy of aripiprazole once-monthly 400 mg as maintenance monotherapy treatment in bipolar I disorder. Study presentations at Psych Congress are as follows:

MDD

- Long-term Efficacy of Adjunctive Brexpiprazole in Major Depressive Disorder (MDD) – Pooled Analysis of Two Short-term Placebo-controlled Studies and of an Open-label, Long-term Extension Study; *Catherine Weiss, Ph.D., et al.*
- Efficacy and Safety of Flexibly-dosed Brexpiprazole for the Adjunctive Treatment of Major Depressive Disorder: A Randomized, Active-Referenced, Placebo-controlled Study; *Mary Hobart, Ph.D., et al.*

Schizophrenia

- Effect of Brexpiprazole on Long-term Remission in Adults with Schizophrenia: Results of an Open-label, Long-term Study; *Ross A. Baker, Ph.D., et al.*

Bipolar I Disorder

- A 52-week, Multicenter, Open-label Study to Evaluate the Effectiveness of Aripiprazole Once-monthly as Maintenance Treatment in Patients with Bipolar I Disorder; *Joseph Calabrese, M.D., et al.*
- Effect on Functioning with Aripiprazole Once Monthly (AOM 400) in the Long-term Treatment of Bipolar I Disorder; *Jessica J. Madera, M.D., et al.*
- Aripiprazole Once-Monthly Maintenance Treatment of Bipolar I Disorder, A Double-Blind, Placebo-Controlled, Randomized Withdrawal Study: Effects on Types of Recurrence and on Recovery; *Joseph Calabrese, M.D., et al.*
- Course of Two Common Adverse Events in Aripiprazole Once-Monthly Maintenance Treatment of

Bipolar I Disorder during a Double-Blind, Placebo-Controlled, Randomized Withdrawal Study; *Joseph Calabrese, M.D., et al.*

- Aripiprazole Once-Monthly Maintenance Treatment of Bipolar I Disorder: A Blinded, Placebo-Controlled, Randomized Study. Effects on Symptoms and Functioning; *Joseph Calabrese, M.D., et al.*

For more information about Psych Congress, please visit: https://www.psychcongress.com/2017.

About Mental Illness

Approximately one in five Americans, or 43.4 million people, experience a mental illness in a given year, including those suffering from bipolar I disorder, MDD and schizophrenia.[1] These serious mental illnesses represent challenging therapeutic areas. For patients with serious mental illness, the main long-term treatment goal is to achieve sustained symptom remission and to prevent relapse, in which long-term treatment may be beneficial.

About Aripiprazole Once-Monthly

Aripiprazole once-monthly is marketed as ABILIFY MAINTENA® for extended-release injectable suspension is an atypical antipsychotic for intramuscular use. It was created by Otsuka in Japan and has been co-developed and co-commercialized by the alliance between Otsuka and Lundbeck. ABILIFY MAINTENA was approved in the U.S. in 2013 for the treatment of adults with schizophrenia and in 2017 for the maintenance monotherapy treatment of adults with bipolar I disorder.[2] Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at increased risk of death. ABILIFY MAINTENA is not approved for the treatment of patients with dementia-related psychosis. ABILIFY MAINTENA is a sterile lyophilized powder that when reconstituted with sterile water for injection, forms a suspension that can be administered by injection once a month (in patients demonstrating tolerability to aripiprazole, the initial injection is accompanied by an overlapping 14-day dosing of their current oral antipsychotic treatment). Subsequent doses of ABILIFY MAINTENA provide uninterrupted medication coverage for up to 30 days.[2] Depot formulations of antipsychotic agents provide patients with concentrations of active drug that remain at a therapeutic range for extended periods of time.[2-3]

The most commonly observed adverse reactions with ABILIFY MAINTENA in patients with schizophrenia (incidence of 5 percent or greater and aripiprazole incidence at least twice that for placebo) were increased weight, akathisia, injection site pain, and sedation.[2]

INDICATIONS and IMPORTANT SAFETY INFORMATION for ABILIFY MAINTENA® (aripiprazole)

INDICATIONS

ABILIFY MAINTENA is an atypical antipsychotic indicated for:

- Treatment of schizophrenia in adults
- Maintenance monotherapy treatment of bipolar I disorder in adults

IMPORTANT SAFETY INFORMATION

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at increased risk of death (1.6 to 1.7 times) compared to placebo-treated patients. ABILIFY MAINTENA is not approved for the treatment of patients with dementia-related psychosis.

Contraindication: Known hypersensitivity reaction to aripiprazole. Reactions have ranged from pruritus/urticaria to anaphylaxis.

Cerebrovascular Adverse Events, Including Stroke: Increased incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, have been reported in clinical trials of elderly patients with dementia-related psychosis treated with oral aripiprazole.

Neuroleptic Malignant Syndrome (NMS): NMS is a potentially fatal symptom complex reported in association with administration of antipsychotic drugs including ABILIFY MAINTENA. Clinical signs of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability. Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. Manage NMS with immediate discontinuation of ABILIFY MAINTENA, intensive symptomatic treatment, and monitoring.

Tardive Dyskinesia (TD): Risk of TD, and the potential to become irreversible, are believed to increase with duration of treatment and total cumulative dose of antipsychotic drugs. TD can develop after a relatively brief treatment period, even at low doses, or after discontinuation of treatment. Prescribing should be consistent with the need to minimize TD. If antipsychotic treatment is withdrawn, TD may remit, partially or completely.

Metabolic Changes: Atypical antipsychotic drugs have caused metabolic changes including:

- **Hyperglycemia/Diabetes Mellitus:** Hyperglycemia, in some cases extreme and associated with ketoacidosis, hyperosmolar coma, or death, has been reported in patients treated with atypical antipsychotics including aripiprazole. Patients with diabetes mellitus should be regularly monitored for worsening of glucose control; those with risk factors for diabetes (e.g., obesity, family history of diabetes), should undergo baseline and periodic fasting blood glucose testing. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

- **Dyslipidemia:** Undesirable alterations in lipids 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.

Pathological Gambling and Other Compulsive Behaviors: Intense urges, particularly for gambling, and the inability to control these urges have been reported while taking aripiprazole. Other compulsive urges have been reported less frequently. Prescribers should ask patients or their caregivers about the development of new or intense compulsive urges. Consider dose reduction or stopping aripiprazole if such urges develop.

Orthostatic Hypotension: ABILIFY MAINTENA may cause orthostatic hypotension and should be used with caution in patients with known cardiovascular disease, cerebrovascular disease, or conditions which would predispose them to hypotension.

Falls: Antipsychotics may cause somnolence, postural hypotension, motor and sensory instability, which may lead to falls causing fractures or other injuries. For patients with diseases, conditions, or medications that could exacerbate these effects, complete fall risk assessments when initiating treatment and recurrently during therapy.

Leukopenia, Neutropenia, and Agranulocytosis: Leukopenia, neutropenia and agranulocytosis have been reported with antipsychotics. Monitor complete blood count in patients with pre-existing low white blood cell count (WBC)/absolute neutrophil count or history of drug-induced leukopenia/neutropenia. Discontinue ABILIFY MAINTENA at the first sign of a clinically significant decline in WBC and in severely neutropenic patients.

Seizures: ABILIFY MAINTENA should be used with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

Potential for Cognitive and Motor Impairment: ABILIFY MAINTENA may impair judgment, thinking, or motor skills. Instruct patients to avoid operating hazardous machinery, including automobiles, until they are certain ABILIFY MAINTENA does not affect them adversely.

Body Temperature Regulation: Use ABILIFY MAINTENA with caution in patients who may experience conditions that increase body temperature (e.g., strenuous exercise, extreme heat, dehydration, or concomitant use with anticholinergics).

Dysphagia: Esophageal dysmotility and aspiration have been associated with ABILIFY MAINTENA. Use caution in patients at risk for aspiration pneumonia.

Alcohol: Advise patients to avoid alcohol while taking ABILIFY MAINTENA.

Concomitant Medication: Dosage adjustments are recommended in patients who are CYP2D6 poor metabolizers and in patients taking concomitant CYP3A4 inhibitors or CYP2D6 inhibitors for greater than 14 days. Avoid concomitant use of CYP3A4 inducers with ABILIFY MAINTENA for greater than 14 days. Dosage adjustments are not recommended for patients with concomitant use of CYP3A4 inhibitors, CYP2D6 inhibitors or CYP3A4 inducers for less than 14 days.

Most Commonly Observed Adverse Reactions: The most commonly observed adverse reactions with ABILIFY MAINTENA in patients with schizophrenia (incidence ≥5% and at least twice that for placebo) were increased weight, akathisia, injection site pain, and sedation.

Injection Site Reactions: In a short-term, clinical trial with ABILIFY MAINTENA in patients with schizophrenia treated with gluteal administered ABILIFY MAINTENA, the percent of patients reporting any injection site-related adverse reaction was 5.4%, and 0.6% for placebo. In an open label study of ABILIFY MAINTENA administered in the deltoid or gluteal muscle, injection site pain was observed at approximately equal rates.

Dystonia: Symptoms of dystonia may occur in susceptible individuals during the first days of treatment and at low doses.

Pregnancy: Neonates exposed to antipsychotic drugs, including ABILIFY MAINTENA, during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms. Consider the benefits and risks of ABILIFY MAINTENA and possible risks to the fetus when prescribing ABILIFY MAINTENA to a pregnant woman. Advise pregnant women of potential fetal risk.

Lactation: Aripiprazole is present in human breast milk. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother and any potential risks to the infant.

To report SUSPECTED ADVERSE REACTIONS, contact Otsuka America Pharmaceutical, Inc. at 1-800-438-9927 or FDA at 1-800-FDA-1088 (www.fda.gov/medwatch).

Please see accompanying FULL PRESCRIBING INFORMATION, including **BOXED WARNING.**

About Brexpiprazole

Brexpiprazole is marketed as REXULTI®, and was approved by the U.S. Food and Drug Administration in July 2015 to treat patients with schizophrenia and as an adjunctive treatment for patients with major depressive disorder (MDD). REXULTI was also approved in February 2017 by Health Canada for the treatment of schizophrenia.

REXULTI was discovered by Otsuka and is co-developed by Otsuka and Lundbeck. The mechanism of action for REXULTI in the adjunctive treatment of major depressive disorder or schizophrenia is unknown. However, the efficacy of REXULTI may be mediated through a combination of partial agonist activity at serotonin 5-HT_{1A} and dopamine D_2 receptors, and antagonist activity at serotonin 5-HT_{2A} receptors. REXULTI exhibits high affinity (sub-nanomolar) for these receptors as well as for noradrenaline $alpha_{1B/2C}$ receptors.

INDICATIONS and IMPORTANT SAFETY INFORMATION for REXULTI® (brexpiprazole)

INDICATIONS

REXULTI is indicated for:

- Use as an adjunctive therapy to antidepressants in adults with major depressive disorder
- Treatment of schizophrenia in adults

IMPORTANT SAFETY INFORMATION

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at increased risk of death. REXULTI is not approved for the treatment of patients with dementia-related psychosis.

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

Antidepressants increase the risk of suicidal thoughts and behaviors in patients aged 24 years and younger. Monitor for clinical worsening and emergence of suicidal thoughts and behaviors. The safety and effectiveness of REXULTI have not been established in pediatric patients.

Contraindication: In patients with known hypersensitivity reaction to brexpiprazole or any of its components. Reactions have included: rash, facial swelling, urticaria and anaphylaxis.

Cerebrovascular Adverse Events, Including Stroke: In clinical trials, elderly patients with dementia randomized to risperidone, aripiprazole, and olanzapine had a higher incidence of stroke and transient ischemic attack, including fatal stroke. REXULTI is not approved for the treatment of patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome (NMS): NMS is a potentially fatal symptom complex reported in association with administration of antipsychotic drugs. Clinical signs of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability. Additional signs may include elevated creatinine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. Manage NMS with immediate discontinuation of REXULTI, intensive symptomatic treatment, and monitoring.

Tardive Dyskinesia (TD): Risk of TD, and the potential to become irreversible, are believed to increase with duration of treatment and total cumulative dose of antipsychotic drugs. TD can develop after a relatively brief treatment period, even at low doses, or after discontinuation of treatment. For chronic treatment, use the lowest dose and shortest duration of REXULTI needed to produce a clinical response. If signs and symptoms of TD appear, drug discontinuation should be considered.

Metabolic Changes: Atypical antipsychotic drugs have caused metabolic changes including:

- **Hyperglycemia/Diabetes Mellitus:** Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics. Assess fasting plasma glucose before or soon after initiation of antipsychotic medication, and monitor periodically during long-term treatment.
- **Dyslipidemia:** Atypical antipsychotics cause adverse alterations in lipids. Before or soon after initiation of antipsychotic medication, obtain a fasting lipid profile at baseline and monitor periodically during treatment.
- **Weight Gain:** Weight gain has been observed in patients treated with REXULTI. Monitor weight at baseline and frequently thereafter.

Leukopenia, Neutropenia, and Agranulocytosis: Leukopenia and neutropenia have been reported with antipsychotics. Agranulocytosis (including fatal cases) has been reported with other agents in this class. Monitor complete blood count in patients with pre-existing low white blood cell count (WBC)/absolute neutrophil count or history of drug-induced leukopenia/neutropenia. Discontinue REXULTI at the first sign of a clinically significant decline in WBC and in severely neutropenic patients.

Orthostatic Hypotension and Syncope: Atypical antipsychotics cause orthostatic hypotension and syncope. Generally, the risk is greatest during initial dose titration and when increasing the dose. Monitor in patients vulnerable to hypotension, and those with cardiovascular and cerebrovascular diseases.

Falls: Antipsychotics may cause somnolence, postural hypotension, motor and sensory instability, which may lead to falls causing fractures or other injuries. For patients with diseases, conditions, or medications that could exacerbate these effects, complete fall risk assessments when initiating treatment and recurrently during therapy.

Seizures: REXULTI may cause seizures and should be used with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

Body Temperature Dysregulation: Use REXULTI with caution in patients who may experience conditions that increase body temperature (e.g., strenuous exercise, extreme heat, dehydration, or concomitant use with anticholinergics).

Dysphagia: Esophageal dysmotility and aspiration have been associated with antipsychotics, including REXULTI, and should be used with caution in patients at risk for aspiration.

Potential for Cognitive and Motor Impairment: REXULTI has the potential to impair judgment, thinking, or motor skills. Patients should not drive or operate hazardous machinery until they are reasonably certain REXULTI does not affect them adversely.

Concomitant Medication: Dosage adjustments are recommended in patients who are known cytochrome P450 (CYP) 2D6 poor metabolizers and in patients taking concomitant CYP3A4 inhibitors or CYP2D6 inhibitors or strong CYP3A4 inducers.

Most commonly observed adverse reactions: In clinical trials, the most common adverse reactions were:

- **Major Depressive Disorder (MDD)** (adjunctive treatment to antidepressant therapy; ≥5% incidence and at least twice the rate of placebo for REXULTI vs. placebo, respectively): akathisia (9% vs. 2%) and weight increase (7% vs. 2%)
- **Schizophrenia** (≥4% incidence and twice incidence of placebo for REXULTI vs. placebo, respectively): weight increased (4% vs. 2%)

Dystonia: Symptoms of dystonia may occur in susceptible individuals during the first days of treatment and at low doses.

Pregnancy: Adequate and well-controlled studies to assess the risks of REXULTI during pregnancy have not been conducted. REXULTI should be used during pregnancy only if the benefit justifies the risk to the fetus.

Lactation: It is not known if REXULTI is excreted in human breast milk. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

To report SUSPECTED ADVERSE REACTIONS, contact Otsuka America Pharmaceutical, Inc. at 1-800- 438-9927 or FDA at 1-800-FDA-1088 (www.fda.gov/medwatch).

Please see accompanying FULL PRESCRIBING INFORMATION, including **BOXED WARNING**.

About Otsuka Pharmaceutical Development & Commercialization, Inc.
Otsuka Pharmaceutical Company is a global healthcare company with the corporate philosophy: "Otsuka–people creating new products for better health worldwide." Otsuka researches, develops, manufactures and markets innovative products, with a focus on pharmaceutical products to meet unmet medical needs and nutraceutical products for the maintenance of everyday health.

In pharmaceuticals, Otsuka is a leader in the challenging area of mental health and also has research programs on several under-addressed diseases including tuberculosis, a significant global public health issue. These commitments illustrate how Otsuka is a "big venture" company at heart, applying a youthful spirit of creativity in everything it does.

Otsuka Pharmaceutical Development & Commercialization, Inc. (OPDC) is dedicated to clinical development of promising drug candidates in mental health, oncology, cardio-renal, and nephrology. Other activities include strategic planning for drug approval, marketing, and lifecycle management to maximize a product's full potential.

OPDC is an indirect subsidiary of Otsuka Pharmaceutical Company, Ltd., which is a subsidiary of Otsuka Holdings Co., Ltd. headquartered in Tokyo, Japan. The Otsuka group of companies employed 45,000 people worldwide and had consolidated sales of approximately USD 11 billion in 2016.

All Otsuka stories start by taking the road less travelled. Learn more about Otsuka in the U.S. at www.otsuka-us.com and connect with us on LinkedIn and Twitter at @OtsukaUS. Otsuka Pharmaceutical Co., Ltd.'s global website is accessible at www.otsuka.co.jp/en/.

About Lundbeck

Lundbeck is a global pharmaceutical company specialized in psychiatric and neurological disorders. For more than 70 years, we have been at the forefront of research within neuroscience. Our key areas of research focus are depression, schizophrenia, Parkinson's disease and Alzheimer's disease.

An estimated 700 million people worldwide are living with psychiatric and neurological disorders and far too many suffer due to inadequate treatment, discrimination, a reduced number of working days, early retirement and other unnecessary consequences. Every day, we strive for improved treatment and a better life for people living with psychiatric and neurological disorders — we call this Progress in Mind.

Our approximately 5,000 employees in 55 countries are engaged in the entire value chain throughout research, development, manufacturing, marketing and sales. Our pipeline consists of several late-stage development programs and our products are available in more than 100 countries. We have production facilities in Denmark, France and Italy. Lundbeck generated revenue of DKK 15.6 billion in 2016 (EUR 2.1 billion; USD 2.2 billion).

In the U.S., Lundbeck employs nearly 1,000 people focused solely on accelerating therapies for brain disorders. With a special commitment to the lives of patients, families and caregivers, Lundbeck U.S. actively engages in hundreds of initiatives each year that support our patient communities. For additional information, we encourage you to visit our corporate site at www.lundbeckus.com and connect with us on Twitter at @LundbeckUS.

Otsuka Contact:
Kimberly Whitefield
Corporate Communications
Otsuka America Pharmaceutical, Inc.
kimberly.whitefield@otsuka-us.com
+1 609 535-9259

Lundbeck Contact:
Nick Przybyciel
Public Affairs
Lundbeck
nprz@lundbeck.com
+1 847 282 5715

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