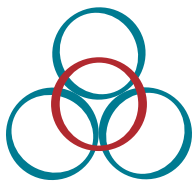


Hong Kong Exchanges and Clearing Limited and The Stock Exchange of Hong Kong Limited take no responsibility for the contents of this announcement, make no representation as to its accuracy or completeness and expressly disclaim any liability whatsoever for any loss howsoever arising from or in reliance upon the whole or any part of the contents of this announcement.



四环医药  
*SihuanPharm*

**Sihuan Pharmaceutical Holdings Group Ltd.**

**四環醫藥控股集團有限公司**

*(incorporated in Bermuda with limited liability)*

**(Stock Code: 0460)**

**VOLUNTARY ANNOUNCEMENT**  
**THE RECOMBINANT HUMAN CD80 MUTANT – Fc FUSION**  
**PROTEIN INJECTION AND**  
**XZP-6877 TABLETS DEVELOPED BY XUANZHU BIOPHARM**  
**WERE APPROVED FOR CLINICAL TRIALS**

The board of directors (the “**Board**”) of Sihuan Pharmaceutical Holdings Group Ltd. (the “**Company**” or “**Sihuan Pharmaceutical**”, together with its subsidiaries, the “**Group**”) is pleased to announce that the recombinant human CD80 mutant - Fc fusion protein injection (drug code: XZP-KM602) and selective DNA Dependent Protein Kinase (DNA-PK) Inhibitor (drug code: XZP-6877 tablets), developed by Xuanzhu Biopharmaceutical Co., Ltd. (“**Xuanzhu Biopharm**”), a non-wholly owned subsidiary of the Group, have been approved by the National Medical Products Administration of the People’s Republic of China (“**China**”) to initiate clinical trials for the treatment of advanced solid tumors.

**About CD80 mutant – Fc fusion protein injection**

XZP-KM602 is a new generation drug of tumor immune, and is a fusion protein composed of the engineered human CD80 extracellular domain and the Fc domain of human IgG1. It largely maintains the structure of natural CD80 and has low immunogenicity. It can enhance the activation of T cells in three pathways, such as by inhibiting PD-L1 and CTLA-4 and promoting the co-stimulation of CD28, thus showing stronger anti-tumor activity. In addition, KM602 has immune memory function, and its anti-tumor activity lasts.

KM602 is compared with FPT155 of Five Prime Therapeutics. FPT155 has the fastest progress in the world and is currently in clinical phase I. Preclinical study shows that KM602 has better anti-tumor efficacy than anti-PD-L1 drugs, anti-CTLA4 immune checkpoint drugs and the similar product, FPT155, and has better safety with the potential to be First-In-Class.

Although there are many drugs for immune checkpoint inhibitors (such as PD-1/PD-L1 drugs) on the market, only some patients benefit. Most tumor patients have low response rate and drug resistance, which may be due to the lack of sufficient T cell co-stimulation in the tumor microenvironment, such as too few CD28 ligands. KM602 enhances the activation of T cells through multiple pathways, and has the potential to break through the low response rate and drug resistance of tumor patients.

KM602 is the first and only CD80 mutant - Fc fusion protein in China, which is expected to fill the market gap in this field in China.

### **About XZP-6877 tablets**

XZP-6877 is a selective DNA dependent protein kinase (DNA-PK) inhibitor independently developed by Xuanzhu Biopharm, which can block the main channels for repairing DNA double-strand breaks (DSBs) caused by radiotherapy or chemotherapy drugs, and improve the sensitivity of tumor cells to radiotherapy and chemotherapy; At the same time, it destroys the stability of telomere DNA structure to inhibit the proliferation and growth of tumor cells. The combination of the two mechanisms can enhance the anti-tumor efficacy and more effectively control tumors.

XZP-6877 has good PK (pharmacokinetics) properties, good oral absorption, high bioavailability, and good safety; It has shown enhanced treatment effect of radiotherapy and chemotherapy on multiple pharmacodynamic models, such as triple negative breast cancer model, small cell lung cancer model, and head and neck cancer model, and has broad spectrum anti-cancer potential. Animal pharmacodynamic models also show that 6877 can prolong survival time, providing a new exploration direction for improving patient survival.

XZP-6877 is the first DNA-PK inhibitor in China, with leading research and development progress and technical advantages. Preclinical data indicate that it has good drug forming ability, and is expected to fill the domestic market gap in this field.

## **About Xuanzhu Biopharm**

Xuanzhu Biopharm is the innovative drug subsidiary of Sihuan Pharmaceutical. It is an innovative pharmaceutical company with roots in China and a global perspective, focusing on major diseases such as digestion, oncology and non-alcoholic steatohepatitis, and is committed to the research and development, production and commercialization of class 1 drugs with core proprietary intellectual property rights to address unmet clinical medical needs. The company has a team with extensive experience in the development and industrialisation of innovative drugs. Having been involved in the research of digestion, oncology and non-alcoholic steatohepatitis for many years, the company has a deep understanding and international vision of the development of new drugs in related fields and their future development direction. The company has two R&D platforms: small molecule chemistry and large molecule biologics. The dual engines drive the company's innovation and development, forming a product pipeline that covers small molecule, monoclonal antibodies, bispecific antibodies, antibody-drug conjugate (ADC) and other types of products. The company adheres to the strategic concept of "innovation driven, promoting the development of new drugs in China and serving human health", and the values of "open innovation, courageous commitment, overcoming difficulties and scientific rigor". With a focus on unmet major clinical needs, the company continues to develop new class 1 drugs with international competitiveness, and is committed to developing into a first-class innovative pharmaceutical company with independent research and development, production, and sales capabilities.

## **About Sihuan Pharmaceutical**

Founded in 2001 and listed on the Main Board of The Stock Exchange of Hong Kong Limited in 2010, Sihuan Pharmaceutical is an international medical aesthetic and biopharmaceutical company led and driven by innovation, with an independent and leading research and development technology platform, a rich global product pipeline, strong product registration capability, a full dosage form production platform with high efficiency and low cost and a mature and excellent sales system. Adhering to the overall strategic objective of "full promotion of a two-wheel drive strategy of its medical aesthetics and biopharmaceutical businesses", Sihuan Pharmaceutical endeavours to build itself into a leading medical aesthetics and biopharmaceutical company in China.

This announcement is being made by the Group on a voluntary basis to update the investing public on the Group's latest business development, and does not constitute, and is not intended to be, an advertisement regarding the use of any medicine, surgical appliance, treatment or orally consumed product.

By order of the Board  
**Sihuan Pharmaceutical Holdings Group Ltd.**  
**Dr. Che Fengsheng**  
*Chairman and Executive Director*

Hong Kong, 27 March 2023

*As at the date of this announcement, the executive directors of the Company are Dr. Che Fengsheng (Chairman), Dr. Guo Weicheng (Deputy Chairman and Chief Executive Officer), Dr. Zhang Jionglong, Ms. Chen Yanling and Ms. Miao Guili; and the independent non-executive directors of the Company are Mr. Patrick Sun, Mr. Tsang Wah Kwong and Dr. Zhu Xun.*