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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 THE GROUP'S INNOVATIVE DRUG LY03021 FOR CLINICAL TRIALS IN THE U.S.

The board of directors (the "**Board**") of Luye Pharma Group Ltd. (the "**Company**", together with its subsidiaries, the "**Group**") announces that the Group has received clearance from the U.S. Food and Drug Administration (FDA) of its Investigational New Drug (IND) application for LY03021, an independently developed next-generation central nervous system (the "**CNS**") investigational drug, to initiate clinical trials in the U.S. LY03021 is intended for the treatment of major depressive disorder. To the knowledge of the Group, LY03021 is the world's first drug candidate to act as a positive allosteric modulator of the gamma-aminobutyric acid type A receptor (the "**$GABA_AR$**") and an inhibitor of the dopamine transporter (the "**DAT**") and norepinephrine transporter (the "**NET**").

Depression poses a substantial public health burden, affecting an estimated 322 million people worldwide. In 2025, an estimated 20 million U.S. adults experienced a major depressive episode in the past year. Depression is often comorbid with other mental disorders, such as anxiety disorders, and may also be accompanied by more serious functional impairments.

The onset of action for existing antidepressants is generally two to four weeks, and a substantial proportion of patients do not achieve full remission. Residual symptoms such as anxiety, low energy and anhedonia may persist after treatment, while adverse drug reactions such as sexual dysfunction may compromise treatment adherence. In addition, although a small number of rapid-acting antidepressants have been approved for marketing, their clinical use is significantly limited by requirements for supervised administration in healthcare settings and high risks of sedation, dissociation, loss of consciousness and abuse. Developing antidepressants that provide rapid and effective symptom control, further improve treatment outcomes and prognosis, and offer both convenience and safety therefore remains a major challenge in antidepressant development.

Developed on TransNEXCEED™, the Group's AI-powered drug discovery platform, LY03021 is a first-in-class, triple-target antidepressant that acts on $GABA_AR$, DAT and NET. It selectively targets the synaptic $\alpha_1\beta_2\gamma_2$ and extrasynaptic $\alpha_4\beta_3\delta$ $GABA_AR$ subtypes, modulating the balance between glutamatergic and GABAergic signaling in the brain to deliver rapid antidepressant and anxiolytic effects. Its high selectivity for extrasynaptic $GABA_ARs$ reduces the risks associated with the excessive activation of synaptic subtypes, including sedation, somnolence, loss of consciousness, and diminished efficacy with long-term treatment. By inhibiting DAT and NET, LY03021 increases dopamine (the "**DA**") and norepinephrine (the "**NE**") levels in the brain, modulating reward and mood pathways to help alleviate core depressive symptoms such as low mood and reduced interest. This activity may also help to address anhedonia commonly experienced by patients with depression, as well as sexual dysfunction associated with treatment or the disease itself. The wake-promoting effects mediated by DA and NE may also counteract CNS depression caused by excessive $GABA_AR$ activation, further improving CNS safety while providing antidepressant effects.

Nonclinical studies showed that LY03021 significantly improved depression- and anxiety-like behaviors in animal models as early as four hours after dosing. With continued dosing, efficacy remained stable through the end of a 56-day study. When LY03021 was administered once a week, its efficacy persisted until Day 7 after dosing. These findings suggest that LY03021 offers both rapid onset of action and sustained efficacy, and support the development of a once-a-week dosing regimen. LY03021 also showed a favorable safety profile, with a no-observed-adverse-effect level (NOAEL) at least 50 times the effective dose. No withdrawal signs associated with physical dependence were observed in animal studies.

LY03021 is another innovative CNS drug candidate being developed by the Group concurrently in China and the U.S., and a Phase I clinical study is currently underway in China. LY03021 has shown a favorable safety and tolerability profile at single doses ranging from 5 mg to 180 mg, with no adverse events of sedation, confusion or loss of consciousness observed. These findings provide preliminary validation of the hypothesis of differential modulation of synaptic and extrasynaptic $GABA_AR$ subtypes and synergy across the three targets. Nonclinical studies have indicated that LY03021 can rapidly and sustainably improve depressive- and anxiety-like behaviors in animal models. It is anticipated that the product may achieve an onset of action at 12 hours post-dose with once-weekly administration clinically, offering the combined advantages of rapid symptom control, sustained efficacy and dosing convenience. Leveraging its unique mechanism of action, it is expected to avoid the sedation risk associated with current rapid-onset therapies, and provide a new therapeutic option for the treatment of CNS disorders. The Group plans to initiate a Phase II clinical trial of LY03021 first in China in 2027, which will evaluate the rapid antidepressant efficacy and safety of a once-a-week dosing regimen at different doses.

The Group has a long-standing focus on CNS therapies, with multiple products launched across China, the U.S., Europe, Japan and other markets, and continues to advance the global development of next-generation innovative drugs. In addition to LY03021, several other differentiated novel chemical entities of the Group are in clinical development. LY03015, the world's only drug candidate targeting both vesicular monoamine transporter 2 (VMAT2) and sigma-1 receptor (Sigma-1R), is intended for the treatment of tardive dyskinesia and chorea associated with Huntington's disease, for which a Phase II clinical trial has been completed in China and a bridging study has been completed in the U.S.; LY03017 is a next-generation serotonin 2A receptor (5-HT_{2A}R) inverse agonist and serotonin 2C receptor (5-HT_{2C}R) antagonist intended for the treatment of psychosis associated with Alzheimer's disease, psychosis associated with Parkinson's disease and other indications; and LY03020 is the world's first dual agonist of trace amine-associated receptor 1 (TAAR1) and 5-HT_{2C}R, intended for the treatment of schizophrenia, psychosis associated with Alzheimer's disease and other indications. Both LY03017 and LY03020 are in Phase II clinical development in China and have been cleared for clinical trials in the U.S.

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

Hong Kong, 17 November 2026

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 Mr. HUANG Liming; 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.