Allergan and Richter Announce Positive Topline Results from Phase III Study of Cariprazine for the Treatment of Bipolar I Depression

Primary endpoint was met in the study evaluating patients with acute bipolar I depression treated with cariprazine 1.5 mg and 3 mg versus placebo

Allergan plans to submit Supplemental New Drug Application (sNDA) to Food and Drug Administration (FDA) in 2nd Half of 2018

DUBLIN, Ireland and BUDAPEST, Hungary – 18 December 2017 – Allergan plc (NYSE: AGN), a leading global pharmaceutical company, and Gedeon Richter Plc., today announced positive topline results for a phase III study of cariprazine for the treatment of adults with major depressive episodes associated with bipolar I disorder (bipolar I depression). This is the second positive pivotal trial of cariprazine for this investigational use.

In this study, the primary efficacy objective was met for both Cariprazine 1.5 mg and 3 mg dose groups ($p<0.05$). Both showed a significantly greater improvement than placebo for the change from baseline to week 6 on the Montgomery-Asberg Depression Rating Scale (MADRS) total score.

"These phase III data provide further support for cariprazine as a potential treatment for adults with bipolar depression, and adds to the growing clinical profile of this compound in mental health disorders," said David Nicholson, Chief Research & Development Officer at Allergan. "Bipolar depression is a serious and impairing condition of bipolar I disorder. At Allergan, we're committed to supporting underserved populations with limited treatment options, and look forward to submitting an sNDA for cariprazine as a treatment option for patients suffering from bipolar I depression."

"There are a limited number of products approved to treat bipolar depression and even fewer products that have been studied and approved to treat the full spectrum of bipolar disorder, from mania through depression. Having another product proven to treat the full range of bipolar disorder would be a welcome addition to the treatment options currently available to the psychiatry community and patients." said Gary Sachs, MD, Associate Clinical Professor of Psychiatry at Harvard Medical School.

"We consider today's positive results a major milestone in the process of making this promising treatment option available for patients suffering from bipolar depression and also widening the therapeutic scope of cariprazine," added Dr István Greiner, Research Director of Gedeon Richter Plc.

In this study, cariprazine was generally well tolerated. Sedation, somnolence, dizziness, akathisia and nausea were the most commonly reported adverse events (reported with a frequency of 5% or greater and at least twice that of placebo). In this study, 5.0% of cariprazine treated patients discontinued due to adverse events versus 2.5% of placebo treated patients.

The company plans to submit a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration in 2nd half of 2018.

About Cariprazine Bipolar I Depression Trial (RGH-MD-54)

RGH-MD-54 is a phase III, randomized, double-blind, placebo-controlled, parallel-group, multicenter, fixed-dose clinical trial in patients with bipolar I depression. A total of 488 patients were randomized in this study aiming to evaluate the efficacy, safety, and tolerability of cariprazine 1.5 mg/day and 3.0 mg/day compared to placebo in patients with bipolar I depression. Subjects underwent a no-drug screening period of approximately 7-14 days, followed by 6 weeks of double-blind treatment and a 1-week, no investigational product safety follow-up period.

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.

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-HT1A receptors and antagonist activity at serotonin 5-HT2A 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-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-HT_{2B} and 5-HT_{2A} receptors with high and moderate binding affinity, respectively 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. The clinical significance of these *in vitro* data is unknown.

VRAYLAR was discovered and co-developed by Gedeon Richter Plc and is licensed, 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 patients suffering from a broad range of mental health illnesses.

Visit www.vraylar.com for more information.

About Allergan plc

Allergan plc (NYSE: AGN), headquartered in Dublin, Ireland, is a bold, global pharmaceutical company and a leader in a new industry model – Growth Pharma. Allergan is 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 for the central nervous system, eye care, medical aesthetics and dermatology, gastroenterology, women's health, urology and anti-infective therapeutic categories.

Allergan is an industry leader in Open Science, a model of research and development, which defines our approach to identifying and developing game-changing ideas and innovation for better patient care. With this approach, Allergan has built one of the broadest development pipelines in the pharmaceutical industry with 55+ mid-to-late stage pipeline programs currently in development.

Allergan's success is powered by our more than 18,000 global colleagues' commitment to being Bold for Life. Together, we build bridges, power ideas, act fast and drive results for our customers and patients around the world by always doing what is right.

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 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; 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, 2016 and Allergan's Quarterly Report on Form 10-Q for the period ended September 30, 2017. Except as expressly required by law, Allergan disclaims any intent or obligation to update these forward-looking statements

About 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, in China and in Latin America. Having reached a market capitalisation of EUR 3.7 billion (US$ 3.9 billion) by the end of 2016, Richter's consolidated sales were approximately EUR 1.3 billion (US$ 1.4 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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