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

Successful Submission of Investigational New Drug (IND) Application to U.S. Food and Drug Administration (FDA) for Self-Developed Innovative Patented Oncology Drug — Pirotinib

The board of directors (the "**Board**") of Sihuan Pharmaceutical Holdings Group Ltd. (the "**Company**", together with its subsidiaries, the "**Group**") announced that the Group's innovative drug research and development division has submitted an Investigational New Drug (IND) application for Pirotinib ("**Pirotinib**" or the "**new drug**"), a self-developed innovative patented oncology drug, on 27 October 2014 (U.S. Time) to the U.S. FDA. This is the first innovative patented drug successfully developed by the Group and submitted to the U.S. FDA, demonstrating that the Group's innovative drug development has entered a stage of international development.

Pirotinib, a novel irreversible pan-epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI), is developed by Shandong Xuanzhu Pharma Co., Ltd. ("**Shandong XuanZhu**"), a wholly-owned subsidiary of the Group, for the treatment of lung cancer, breast cancer, gastric cancer as well as other malignancies with unmet medical needs.

Preclinical *in vitro* and *in vivo* studies demonstrate that Pirotinib not only shows high efficacy in tumors harboring EGFR activation mutations, but also effectively overcomes the drug resistance induced by the first-generation EGFR TKIs. When compared to the same class of drugs were recently approved for commercial use,

Pirotinib shows superior activity against the acquired drug resistance mutation due to its excellent efficacy, distinct pharmacokinetics profiles and tissue distribution, and excellent safety profiles. Furthermore, recent studies have discovered novel oncogenic mutations in the EGFR family in malignancies such as lung and gastric cancers. Pirotinib has exhibited astonishing inhibition on the oncogenic transformation caused by these newly-discovered mutations. Shandong XuanZhu will explore to address these unmet medical needs in the targeted patient population in clinical trials. The patent for Pirotinib has been issued in the People's Republic of China ("**China**"), and the drug has entered the substantive examination stage in the United States, Japan, Europe, and Hong Kong.

The IND application for clinical trial approval (Category 1.1) of Pirotinib to the China Food and Drug Administration (CFDA) was filed on 30 September 2013, and is currently under regulatory review. Shandong XuanZhu is working closely with Covance on the clinical development of Pirotinib in the United States. We expect clinical trials for Pirotinib to be open in the United States in the beginning of 2015 if the process undergoes smoothly.

Due to the rapidly aging population and environmental pollution, the global incidence of cancer will continue to grow, while the situation in China is even more worrisome. Cancer and cardio-cerebral vascular disease are the two major disease areas with the highest fatality rates, and the global oncology drug market has reached USD 91 billion by the end of 2013. According to statistics from MENET, China's average cancer incidence rate is already more than three thousandths, while the incidence rate among urban residents exceeds five thousandths, and the number of newly diagnosed cancer patients has reached more than 3.12 million annually. China's oncology drug market reached RMB 85 billion (including immunity enhancers) in 2013. As the incidence of cancer continues to grow on the back of a rapidly aging population and urbanization, the oncology market in China is projected to reach RMB 100 billion in two years. Thus, there is tremendous market potential for innovative and effective oncology treatment.

Pirotinib is the first innovative patented oncology drug developed by the Group. The successful IND submission of Pirotinib both in China and the United States marks the Group's entry into a new stage of oncology drug discovery and development. In addition, the successful IND submission in U.S. also showcases that the Group's innovative drug research and development capabilities have reached international standards, laying a firm foundation for international collaboration in the future.

This announcement is being made by the Company on a voluntary basis to let the investing public understand the Group's latest business developments, 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.
Che Fengsheng
Chairman and Executive Director

Hong Kong, 28 October 2014

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) and Mr. Meng Xianhui; the non-executive directors of the Company are Dr. Zhang Jionglong and Mr. Homer Sun; and the independent non-executive directors of the Company are Mr. Patrick Sun, Mr. Tsang Wah Kwong and Mr. Zhu Xun.