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)

INSIDE INFORMATION ANNOUNCEMENT

CONDITIONAL MARKETING APPROVAL OBTAINED IN CHINA FOR PUYOUHENG (PUCOTENLIMAB INJECTION) FOR THE TREATMENT IN HIGH LEVELS OF MICROSATELLITE INSTABILITY/DEFICIENT MISMATCH REPAIR (MSI-H/DMMR)

A. INTRODUCTION

This announcement is made by Lepu Biopharma Co., Ltd. (the "**Company**") pursuant to Rule 13.09 of the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited (the "**Listing Rules**") and the Inside Information Provisions (as defined in the Listing Rules) under Part XIVA of the Securities and Futures Ordinance (Chapter 571, Laws of Hong Kong).

The board of directors of the Company (the "**Board**") is pleased to announce that, the National Medical Products Administration (the "**NMPA**") has recently granted conditional marketing approval in China for 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 their ligands PD-L1 and PD-L2, for the treatment of patients in high levels of microsatellite instability/deficient mismatch repair ("**MSI-H/dMMR**") solid tumors: including patients with advanced colorectal cancer who have experienced disease progression after previous therapy with fluorouracil, oxaliplatin and irinotecan as well as patients with other advanced solid tumours who have experienced disease progression after previous first-line therapy and no satisfactory treatment alternatives.

B. ABOUT MSI-H/dMMR

Microsatellite instability ("**MSI**") refers to any change in microsatellite length due to either insertion or deletion of repeating units in a microsatellite in a tumor, compared to normal tissue, leading to the appearance of new microsatellite alleles. The impairment of the mismatch repair ("**MMR**") system can cause such changes. Microsatellite instability-high ("**MSI-H**") or deficient mismatch repair ("**dMMR**") has been observed in various cancers, the occurrence rate of which in endometrial cancer, colorectal cancer or gastric cancer, and other cancers is nearly 30%, about 20% and about or less than 5%, respectively. MSI-H/dMMR tumors are more likely to respond to immunotherapies than tumors with fewer mutations due to the significantly increased number of somatic mutations which express a large number of neoantigens.

C. ABOUT PUYOUHENG (PUCOTENLIMAB INJECTION)

PUYOUHENG (Pucotenlimab Injection) 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 their ligands PD-L1 and PD-L2. PUYOUHENG (Pucotenlimab Injection) 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 (Pucotenlimab Injection) 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, and it has shown encouraging clinical efficacy profile.

The approval is mainly based on a multi-center, open-label, Phase II clinical study, the primary endpoint of which is the objective response rate (the "**ORR**") evaluated by the Independent Review Committee (the "**IRC**") according to RECIST1.1. As of December 4, 2021, the study had enrolled a total of 100 patients with histologically diagnosed advanced solid tumors which were identified by the central laboratory as MSI-H/dMMR tumors. The enrolled patients received intravenous drip of PUYOUHENG (Pucotenlimab Injection) once every three weeks ("**Q3W**") at the dose level of 200 mg. The median follow-up period for the population was 22.5 months, and the ORR was 49.0% (95% CI: 38.86%, 59.20%) with 9 patients realizing complete response and 40 patients realizing partial response; in the subgroup of patients with colorectal cancer who had failed treatment with triple therapy (fluorouracil, oxaliplatin and irinotecan), the ORR was 50.0% (95% CI: 31.30%, 68.70%). The results of the study indicate that PUYOUHENG (Pucotenlimab Injection) as monotherapy is safe and efficacious for the treatment of patients with advanced unresectable or metastatic MSI-H/dMMR tumors that failed prior standard treatment, the expected clinical endpoints have been achieved and the patients can gain significant benefits from the treatment.

Note: The above data come from CSR.

As of the date of this announcement, other than the approval of PUYOUHENG (Pucotenlimab Injection) in MSI-H/dMMR granted by the NMPA, the NMPA has accepted the new drug application of PUYOUHENG (Pucotenlimab Injection) in melanoma in July 2021, and the use of PUYOUHENG (Pucotenlimab Injection) in advanced gastric cancer/gastroesophageal junction carcinoma in second-line therapy has entered into the Phase III registrational trial stage.

D. IMPACT ON THE COMPANY

PUYOUHENG (Pucotenlimab Injection) is the first innovative biological drug developed by the Company and approved for marketing. The approved indication for the MSI-H/dMMR solid tumours are screened by specific MSI-H/dMMR solid tumour markers rather than by cancer type, covering a wide range of patient groups. PUYOUHENG (Pucotenlimab Injection), being approved for marketing, will offer more treatment options to patients.

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

Shanghai, the PRC, July 22, 2022

As at the date of this announcement, the board of directors of the Company comprises Dr. Pu Zhongjie as chairman and executive director, Dr. Sui Ziye as executive director and chief executive officer, Dr. Hu Chaohong as executive director and co-chief executive officer, 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.