Allergan and Gedeon Richter Plc. Receive FDA Approval of VRAYLAR™ (cariprazine) for Treatment of Manic or Mixed Episodes of Bipolar I Disorder and Schizophrenia in Adults

- The safety and efficacy of oral, once-daily VRAYLAR was established in a clinical trial program involving more than 2,700 patients

Bipolar I disorder and schizophrenia are highly complex conditions requiring additional treatment options because response to medications vary from patient to patient -

DUBLIN, Ireland and BUDAPEST, Hungary, 17 September 2015-- Allergan plc (NYSE: AGN) and Gedeon Richter Plc. announced today that the U.S. Food and Drug Administration (FDA) has approved VRAYLAR™ (cariprazine) capsules, an atypical antipsychotic, for the acute treatment of manic or mixed episodes associated with bipolar I disorder and for treatment of schizophrenia in adults.

“We are pleased with the FDA approval of VRAYLAR™, which represents an important new treatment option for adults living with bipolar I disorder and schizophrenia to help address the unmet medical needs of people with these complex conditions,” said David Nicholson, Executive Vice President and President of Global R&D brands of Allergan. “This approval reinforces our deep commitment to the mental health community, as we continue to build our robust CNS portfolio.”

Bipolar I disorder and schizophrenia are chronic and disabling mental health disorders. Bipolar I disorder, also known as manic-depressive illness, is a disorder of the brain that is characterized by fluctuations in mood, energy, activity levels, and the ability to carry out day-to-day tasks. Schizophrenia is characterized by delusions, hallucinations, disorganized speech and behavior, and other symptoms that cause social or occupational dysfunction.

“Bipolar I disorder and schizophrenia are serious, chronic and treatable conditions. The symptoms and response to treatment vary from patient to patient making these conditions challenging to manage,” said Gary Sachs, MD, Founding Director of the Bipolar Clinic and Research Program at the Massachusetts General Hospital and Associate Professor of Psychiatry at Harvard Medical School.

The FDA approval of VRAYLAR™ is based on the results of three 3-week controlled trials in adults with manic or mixed episodes of bipolar I disorder and three 6-week placebo-controlled trials in adults with schizophrenia. In these clinical trials involving more than 2,700 adults, VRAYLAR™ demonstrated improvement compared to placebo as measured by Young Mania Rating Scale (YMRS) total scores in patients with bipolar mania and by Positive and Negative Syndrome Scale (PANSS) total scores in patients with schizophrenia. VRAYLAR™ also demonstrated efficacy as measured by the Clinical Global Impressions-Severity (CGI-S) rating scale, the secondary efficacy endpoints for both conditions.

“This approval is a notable achievement for Gedeon Richter’s discovery platform,” said Erik Bogsch, Managing Director of Gedeon Richter Plc. “Despite the variety of treatments available for the millions living with bipolar I disorder and schizophrenia, unmet needs remain and we are proud to offer an additional option to help patients manage their symptoms.”

The most commonly reported adverse reactions (incidence ≥ 5% and at least twice the rate of placebo) in bipolar mania were extrapyramidal symptoms, akathisia, dyspepsia, vomiting, somnolence, and restlessness and in schizophrenia were extrapyramidal symptoms and akathisia.

About Bipolar I Disorder

Bipolar disorder affects approximately 3.6 million people in the United States. Bipolar I disorder is also known as manic-depressive illness. People with bipolar I disorder experience "mood episodes" ranging from manic episodes (i.e., overexcited, extreme irritability, racing thoughts, difficulties with sleep), depressive episodes (i.e., extreme sadness, fatigue, hopelessness), or mixed episodes (a combination of both mania and depression).

About Schizophrenia

Schizophrenia is a chronic and disabling disorder that affects more than 2.6 million American adults. It imposes significant burden on patients, their families, and society. Symptoms fall into three broad categories: positive symptoms (hallucinations, delusions, thought disorders, and movement disorders), negative symptoms (such as loss of motivation and social withdrawal), and cognitive symptoms (problems with executive functioning, focusing, and working memory).

About VRAYLAR™ (cariprazine)

VRAYLAR™ is an oral, once daily atypical antipsychotic approved for the acute treatment of adult patients with manic or mixed episodes associated with bipolar I disorder, with a recommended dose range of 3 to 6 mg/day and for the treatment of schizophrenia in adults, with a recommended dose range of 1.5 to 6 mg/day. The safety and efficacy of VRAYLAR™ was studied in a clinical trial program of more than 2,700 patients with these conditions.

While the mechanism of action of VRAYLAR™ in schizophrenia and bipolar I disorder is unknown, the efficacy of VRAYLAR™ could be mediated through a combination of partial agonist activity at central dopamine D_2 and serotonin 5-HT_{1A} receptors and antagonist activity at serotonin 5-HT_{2A} receptors.

Pharmacodynamically, cariprazine acts as a partial agonist at the dopamine D_3 and D_2 receptors with high binding affinity and at the serotonin 5-HT_{1A} receptors. Cariprazine acts as an antagonist at 5-HT_{2B} and 5-HT_{2A} receptors with high and moderate binding affinity as well as it binds to the histamine H_1 receptors. Cariprazine shows lower binding affinity to the serotonin 5-HT_{2C} and α_{1A}- adrenergic receptors and has no appreciable affinity for cholinergic muscarinic receptors.

VRAYLAR™ was discovered and co-developed by Gedeon Richter Plc and is licensed to Actavis, now Allergan, in the U.S. and Canada.

Cariprazine is also being investigated for the treatment of bipolar depression and as adjunctive treatment for major depressive disorder in adults.

Visit www.VRAYLAR.com for more information on this once daily option for the acute treatment of manic or mixed episodes associated with bipolar I disorder and for the 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 an increased risk of death. VRAYLAR™ is not approved for treatment of patients with dementia-related psychosis.

Contraindication: VRAYLAR™ is contraindicated in patients with known hypersensitivity. Reactions have included rash, pruritus, urticaria, and events suggestive of angioedema.

Cerebrovascular Adverse Reactions, Including Stroke: In clinical trials with antipsychotic drugs, elderly subjects with dementia had a higher incidence of cerebrovascular adverse reactions, including fatalities vs placebo. VRAYLAR™ is not approved for the treatment of patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome (NMS): NMS, a potentially fatal symptom complex, has been reported with antipsychotics drugs. NMS may cause hyperpyrexia, muscle rigidity, delirium, and autonomic instability. Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. Manage with immediate discontinuation, intensive symptomatic treatment, and monitoring.

Tardive Dyskinesia (TD): Risk of developing TD (a syndrome of potentially irreversible, involuntary dyskinetic movements) and the likelihood it will become irreversible may increase with the duration of treatment and the cumulative dose. The syndrome can develop after a relatively brief treatment period, even at low doses, or after treatment discontinuation. If signs and symptoms of TD appear, drug discontinuation should be considered.

Late-Occurring Adverse Reactions: Adverse events may first appear several weeks after initiation of VRAYLAR™, probably because plasma levels of cariprazine and its major metabolites accumulate over time. Monitor for adverse reactions and patient response for several weeks after starting VRAYLAR™ and after each dosage increase. Consider reducing the dose or discontinuing the drug.

Metabolic Changes: Atypical antipsychotics have caused metabolic changes, such as:

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

Leukopenia, Neutropenia, and Agranulocytosis: Leukopenia/neutropenia have been reported with antipsychotics, including VRAYLAR™. Agranulocytosis (including fatal cases) has been reported with other 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 VRAYLAR™ 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, with the greatest risk during initial titration and with dose increases. Monitor orthostatic vital signs in patients predisposed to hypotension and in those with cardiovascular/cerebrovascular diseases.

Seizures: Use VRAYLAR™ with caution in patients with history of seizures or with conditions that lower the seizure threshold.

Potential for Cognitive and Motor Impairment: Somnolence was reported with VRAYLAR™. Caution patients about performing activities requiring mental alertness (eg, operating hazardous machinery or a motor vehicle).

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

Dysphagia: Esophageal dysmotility and aspiration have been associated with antipsychotics. Antipsychotic drugs, including VRAYLAR™, should be used cautiously in patients at risk for aspiration.

Drug Interactions: Strong CYP3A4 inhibitors increase VRAYLAR™ concentrations, so VRAYLAR dose reduction is recommended. Concomitant use with CYP3A4 inducers is not recommended.

Adverse Reactions: In clinical trials, the most common adverse reactions (≥5% and at least twice the rate of placebo) are listed below. Dose-related increase in certain adverse reactions was observed, particularly above the maximum recommended dose of 6 mg/day.

- Schizophrenia: The incidences within the recommended dose range (VRAYLAR™ 1.5 – 3 mg/day and 4.5 – 6 mg/day vs placebo) were: extrapyramidal symptoms (15%, 19% vs 8%) and akathisia (9%, 13% vs 4%)
- Bipolar mania: The incidences within the recommended dose range (VRAYLAR™ 3 – 6 mg/day vs placebo) were: extrapyramidal symptoms (26% vs 12%), akathisia (20% vs 5%), dyspepsia (7% vs 4%), vomiting (10% vs 4%), somnolence (7% vs 4%), and restlessness (7% vs 2%)

Please also see the full Prescribing Information, including Boxed Warning.

About Allergan

Allergan plc (NYSE: AGN), headquartered in Dublin, Ireland, is a unique, global pharmaceutical company and a leader in a new industry model – Growth Pharma. Allergan is focused on developing, manufacturing and commercializing innovative branded pharmaceuticals, high-quality generic and over-the-counter medicines and biologic products for patients around the world.

Allergan markets a portfolio of best-in-class products that provide valuable treatments for the central nervous system, eye care, medical aesthetics, gastroenterology, women's health, urology, cardiovascular and anti-infective therapeutic categories, and operates the world's third-largest global generics business, providing patients around the globe with increased access to affordable, high-quality medicines. Allergan is an industry leader in research and development, with one of the broadest development pipelines in the pharmaceutical industry and a leading position in the submission of generic product applications globally.

With commercial operations in approximately 100 countries, Allergan is committed to working with physicians, healthcare providers and patients to deliver innovative and meaningful treatments that help people around the world live longer, healthier lives.

For more information, visit Allergan's website at www.allergan.com.

Forward-Looking Statement

Statements contained in this press release that refer to future events or other non-historical facts are forward-looking statements that reflect Allergan's current perspective of existing trends and information as of the date of this release. Except as expressly required by law,

Allergan disclaims any intent or obligation to update these forward-looking statements. Actual results may differ materially from Allergan's current expectations depending upon a number of factors affecting Allergan's business. These factors include, among others, the risks associated with acquisition transactions; the difficulty of predicting the timing or outcome of FDA approvals or actions, if any; the impact of competitive products and pricing; market acceptance of and continued demand for Allergan's products; difficulties or delays in manufacturing; and other risks and uncertainties detailed in Allergan's periodic public filings with the Securities and Exchange Commission, including but not limited to Allergan's Quarterly Report on Form 10-Q for the quarter ended 31 March, 2015 (such periodic public filings having been filed under the "Actavis plc" name) and from time to time in Allergan's other investor communications . Except as expressly required by law, Allergan disclaims any intent or obligation to update these forward-looking statements.

About Gedeon Richter

Gedeon Richter Plc. (www.richter.hu), headquartered in Budapest/Hungary, is a major pharmaceutical company in Central Eastern Europe, with an expanding direct presence in Western Europe. Richter's consolidated sales were approximately EUR 1.1 billion (US$ 1.5 billion), while its market capitalization amounted to EUR 2.1 billion (US$ 2.5 billion) in 2014. The product portfolio of Richter covers almost all important therapeutic areas, including gynaecology, central nervous system, and cardiovascular areas. Having the largest R&D unit in Central Eastern Europe, Richter's original research activity focuses on CNS disorders. With its widely acknowledged steroid chemistry expertise, Richter is a significant player in the female healthcare field worldwide. Richter is also active in biosimilar product development.

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