LEPU BIOPHARMA CO., LTD.
樂普生物科技股份有限公司

(A joint stock company incorporated in the People's Republic of China with limited liability)

(Stock Code: 2157)

VOLUNTARY ANNOUNCEMENT

CONDITIONAL MARKETING APPROVAL OBTAINED IN CHINA FOR PUYOUHENG (PUCOTENLIMAB INJECTION) FOR THE TREATMENT OF INOPERABLE OR METASTATIC MELANOMA

A. INTRODUCTION

This announcement is made by Lepu Biopharma Co., Ltd. (the "**Company**", together with its subsidiaries, the "**Group**") on a voluntary basis.

The board of directors of the Company (the "**Board**") is pleased to announce that, the National Medical Products Administration (the "**NMPA**") of the People's Republic of China (the "**PRC**") has recently granted an approval to PUYOUHENG (Pucotenlimab Injection), a humanized antagonist monoclonal antibody ("**mAb**") to human programmed cell death protein 1 ("**PD-1**"), which can antagonize the PD-1 signal to restore the capability of the immune cells to kill cancer cells through blocking PD-1 binding to its ligands PD-L1 and PD-L2, for the treatment of inoperable or metastatic melanoma after systemic therapy failure.

B. ABOUT MELANOMA

Melanoma is a type of malignancies that develops from melanocytes and is the most fatal skin cancer as it accounts for lower than 5% in all skin cancers but contributes to more than 75% of all deaths from skin cancers. For malignant melanoma in the early stage, surgery is the main treatment; for advanced melanoma, treatment is limited and has poor prognosis. As an innovative humanized anti-PD-1 mAb drug, pucotenlimab innovatively improves half-life through triple mutations and achieves binding with PD-1 with high affinity, thereby restoring the capability of the immune cells to kill cancer cells by blocking PD-1 binding to its ligands PD-L1 and PD-L2.

PUYOUHENG has high affinity and good stability in binding to PD-1 and has demonstrated superior anti-tumour efficacy in preclinical and clinical trials.

C. ABOUT PUYOUHENG (PUCOTENLIMAB INJECTION)

PUYOUHENG is a humanized immunoglobulin G4 mAb against human PD-1 independently developed by the Company, which can bind with PD-1 with high affinity to restore the capability of the immune cells to kill cancer cells by blocking PD-1 binding to its ligands PD-L1 and PD-L2.

PUYOUHENG employs an innovative molecular design to extend its half-life and demonstrated strong clinical anti-tumor activity and a favorable safety profile. It innovatively employs antibody engineering techniques to introduce triple mutations in Fc portion to increase FcRn binding, thereby significantly improving its half-life and leading to encouraging clinical efficacy and drug compliance of patients. Compared with all competing anti-PD-1 antibodies that were marketed or had entered a Phase III clinical trial, PUYOUHENG demonstrated an average half-life of 21.8 days (single dose). Furthermore, the extension of the half-life did not cause any additional adverse event, it has shown encouraging clinical efficacy. In July 2022, PUYOUHENG has obtained marketing approval for the treatment of advanced solid tumours with high levels of microsatellite instability ("**MSI-H**") or deficient mismatch repair ("**dMMR**").

The approval is mainly based on a single-arm, open-label, registrational Phase II clinical study, and the primary endpoint of such trial is objective response rate (ORR) evaluated by the Independent Review Committee (IRC) according to RECIST 1.1. A total of 119 patients were enrolled and as of July 30, 2021, the ORR evaluated by the IRC was 20.2% (95% CI: 13.4-28.5) with 1 patient achieving complete response and 23 patients achieving partial response. The results of the study indicate that PUYOUHENG has significant benefit in treatment of inoperable or metastatic melanoma after systemic therapy failure, met the primary endpoint criteria and had good safety profile.

Note: The data source is the label of the PUYOUHENG (Pucotenlimab Injection).

As of the date of this announcement, other than the approvals of PUYOUHENG (Pucotenlimab Injection) in MSI-H/dMMR and in melanoma, both granted by the NMPA, we are conducting clinical trial of PUYOUHENG (Pucotenlimab Injection) in advanced gastric cancer/ gastroesophageal junction carcinoma.

In addition, the Company has been accelerating its developments on various solid tumours and has been actively working on immuno-oncology combination therapies, including the treatment of cancers with the high prevalence such as gastric cancer, liver cancer and lung cancer.

D. IMPACT ON THE COMPANY

PUYOUHENG (Pucotenlimab Injection) is the first innovative biological drug that is developed by the Company and approved for marketing. The approved indication for the MSI-H/dMMR solid tumours and Melanoma, covering a wide range of patient groups. PUYOUHENG (Pucotenlimab Injection), being approved for marketing, will offer more treatment options to patients. The Company will continue to strengthen its overseas business development in the international market and the international clinical development and business development with global collaborators.

In respect of international development, the Company will promote the joint development, collaboration and license of new drugs globally.

By order of the Board
Lepu Biopharma Co., Ltd.
Dr. Pu Zhongjie
Chairman of the Board and Executive Director

Shanghai, the PRC, September 29, 2022

As at the date of this announcement, the board of directors of the Company comprises Dr. Pu Zhongjie (Chairman), Dr. Sui Ziye (Chief Executive Officer) and Dr. Hu Chaohong (Co-Chief Executive Officer) as executive Directors; Ms. Pu Jue, Mr. Yang Hongbing and Mr. Lin Xianghong as non-executive Directors; and Mr. Zhou Demin, Mr. Yang Haifeng and Mr. Fengmao Hua as independent non-executive directors.