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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

APPROVAL OBTAINED FOR CLASS 1 INNOVATIVE ANTIDEPRESSANT LY03021 FOR CLINICAL TRIALS IN CHINA

The board of directors (the "**Board**") of Luye Pharma Group Ltd. (the "**Company**", together with its subsidiaries, the "**Group**") announces that the Center for Drug Evaluation of China's National Medical Products Administration has approved its Investigational New Drug application for LY03021, intended for the treatment of Major Depressive Disorder ("**MDD**"). LY03021 has been designated as a Class 1 innovative drug in China.

LY03021 is an inhibitor of the norepinephrine transporter ("**NET**") and the dopamine transporter ("**DAT**"), as well as a gamma-aminobutyric acid type A receptor-positive allosteric modulator ($GABA_AR$ PAM). Independently developed on the Group's New Chemical Entity/ New Therapeutic Entity (NCE/NTE) platform, this innovative antidepressant acts on the three targets above, featuring a novel mechanism of action ("**MoA**") that makes it a potential first-in-class drug. As far as the Company is aware, no other investigational drug with the same MoA is currently being developed.

MDD is a mood disorder characterized by significant and persistent depressive symptoms that impair social functions. Epidemiological data shows a lifetime prevalence of 3.4% and a 12-month prevalence of 2.1% for MDD in China, both of which are also increasing. This disorder has a high recurrence rate, a high suicide rate, and a high disability rate, placing a serious burden to patients, their family members, and the general public. Existing antidepressants have low response and remission rates, and it is common to observe a slow onset of action, residual symptoms, a high recurrence risk, and multiple adverse reactions in patients taking them. Therefore, how to quickly and effectively control the clinical symptoms of MDD and further improve treatment efficacy and patient prognosis become a challenge in the current development of antidepressant drugs.

LY03021 acts on three targets: NET, DAT, and $GABA_AR$. By targeting synaptic $GABA_A$ receptors (subtype $\alpha_1\beta_2\gamma_2$) and extrasynaptic $GABA_A$ receptors (subtype $\alpha_4\beta_3\delta$), this drug helps GABA activate $GABA_A$ receptors, regulates the glutamate/GABA balance in the brain, inhibits the excessive activation of the hypothalamic-pituitary-adrenal (HPA) axis, and rapidly exerts antidepressant effects. At the same time, it also increases norepinephrine ("**NE**") and dopamine ("**DA**") levels in the brain by inhibiting NET and DAT, significantly improving core symptoms, anhedonia, and sexual dysfunction in MDD patients. Through the wake-promoting effects of NE and DA, it also eliminates adverse reactions such as sedation, drowsiness, and loss of consciousness caused by GABA receptor activation.

Non-clinical studies have shown that LY03021 significantly inhibited depressive symptoms in animal models 24 hours after administration, and continuous administration could maintain the efficacy until the end of the 21-day study, demonstrating rapid onset and sustained efficacy with long-term and continuous administration. This drug also has a good safety profile, as its NOAEL (no-observed-adverse-effect-level) is 50 times above its effective dose.

There is a huge demand for CNS drugs, including those for treating MDD. However, progress of new drug development in this area has been relatively slow. The Group has developed a range of internationally competitive innovative drugs and formulations, making it a leader in this therapeutic area. The Group's product portfolio includes: Erzofri® (paliperidone palmitate) extended-release injectable suspension and Rykindo® (risperidone) 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 launched in China. In addition, the Group is conducting clinical studies for several Class 1 innovative drugs, such as LY03020, a dual agonist targeting TAAR1/5-HT_{2C}R, and LY03015, which targets VMAT2 and Sigma1.

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

Hong Kong, 11 November 2024

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.