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

ERZOFRI® (PALIPERIDONE PALMITATE) EXTENDED-RELEASE INJECTABLE SUSPENSION APPROVED BY THE FDA FOR TREATMENT OF SCHIZOPHRENIA AND SCHIZOAFFECTIVE DISORDER

The board of directors (the "**Board**") of Luye Pharma Group Ltd. (the "**Company**", together with its subsidiaries, the "**Group**") announces that ERZOFRI® (paliperidone palmitate) extended-release injectable suspension (also known as LY03010), an innovative formulation independently developed by the Group, has received marketing approval from the U.S. Food and Drug Administration (the "**FDA**") for treatment of schizophrenia in adult patients and for treatment of schizoaffective disorder in adults as monotherapy and as an adjunct to mood stabilizers or antidepressants.

Both schizophrenia and schizoaffective disorder are two types of severe, chronic psychiatric disorders characterized by recurring relapses. Antipsychotic medications play an important role in treating and controlling symptoms of schizophrenia and schizoaffective disorder, but patient adherence to antipsychotics is generally poor. Using long-acting injectable (LAI) antipsychotics is effective in improving patient adherence by reducing dosing frequency and can also reduce the risk of patients not adhering to their dosing regime without the knowledge of their healthcare providers.

ERZOFRI®, administered once per month, is the first patented paliperidone palmitate long-acting injection developed by a Chinese Company to be approved in the U.S. with independent intellectual property rights. The product was granted a patent in the U.S. (Patent No. 11,666,573) in 2023, which will expire in 2039. ERZOFRI® obtained marketing approval as a new drug under the 505(b)(2) pathway in the U.S.

Publicly available information shows that Paliperidone Palmitate Long-acting Injection generated sales of US$2.897 billion in the U.S. market in 2023. ERZOFRI® will provide patients with a new treatment option after being marketed.

ABOUT ERZOFRI®

What is ERZOFRI® (paliperidone palmitate) extended-release injectable suspension?

ERZOFRI® is an atypical antipsychotic indicated for:

- The treatment of schizophrenia in adults.
- The treatment of schizoaffective disorder in adults as monotherapy and as an adjunct to mood stabilizers or antidepressants.

IMPORTANT SAFETY INFORMATION FOR ERZOFRI®

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. ERZOFRI® is not approved for use in patients with dementia-related psychosis.

CONTRAINDICATIONS: ERZOFRI® is contraindicated in patients with a known hypersensitivity to either paliperidone or risperidone, or to any of the excipients in the ERZOFRI® formulation. Hypersensitivity reactions, including anaphylactic reactions and angioedema, have been reported in patients treated with risperidone and in patients treated with paliperidone.

WARNINGS AND PRECAUTIONS

Cerebrovascular Adverse Reactions: In clinical trials in elderly patients with dementia-related psychosis, increased risk of cerebrovascular adverse reactions (cerebrovascular accidents and transient ischemic attacks), including fatalities, have been reported in patients taking atypical antipsychotic medications compared to placebo. ERZOFRI is not approved for the treatment of patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome (NMS): NMS, a potentially fatal symptom complex, has been reported in association with antipsychotic drugs. Manage with immediate discontinuation and close monitoring.

QT Prolongation: Paliperidone causes a modest increase in the corrected QT (QTc) interval. The use of paliperidone should be avoided in combination with other drugs that are known to prolong QTc. Paliperidone should also be avoided in patients with congenital long QT syndrome and in patients with a history of cardiac arrhythmias.

Tardive Dyskinesia (TD): TD, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to predict which patients will develop the syndrome. Whether antipsychotic drug products differ in their potential to cause TD is unknown.

The risk of developing TD and the likelihood that it will become irreversible appear to increase with the duration of treatment and the cumulative dose. The syndrome can develop after relatively brief treatment periods, even at low doses. It may also occur after discontinuation of treatment. TD may remit, partially or completely, if antipsychotic treatment is discontinued. Antipsychotic treatment itself may suppress (or partially suppress) the signs and symptoms of the syndrome and may thus mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown.

If signs and symptoms of TD appear in a patient treated with ERZOFRI®, drug discontinuation should be considered. However, some patients may require treatment with ERZOFRI® despite the presence of the syndrome.

Metabolic Changes: Atypical antipsychotic drugs have been associated with metabolic changes, including hyperglycemia, dyslipidemia, and body weight gain.

- **Hyperglycemia and Diabetes Mellitus:** Hyperglycemia and diabetes mellitus, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, have been reported in patients treated with all atypical antipsychotics. Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening glucose control. Patients with risk factors for diabetes mellitus who are starting treatment with atypical antipsychotics, including ERZOFRI®, should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

- **Dyslipidemia:** Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics.

- **Weight Gain:** Weight gain has been observed with atypical antipsychotic use. Monitoring weight is recommended.

Orthostatic Hypotension and Syncope: Paliperidone can induce orthostatic hypotension and syncope in some patients. Use ERZOFRI® with caution in patients with known cardiovascular disease (e.g., heart failure, history of myocardial infarction or ischemia, conduction abnormalities), cerebrovascular disease, or conditions that predispose the patient to hypotension. Monitoring of orthostatic vital signs should be considered in patients who are vulnerable to hypotension.

Falls: Somnolence, postural hypotension, motor and sensory instability have been reported with the use of antipsychotics, including paliperidone palmitate, which may lead to falls and, consequently, fractures or other fall-related injuries. For patients, particularly the elderly, with diseases, conditions, or medications that could exacerbate these effects, assess the risk of falls when initiating antipsychotic treatment and recurrently for patients on long-term antipsychotic therapy.

Leukopenia, Neutropenia, and Agranulocytosis: Events of leukopenia, neutropenia, and agranulocytosis have been reported temporally related to antipsychotic agents. Patients with a history of a clinically significant low white blood cell count (WBC)/absolute neutrophil count (ANC) or past drug-induced leukopenia/neutropenia should have their complete blood count (CBC) monitored frequently during the first few months of therapy. Discontinuation of ERZOFRI® should be considered at the first sign of a clinically significant decline in WBC in the absence of other causative factors.

Monitor patients with clinically significant neutropenia for fever or other symptoms or signs of infection and treat promptly if such symptoms or signs occur. Discontinue ERZOFRI® in patients with absolute neutrophil count <1000/mm^3 and follow their WBC until recovery.

Hyperprolactinemia: Like other drugs that antagonize dopamine D2 receptors, paliperidone elevates prolactin levels and the elevation persists during chronic administration. Paliperidone has a prolactin-elevating effect similar to that seen with risperidone, a drug that is associated with higher levels of prolactin than other antipsychotic drugs. Long-standing hyperprolactinemia, when associated with hypogonadism, can lead to decreased bone density in males and females.

Potential for Cognitive and Motor Impairment: Antipsychotics, including ERZOFRI®, have the potential to impair judgement, thinking, and motor skills. Patients should be cautioned about performing activities requiring mental alertness, such as operating hazardous machinery or operating a motor vehicle, until they are reasonably certain that paliperidone therapy does not adversely affect them.

Seizures: ERZOFRI® should be used cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold.

Dysphagia: Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Antipsychotic drugs, including ERZOFRI®, should be used cautiously in patients at risk for aspiration.

Priapism: Priapism has been reported with oral paliperidone during post-marketing surveillance. Severe priapism may require surgical intervention.

Disruption of Body Temperature Regulation: Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. Appropriate care is advised when prescribing ERZOFRI® to patients who will be experiencing conditions which may contribute to an elevation in core body temperature, such as exercising strenuously, exposure to extreme heat, receiving anticholinergic medications, or dehydration.

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥ 5% and occurring at least twice as often as placebo) were injection site reactions, somnolence/sedation, dizziness, akathisia, and extrapyramidal disorder.

DRUG INTERACTIONS

An additive effect may occur when co-administered ERZOFRI with drugs that may cause orthostatic hypotension.

Avoid using a strong inducer of CYP3A4 and/or P-glycoprotein (P-gp) during a dosing interval for ERZOFRI®. If concomitant use is necessary, consider using paliperidone extended-release tablets.

USE IN SPECIFIC POPULATIONS

Pregnancy: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure. There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to atypical antipsychotics, including ERZOFRI®, during pregnancy. Healthcare providers are encouraged to register patients by contacting the National Pregnancy Registry for Atypical Antipsychotics at 1-866-961-2388 or online at http://womensmentalhealth.org/clinicaland-research-programs/pregnancyregistry/.

Lactation: Infants exposed to ERZOFRI through breastmilk should be monitored for excess sedation, failure to thrive, jitteriness, and extrapyramidal symptoms (tremors and abnormal muscle movements).

Fertility: Based on the pharmacologic action of paliperidone (D2 receptor antagonism), treatment with ERZOFRI® may result in an increase in serum prolactin levels, which may lead to a reversible reduction in fertility in females of reproductive potential.

Pediatric Use: Safety and effectiveness of ERZOFRI® in pediatric patients have not been established.

Please see full Prescribing Information at https://www.luye.cn/lvye_en/erzofri.pdf, including BOXED WARNING, for ERZOFRI®.

ABOUT THE CLINICAL TRIALS OF ERZOFRI®

The U.S. FDA approval of ERZOFRI® is based on the results of an open-label, randomized, multiple-dose, parallel-group study that enrolled 281 patients (aged 18-65) with schizophrenia or schizoaffective disorder (NCT04922593), designed to evaluate the PK profile of ERZOFRI® and its relative bioavailability compared with the listed drug INVEGA SUSTENNA®. ERZOFRI® was demonstrated to be bioequivalent to the listed drug at steady state after multiple administrations. Compared with the listed drug, the initial dosing was optimized for ERZOFRI® by omitting the injection on Day 8 after the first injection, resulting in a comparable total drug exposure.

The safety profile of ERZOFRI® is consistent with the known safety profile of the listed drug.

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

Hong Kong, 28 July 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.