



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 NDA OF INSULIN DEGLUDEC AND INSULIN
ASPART INJECTION, DEVELOPED BY HUISHENG
BIOPHARMACEUTICAL, ACCEPTED BY NMPA

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 insulin degludec and insulin aspart injection (the “**Product**”), developed by the Group’s non-wholly owned subsidiary, Huisheng Biopharmaceutical Co., Ltd. (“**Huisheng Biopharmaceutical**”), was accepted by the National Medical Products Administration (the “**NMPA**”) of the People’s Republic of China (“**China**”). It is the first biosimilar of insulin degludec and insulin aspart injection that has been applied for New Drug Application (“**NDA**”) and accepted in China.

Insulin degludec and insulin aspart injection is a soluble double insulin preparation, consisting of 70% of insulin degludec and 30% of insulin aspart, after subcutaneous injection, exert their respective pharmacokinetic effects. The basal insulin, insulin degludec, forms a stable soluble multi hexamers when injected into the subcutaneous tissue resulting in a subcutaneous insulin degludec depot. The monomers gradually separate from this depot and are continuously and slowly absorbed into the circulatory system. It reversibly binds to albumin through fatty acid side chains, thereby achieving an ultra long and stable hypoglycemic effect. The mealtime insulin, insulin aspart, after injection, quickly enters the bloodstream in the form of monomers, providing the hypoglycemic effect of insulin during meals. The Product is characterized as a combination of basal insulin and mealtime insulin. The Product can satisfy both basal and mealtime insulin needs in one injection, quickly control fasting and postprandial blood glucose, and better reduce HbA1c. Compared with the use of insulin glargine and insulin apart, the Product has a significantly lower risk of nocturnal hypoglycemia and is more conducive to blood glucose regulation in patients with diabetes. As a non-co-crystalline compound, the Product can be used without mixing, which enhances the convenience of the Product and avoids the injection risk of mixing preparations. In addition, compared to basal insulin and mealtime insulin treatment, the Product can reduce the number of injections, thereby helping to improve patient compliance and reduce medical burden.

Insulin degludec and insulin aspart injection is included in the National Reimbursement Drug List, and with its product advantages, it will be easier to be chosen by doctors and patients in the future. According to the financial report of Novo Nordisk, the sales revenue of insulin degludec and insulin aspart injection in Greater China was approximately \$175 million in 2022, an increase of 330% compared to 2021.

About Huisheng Biopharmaceutical

Huisheng Biopharmaceutical is a biopharmaceutical company under Sihuan Pharmaceutical, a large domestic pharmaceutical and medical aesthetics group, focusing on the areas of diabetes and complications. After eight years of construction and development, Huisheng Biopharmaceutical has become one of the few company in China that has achieved full product coverage in the field of diabetes and related complications, and integrated the whole industrial chain of R&D, production and sales. the company currently has a world-class R&D team of more than 200 people with rich experience in diabetes drug research and development. At present, it has more than 40 products in the research product pipeline of diabetes and complications, covering a full range of second-, third-, and new-generation insulin (covering basic, premixed and quick-acting etc.), innovative drugs with the latest mechanism, such as SGLT-2i, GLP-1a, and other hypoglycemic drugs and complication drugs. Huisheng Biopharmaceutical is committed to providing full-process, all-round integrated treatment solutions for diabetic patients, serving patients and making health easier.

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