



LI CHEN Ph.D.

Founder, Executive Director, CEO

Dr. Li Chen, Executive Director and Chief Executive Officer, founded and leads Hua Medicine to discover and develop clinically differentiated medicine in China for Global. Under his leadership, Hua Medicine has successfully brought a disease modifying first-in-class glucokinase activator (GKA) HuaTangNing (华堂宁®) (dorzagliatin tablets, HMS5552) into the China market. Dorzagliatin is approved by the National Medical Products Administration (NMPA) of China for type 2 diabetes with its unique mechanism of action in restoring the impaired glucose homeostasis.

Q: What motivates you to develop new medicines for diabetes?

Dr. Chen: In 2010, Professor Wenying Yang, a leading Chinese expert in diabetes, published an epidemiological study on diabetes prevalence in China. In this study, Professor Yang's team used the oral glucose tolerance test to diagnose diabetes and prediabetes. The results showed that the prevalence of diabetes and prediabetes in China had already reached 9.7% and 15.5%, respectively, making China the country with the highest number of diabetes cases globally. It was this paper that inspired me to focus on the field of diabetes and metabolic disorders. I selected glucokinase (GK) as a therapeutic target for diabetes due to my involvement in the development of glucokinase activators (GKAs) at Roche during that time. GK is a glucose sensor, regulating the secretion of key hormones such as insulin, glucagon, and glucagon-like peptide-1 (GLP-1) in response to fluctuations in blood glucose levels, thereby maintaining glucose homeostasis. Recognizing the critical role of GK in glucose metabolism, we developed dorzagliatin, a GKA designed to restore proper glucose regulation.

Q: What led to your success in the development of GKA?

Dr. Chen: First, the mechanism of action of dorzagliatin is unique. It functions as an ectopic allosteric GK full activator, with minimal impact on GK's Hill coefficient, thereby preserving the kinetic cooperativity between GK and glucose. This ensures that GK is activated in response to changes in blood glucose levels. Furthermore, dorzagliatin acts on

GK targets in three key organs involved in blood glucose regulation—the pancreas, liver, and intestines—activating GK within these organs to restore physiological glucose homeostasis. Secondly, Hua Medicine has consistently employed a steady and methodical approach, focusing on generating robust data to support the regulatory approval and clinical application of dorzagliatin. In 2017, we launched a multicenter phase 3 clinical trial involving 110 hospitals across China. At the time, conducting such a large-scale, randomized controlled trial for a first-in-class drug in China was rare. However, the broad geographic distribution of research centers allowed more medical professionals to gain firsthand experience with this novel GKA and ensured that our patient population was more representative. Finally, dorzagliatin has garnered strong support and trust from both the government and the clinical community. These factors, combined with the strength of scientific research, have served as both internal and external drivers of our success.

Q: What are your visions for the future of diabetes treatment?

Dr. Chen: First, I believe that GKAs hold significant therapeutic potential for diseases currently considered complications of diabetes, such as diabetes-related cognitive impairment, which are driven by dysregulation of glucose homeostasis. Secondly, since GK is upstream of both glucose and lipid metabolism pathways, it may play a key role in weight management, promoting muscle mass while reducing body fat. This presents novel strategies

for managing diabetes and related metabolic disorders. Thirdly, our team is investigating the excessive secretion of insulin, GLP-1, and other hormones caused by hyperactive glucokinase. We are developing allosteric modulators or inhibitors to downregulate glucokinase activity in order to address this challenge. Additionally, we are investigating the potential of combining GKAs with existing diabetes treatments, aiming to provide physicians with a broader range of therapeutic options. In summary, as a glucose sensor, GK presents important scientific questions and offers promising clinical applications not only for the treatment of diabetes and its complications but also for potentially broader medical fields.

Hua Medicine

Hua Medicine is an innovative drug development and commercialization company based in Shanghai, China, with companies in the United States and Hong Kong, China. Hua Medicine focuses on developing novel therapies for patients with unmet medical needs worldwide. Based on global resources, Hua Medicine teams up with global high-calibre people to develop breakthrough technologies and products, which contribute to innovation in diabetes care. Hua Medicine's cornerstone product HuaTangNing (华堂宁®) (dorzagliatin tablets), targets the glucose sensor glucokinase, restores glucose sensitivity in patients with type 2 diabetes, and stabilizes imbalances in blood glucose levels in patients.