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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**

**PATIENT ENROLLMENT COMPLETED FOR THE PHASE 2 CLINICAL STUDY OF NEW CLASS 1 DRUG LY03014 IN CHINA**

The board of directors (the “**Board**”) of Luye Pharma Group Ltd. (the “**Company**”, together with its subsidiaries, the “**Group**”) announces that the new Class 1 drug LY03014 (“**LY03014**”) developed by the Group has completed the patient enrollment for its phase 2 clinical trial in China. LY03014 is a small molecule G protein biased at mu-opioid receptor (“**MOR**”) agonist, and is indicated for the treatment of moderate to severe acute postoperative pain and breakthrough cancer pain.

The phase 2 clinical trial is a multi-center, randomized, double-blind, placebo- and positive-controlled parallel study to preliminarily evaluate the analgesic efficacy and safety of LY03014 in patients with moderate to severe postoperative pain after abdominal surgery.

Opioids are commonly used to treat moderate-to-severe acute postoperative pain and breakthrough cancer pain. Opioids are used with the aim to improving the quality of life of patients with moderate-to-severe pain. However, opioids for medical use currently available in the marketplace present a common risk of Opioid-induced Respiratory Depression (OIRD), which is a major cause of death in clinical practice.

As a novel analgesic, LY03014 can separate analgesia and respiratory depression, and is expected to meet the unmet clinical needs above. The results of its phase 1 clinical trials show that a single intravenous infusion of LY03014 can significantly improve the pain threshold and pain tolerance of subjects with a good overall safety profile. Non-clinical studies show that LY03014 has good blood-brain barrier permeability and a good pharmacokinetic profile. A proof-of-concept (“**POC**”) study shows that compared to conventional MOR agonists, LY03014 completely separated the G protein pathway and the  $\beta$ -arrestin2 pathway, which mainly alleviates adverse effects associated with MOR

activation, such as respiratory depression, constipation, and opioid tolerance. The POC study also shows that at equianalgesic doses, LY03014 was less likely to cause respiratory depression, gastrointestinal dysfunction, or opioid tolerance than morphine. Another promising feature of LY03014 observed in studies is that unlike other G protein biased MOR agonists, it did not cause QTc prolongation, which can lead to potentially fatal arrhythmias and liver toxicity. The research results were published in the *European Journal of Medicinal Chemistry*, an international academic journal.

It has been reported that globally, over 300 million patients receive surgeries each year, and more than 80% of them suffer from postoperative pain, of which about 75% is acute. In China, approximately 4.57 million new cancer cases were reported in 2020. For patients with malignant tumors, pain is one of the most common symptoms. It is estimated that about 80% of tumor patients would develop cancer pain during their disease treatment and the incidence of breakthrough cancer pain among these patients ranges from 33% to 95%.

According to the data from IQVIA CHPA, the sales amount of China's anesthesia and analgesia market in 2022 reached RMB37.3 billion, representing a compound annual growth rate ("CAGR") of 7.7% from 2018 to 2022. Among them, the sales amount of opioids in 2022 reached RMB19.0 billion, representing a CAGR of 10.4% from 2018 to 2022, and the growth rate exceeded the average growth rate of the entire anesthesia and analgesia field.

The Company believes that LY03014 has the potential to address the prevailing clinical demands and has good market potential in China. It, together with the other oncology products of the Group, creates a comprehensive product portfolio. Leveraging on the Group's existing resources and advantages in oncology, the addition of LY03014 will help accelerate the Company's coverage and development in this field.

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

Hong Kong, 6 July 2023

*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. SUN Xin; 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.*