LUYE PHARMA GROUP LTD.

绿叶制药集团有限公司

(Incorporated in Bermuda with limited liability)

(Stock Code: 02186)

VOLUNTARY ANNOUNCEMENT

FIRST PATIENT ENROLLED FOR THE PHASE 2 CLINICAL STUDY OF THE GROUP'S NEW DRUG LY03015 IN CHINA

The board of directors (the "**Board**") of Luye Pharma Group Ltd. (the "**Company**", together with its subsidiaries, the "**Group**") announces that the Group's Class 1 new drug, LY03015 has completed the enrollment of the first patient in China for a Phase II clinical trial. LY03015 is a VMAT2 (vesicular monoamine transporter 2) inhibitor and a Sigma-1 receptor agonist, intended for the treatment of tardive dyskinesia ("**TD**") and Huntington's disease ("**HD**"). It is being developed in both China and the U.S., which will further strengthen the company's central nervous system ("**CNS**") portfolio.

TD is an abnormal, involuntary movement disorder associated with the long-term use of dopamine receptor blockers such as antipsychotics. It is primarily characterized by involuntary, rhythmic, repetitive and stereotyped movements. In 67% to 89% of TD patients, involuntary movements persist permanently, leading to a high rate of disability. Among patients taking antipsychotics, the average prevalence of TD reaches 25.3%. HD is an autosomal dominant neurodegenerative disorder, with typical symptoms including choreiform involuntary movements, cognitive impairment, and psychiatric or behavioral abnormalities.

VMAT2 inhibitors are currently the only drugs with proven clinical efficacy and safety in the treatment of TD and HD. However, there are still varying degrees of clinical challenges to the currently marketed VMAT2 inhibitors, such as insufficient efficacy due to serious adverse reactions caused by off-target effects, drug metabolism problems, black box warnings for the increased risk of depression and suicidal thoughts and behaviors, or warnings regarding increased cardiovascular risk.

LY03015 is a next-generation VMAT2 inhibitor developed by the Group on its New Chemical Entity/New Therapeutic Entity (NCE/NTE) platform. It works by inhibiting the transport function of VMAT2, reducing the release of dopamine (DA) from presynaptic neurons, thereby decreasing the DA-induced stimulation of hypersensitive D2 receptors without blocking D2 receptors on the postsynaptic membrane, thus alleviating the symptoms of TD and HD. Meanwhile, LY03015 is potent in agonizing Sigma-1 receptors. The activation of Sigma-1 receptor pathways reduces oxidative stress, provides neuroprotection, and improves cognitive function. This helps to treat TD and HD through multiple mechanisms, leading to better clinical therapeutic outcomes.

Preclinical studies show that LY03015 is superior to the marketed VMAT2 inhibitors in terms of vitro and in vivo pharmacologic and pharmacokinetic properties, having no off-target effects and better cardiac safety. A Phase I clinical trial shows that LY03015 is generally safe and well-tolerated with a relatively long half-life, which can be administered orally once a day. Compared with the marketed VMAT2 inhibitors, LY03015 is not metabolized by CYP2D6, thereby reducing the risk of drug interactions mediated by this enzyme.

The Phase II clinical trial of LY03015 to be conducted in China is a multicenter, randomized, double-blind, and placebo-controlled study in TD patients.

Data from IQVIA shows that the combined worldwide sales for the three originator drugs based on VMAT2 inhibitors approved for marketing by the U.S. FDA were approximately USD 3.069 billion, representing a 42% growth from 2022. In the first half of 2024, their combined worldwide sales were approximately USD 1.812 billion, growing 28% year-on-year.

There is a huge demand for CNS drugs, including those for treating TD and HD. However, new drug development in this therapeutic area has been relatively slow. The Group has developed a range of internationally competitive innovative drugs and formulations, and has become a leader among Chinese pharmaceutical companies in this therapeutic area. Examples include: Erzofri® (paliperidone palmitate) extended-release injectable suspension and Rykindo® (risperidone) for extended-release injectable suspension, both of which have been approved for marketing in the U.S.; and Ruoxinlin® (Toludesvenlafaxine Hydrochloride Extended-Release Tablets) and Jinyouping® (Rotigotine Microspheres for Injection), both of which have been launched in China. In addition, the Group is also conducting clinical studies for several drugs filed under China's Class 1 pathway, such as LY03020, a dual TAAR1/5-HT_{2C}R agonist, and LY03021, which targets NET/DAT/$GABA_A$R.

By Order of the Board
LUYE PHARMA GROUP LTD.
Liu Dian Bo
Chairman

Hong Kong, 15 January 2025

As at the date of this announcement, the executive directors of the Company are Mr. LIU Dian Bo, Mr. YANG Rong Bing, Mr. YUAN Hui Xian and Ms. ZHU Yuan Yuan; the non-executive directors of the Company are Mr. SONG Rui Lin and Dr. LYU Dong; and the independent non-executive directors of the Company are Mr. ZHANG Hua Qiao, Professor LO Yuk Lam, Mr. LEUNG Man Kit, Mr. CHOY Sze Chung Jojo and Ms. XIA Lian.