Gedeon Richter and Allergan Receive U.S. FDA Approval For Expanded Use of VRAYLAR® (cariprazine) in the Treatment of Bipolar Depression

- New Indication Makes VRAYLAR® First and Only Dopamine and Serotonin Partial Agonist to Treat the Full Spectrum of Bipolar I Symptoms in Manic, Mixed, and Depressive Episodes -

Budapest, Hungary and Dublin, Ireland – 28 May 2019 – Gedeon Richter Plc. and Allergan plc (NYSE: AGN) today announced that the U.S. Food and Drug Administration (FDA) has approved a supplemental New Drug Application (sNDA) for VRAYLAR® (cariprazine) for expanded use to treat depressive episodes associated with bipolar I disorder (bipolar depression) in adults. VRAYLAR® is also approved in the U.S. to treat manic or mixed episodes associated with bipolar I disorder in adults. There are nearly 11 million adults in the U.S. living with bipolar disorder,[1] a condition that causes extreme shifts in mood, energy, and activity levels.[2]

"Treating bipolar disorder can be very difficult because people living with the illness experience a range of depressive and manic symptoms, sometimes both at the same time, and this FDA approval gives healthcare providers a new option to treat the full spectrum of bipolar I disorder symptoms, specifically manic, mixed, and depressive episodes, with just one medication," said Dr. Stephen Stahl, Professor of Psychiatry at the University of California San Diego and lead author of the post hoc analysis, *Cariprazine Efficacy in Patients with Bipolar Depression and Concurrent Manic Symptoms*. "Treating depression, mania and mixed episodes with a single medication is important for people living with, and healthcare providers treating, this complex illness. This approval can streamline a treatment decision while helping to stabilize the disorder."

Seventy percent of people living with bipolar disorder receive at least one misdiagnosis and consult an average of four doctors over approximately 10 years before being accurately diagnosed.[3] Many patients take multiple medications to treat the symptoms of this condition.

The FDA approval for the expanded indication of VRAYLAR® is based on three pivotal trials, including RGH-MD-53, RGH-MD-54 and RGH-MD-56, in which cariprazine demonstrated greater improvement than placebo for the change from baseline to week six on the Montgomery Asberg Depression Rating scale (MADRS) total score. In all three studies, the VRAYLAR® 1.5 mg dose demonstrated statistical significance over placebo; additionally, in RGH-MD-54, the VRAYLAR® 3 mg dose demonstrated statistical significance over placebo. Common adverse events reported in the pivotal trials were nausea, akathisia, restlessness, and extrapyramidal symptoms.

“This approval represents an important milestone in our efforts to help patients and prescribing healthcare providers effectively manage bipolar I disorder and demonstrates our ongoing focus on mental health,” said David Nicholson, Chief Research & Development Officer at Allergan. “We are committed to developing therapies for complex mental health disorders including VRAYLAR® which is currently in phase III clinical trials for the treatment of Major Depressive Disorder.”

“This approval is considered a notable achievement in the development process of cariprazine, our flagship product,” said Dr. István Greiner, Research Director of Gedeon Richter Plc. “We are pleased that more and more patient groups suffering from psychiatric disorders will get access to cariprazine as a treatment option.”

About VRAYLAR® (cariprazine)

VRAYLAR® is an oral, once daily atypical antipsychotic approved for the acute treatment of adults with manic or mixed episodes associated with bipolar I disorder (3 to 6 mg/day) and for the treatment of depressive episodes associated with bipolar I disorder (bipolar depression) in adults (1.5 or 3 mg/day). VRAYLAR® is also approved for the treatment of schizophrenia in adults (1.5 to 6 mg/day).

While the mechanism of action of VRAYLAR® is unknown, the efficacy of VRAYLAR® could be mediated through a combination of partial agonist activity at central dopamine D_2 and serotonin $5\text{-}HT_{1A}$ receptors and antagonist activity at serotonin $5\text{-}HT_{2A}$ receptors. Pharmacodynamic studies with cariprazine have shown that it acts as a partial agonist with high binding affinity at dopamine D_3, dopamine D_2, and serotonin $5\text{-}HT_{1A}$ receptors. Cariprazine demonstrated up to ~8-fold greater *in vitro* affinity for dopamine D_3 vs D_2 receptors. Cariprazine also acts as an antagonist at serotonin $5\text{-}HT_{2B}$ and $5\text{-}HT_{2A}$ receptors with high and moderate binding affinity, respectively as well as it binds to the histamine H_1 receptors.

VRAYLAR® shows lower binding affinity to the serotonin $5\text{-}HT_{2C}$ and α_{1A}- adrenergic receptors and has no appreciable affinity for cholinergic muscarinic receptors. The clinical significance of these *in vitro* data is unknown.

VRAYLAR® was discovered and co-developed by Gedeon Richter Plc and is licensed by Allergan, in the U.S. and Canada. For more than a decade both companies have conducted over 20 clinical trials enrolling thousands of patients worldwide to evaluate the efficacy and safety of cariprazine for people living with a broad range of mental health illnesses.

Visit www.vraylar.com for more information.

About Bipolar I Disorder and Bipolar I Depression

There are nearly 11 million adults in the U.S. living with bipolar disorder,[1] a condition that causes periods of severe changes in mood, energy, and activity levels.[2] These periods are often called "episodes." Experiencing just one manic episode is enough to be diagnosed with bipolar I disorder. Although there is no known cure, its symptoms may be managed.[4]

Bipolar depression refers to the depressive episodes of bipolar I disorder. People living with bipolar I disorder can have manic and depressive episodes, as well as mixed episodes that feature both manic and depressive symptoms at the same time. Depressive symptoms are three times more prevalent than manic symptoms and constitute a larger portion of the patient's life spent unwell.[5] Bipolar I depression typically lasts at least two weeks and can be difficult to differentiate from major depression during diagnosis. If misdiagnosed with major depressive disorder, people may be given an antidepressant which, when taken as a monotherapy by someone with bipolar disorder, can induce a manic episode.[6]

About Allergan plc

Allergan plc (NYSE: AGN), headquartered in Dublin, Ireland, is a global pharmaceutical leader focused on developing, manufacturing and commercializing branded pharmaceutical, device, biologic, surgical and regenerative medicine products for patients around the world. Allergan markets a portfolio of leading brands and best-in-class products primarily focused on four key therapeutic areas including medical aesthetics, eye care, central nervous system and gastroenterology. As part of its approach to delivering innovation for better patient care, Allergan has built one of the broadest pharmaceutical and device research and development pipelines in the industry.

With colleagues and 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 every day.

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 on existing trends and information as of the date of this release. 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 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; the impact of uncertainty around timing of generic entry related to key products, including RESTASIS®, on our financial results; risks associated with divestitures, acquisitions, mergers and joint ventures; risks related to impairments; uncertainty associated with financial projections, projected cost reductions, projected debt reduction, projected synergies, restructurings, increased costs, and adverse tax consequences; 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 Annual Report on Form 10-K for the year ended December 31, 2018and Allergan's Quarterly Report on Form 10-Q for the period ended March 31, 2019. Except as expressly required by law, Allergan disclaims any intent or obligation to update these forward-looking statements.

About Gedeon Richter Plc.

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, in China and in Latin America. Having reached a market capitalisation of EUR 3.2 billion (USD 3.6 billion) by the end of 2018, Richter's consolidated sales were approximately EUR 1.4 billion (USD 1.6 billion) during the same year. The product portfolio of Richter covers many important therapeutic areas, including Women's Healthcare, 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 Women's Healthcare field worldwide. Richter is also active in biosimilar product development.

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