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 DOSED IN A PHASE II CLINICAL STUDY IN CHINA FOR NEW CLASS 1 DRUG LY03014

The board of directors (the "**Board**") of Luye Pharma Group Ltd. (the "**Company**", together with its subsidiaries, the "**Group**") announces that the first patient has been dosed in a Phase II clinical study for new Class 1 drug LY03014 developed by the Group in the People's Republic of China ("**China**"). LY03014 is a small molecule Gi 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 II 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 the most commonly medications for moderate to severe acute postoperative pain and breakthrough cancer pain in clinical practice. On one hand, opioids can significantly improve the quality of life for patients with moderate to severe pain. They are administered for no more than 72 hours after an operation, so there is no addiction concern. On the other hand, respiratory depression is a major cause of death resulting from the usage of opioids. Therefore, all opioids available in the market have a black box warning. Furthermore, fatal respiratory depression is also the most principal risk factor in using opioids currently available to manage postoperative pain and breakthrough cancer pain.

As a novel analgesic, LY03014 can separate respiratory depression and analgesia, and is expected to meet the unmet clinical needs above. The results of its Phase I clinical trials show that a single intravenous infusion of LY03014 can significantly improved the pain tolerance of the subjects and has good security overall. 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 Gi pathway and the β-arrestin2 pathway, which mainly mediates 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 Gi 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 authoritative international academic journal.

Globally, it is estimated that there are approximately more than 300 million patients receiving surgeries in a year. More than 80% of them suffer from postoperative pain, of which about 75% is acute postoperative pain. In China, approximately 4.57 million new cancer cases were reported in 2020. For cancer patients, pain is one of the most common and unbearable symptoms. The incidence of pain is about 25% in newly diagnosed cancer patients and 60 to 80% in patients with advanced cancer, of which one-third have severe pain.

According to the data from IQVIA CHPA, the sales amount of China's anesthesia and analgesia market in 2021 reached RMB38.8 billion, representing a compound annual growth rate ("**CAGR**") of 13.6% from 2017 to 2021. Among them, the sales amount of opioids in 2021 reached RMB18.1 billion, representing a CAGR of 16.6% from 2017 to 2021, 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, 29 November 2022

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 and Mr. CHOY Sze Chung Jojo.