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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 FINAL ANALYSIS RESULTS OF THE PHASE 3 CLINICAL STUDY (BRIGHT-2) OF BIREOCICLIB IN COMBINATION WITH FULVESTRANT FOR THE TREATMENT OF HR+/HER2- ADVANCED BREAST CANCER PUBLISHED IN TOP-TIER INTERNATIONAL JOURNAL *JAMA ONCOLOGY*

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 final analysis results of the Phase 3 BRIGHT-2 clinical study of Bireociclib, a novel CDK2/4/6 inhibitor independently developed by Xuanzhu Biopharmaceutical Co., Ltd. ("**Xuanzhu Biopharm**") (Stock Code: 02575.HK), a non wholly-owned subsidiary of the Group, were officially published online recently, in the top-tier international medical journal *JAMA Oncology* (Journal of the American Medical Association – Oncology, Medicine Category 1, Impact Factor 20.1).

## ABOUT THE BRIGHT-2 STUDY AND ITS FINAL ANALYSIS

The BRIGHT-2 study is a randomized, double-blind, placebo-controlled, multicenter Phase 3 clinical trial conducted in China, designed to evaluate the efficacy and safety of Bireociclib in combination with Fulvestrant in patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) ("**HR+/HER2-**") advanced breast cancer who had progressed on or after prior endocrine therapy. This study was led by Academician Xu Binghe from the Cancer Hospital of the Chinese Academy of Medical Sciences and conducted across 64 hospitals nationwide.

Xuanzhu Biopharm previously announced the interim analysis results of the BRIGHT-2 study in the journal *Nature Communications* in April 2025. The publication now released represents the final analysis results, incorporating an additional 11 months of observation beyond the interim analysis, with the median follow-up time extended to 19 months, further revealing the maturity and robustness of the survival benefit of Bireociclib.

**SUMMARY OF KEY RESEARCH FINDINGS**

The final analysis results of the BRIGHT-2 study demonstrate that Bireociclib in combination with Fulvestrant provides patients with clinically meaningful and durable robust benefits.

In patients with progression after prior endocrine therapy, the median progression-free survival (mPFS) in the Bireociclib combination group was further extended from 12.9 months in the interim analysis to 14.7 months, significantly superior to the 7.3 months in the placebo combination group, successfully reducing the risk of disease progression or death by 46% (HR=0.54; 95% CI, 0.40–0.74; P<0.001). These data demonstrate the durability of its antitumor effect. More notably, the results assessed by Blinded Independent Central Review (BICR) demonstrated that the median progression-free survival (mPFS) in the Bireociclib combination therapy group reached 17.5 months, which was significantly superior to 7.3 months in the placebo group. This regimen reduced the risk of disease progression or death by 53% (HR=0.47; 95% CI, 0.34–0.65; P<0.001).

In terms of depth of clinical response, the final analysis of the BRIGHT-2 study demonstrated a highly competitive objective response rate (ORR). Among subjects with measurable lesions, the ORR in the Bireociclib group reached 50.3%, significantly higher than the 16.7% in the control group. Notably, the median time to first response in patients achieving tumor response in the Bireociclib group was the same as in the control group at 3.7 months, but the maximum range far exceeded the control group, reaching 22.8 months, and the tumor shrinkage effect persisted over multiple treatment cycles; as of the data cutoff date, the median duration of response (mDOR) in this group had not yet been reached. Combined with the previously demonstrated 29.8% response rate and 15.2-month median DoR of Bireociclib monotherapy, these combination therapy data further prove that high levels of objective response can effectively translate into long-term progression-free survival benefits for patients.

Addressing the high heterogeneity of HR+/HER2- advanced breast cancer, the BRIGHT-2 study provided evidence supporting specific clinically at-risk populations through detailed subgroup analyses. The study observed consistent benefit from Bireociclib treatment regardless of whether patients had primary endocrine resistance, were premenopausal/perimenopausal, or had a disease-free interval (DFI) ≤24 months and other high-risk factors. In exploratory molecular marker analyses, patients with refractory disease harboring ESR1, PIK3CA, or TP53 mutations also showed consistent PFS improvement after Bireociclib treatment. Furthermore, in the exploratory analysis of overall survival (OS), the hazard ratio (HR) for premenopausal/perimenopausal subjects reached 0.38, indicating the significant potential of Bireociclib for implementing individualized treatment strategies in this high-risk specific subgroup.

Regarding the balance between pharmacological mechanism and safety, Bireociclib embodies a scientific design concept. As a highly selective CDK4 inhibitor, its inhibitory effect on CDK6 is relatively weaker, a feature that helps alleviate CDK6-mediated hematopoietic suppression, thereby endowing the drug with favorable hematological safety. Based on this mechanistic background, Bireociclib adopts a continuous twice-daily (BID) dosing regimen, capable of maintaining stable steady-state drug exposure levels and depth of target inhibition. Safety data show that the most common adverse events such as diarrhea and neutropenia mostly occur early in treatment and are effectively controlled through clinical management and dose adjustments, with no observed cumulative toxicity. The BRIGHT-2 study provides important evidence-based medical evidence for the application of Bireociclib in Chinese clinical practice, offering a more ideal treatment option for patients with endocrine-resistant disease by ensuring efficacy while employing a differentiated toxicity management model.

**ABOUT BIREOCICLIB**

Bireociclib Tablets (brand name: Xuan Yue Ning), as the first approved CDK2/4/6 inhibitor in China, possesses a unique multi-target synergistic mechanism of action, offering advantages such as potent inhibition of tumor cell proliferation and a significant reduction in hematological toxicity commonly associated with traditional CDK4/6 inhibitors. Bireociclib was approved by the National Medical Products Administration in May 2025 and March 2026, for use in combination with Fulvestrant for the treatment of patients with HR+/HER2- advanced or metastatic breast cancer whose disease has progressed after prior endocrine therapy; as a monotherapy for HR+/HER2- advanced or metastatic breast cancer patients who have progressed after receiving two or more lines of endocrine therapies and one chemotherapy in the metastatic stage; and in combination with aromatase inhibitor ("**AI**") for the treatment of first-line treatment of HR+/HER2- advanced breast cancer, making it the first and only CDK2/4/6 inhibitor in China approved for a monotherapy indication. In December 2025, the two indications of Bireociclib Tablets approved in May 2025 have been included in the *National Reimbursement Drug List for Basic Medical Insurance, Maternity Insurance and Work-Related Injury Insurance (2025)*, effective on January 1, 2026.

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, 24 March 2026

*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.*