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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

NDA OF BIREOCICLIB TABLETS' NEW INDICATION, IN COMBINATION WITH AROMATASE INHIBITOR FOR FIRST-LINE TREATMENT OF HR+/HER2- ADVANCED BREAST CANCER, ACCEPTED BY NMPA

The board of directors (the “**Board**”) of Sihuan Pharmaceutical Holdings Group Co., Ltd. (the “**Company**” or “**Sihuan Pharmaceutical**”, together with its subsidiaries, the “**Group**”) is pleased to announce that the New Drug Application (the “**NDA**”) for a new additional indication of Bireociclib Tablets (Trade Name: Xuan Yue Ning) (the “**Product**”), a Class 1 innovative drug independently developed by the Group’s non-wholly owned subsidiary Xuanzhu Biopharmaceutical Co., Ltd. (the “**Xuanzhu Biopharm**”), has been accepted for review by the National Medical Products Administration (the “**NMPA**”) of China. The specific indication accepted is: combined with aromatase inhibitors as the initial endocrine therapy for patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) (“**HR+/HER2-**”) advanced breast cancer, and the treatment for patients who progressed after adjuvant therapy with Tamoxifen or Toremifene. **This is the third indication for the Product to apply for NDA.**

Bireociclib is a CDK4/6 (cell cyclin-dependent kinase 4 and 6) inhibitor independently developed by Xuanzhu Biopharm. Leveraging its unique polypharmacology targeting CDK2/4/6/9, it effectively inhibits tumor cell proliferation while significantly reduces hematological toxicity such as grade 3/4 neutropenia commonly seen in traditional CDK4/6 inhibitors, and improves patient treatment tolerance. **With previously approved two major indications: in combination with Fulvestrant for second-line endocrine treatment and monotherapy for posterior line treatment, the Product will now cover all HR+/HER2- advanced breast cancer patients across the first-line, second-line, and later-line treatment settings. This will further optimize the overall management layout of breast cancer,** and provide more precise treatment options for domestic patients.

Breast cancer is the most common malignant tumor among women worldwide. According to the latest data released by the International Agency for Research on Cancer (IARC) in the journal Nature Medicine in 2025, there were 2.3 million newly diagnosed cases of breast cancer worldwide in 2022, and it is expected to reach 3.2 million newly diagnosed cases by 2050. Among them, about 70% of breast cancer patients are HR+/HER2- subtypes, which have a huge demand for treatment. The global market size of CDK4/6 inhibitor drugs was nearly US\$13 billion in 2024, year-on-year growth of approximately 18%.

The acceptance of the new indication NDA of Bireociclib is not only a strong proof of the Group's innovative research and development (R&D) capability, but also means that we have taken a solid step on the road to providing more effective treatment for breast cancer patients. In the future, Sihuan Pharmaceutical will continue to adhere to its innovation-driven development philosophy, increase investment in R&D, accelerate the transformation of innovative achievements, and contribute more to the health and well-being of patients worldwide.

ABOUT XUANZHU BIOPHARM

Xuanzhu Biopharmaceutical 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. The company has a first-class R&D team, all core personnel have years of experience in new drug research and development. 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 chemistry, large molecule biopharmaceuticals, antibody-drug conjugate (ADC) and other types of products. With a focus on unmet major clinical needs, the company 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 pharmaceutical company led 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 goal for the “full promotion of a two-wheel drive strategy of its medical aesthetics and biopharmaceutical businesses”, Sihuan Pharmaceutical endeavors to build itself into a leading medical aesthetics and biopharmaceutical company in China.

This announcement is being made by the Company 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, 9 June 2025

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. Tsang Wah Kwong, Dr. Zhu Xun and Mr. Wang Guan.