Li Chen – Founder, Executive Director & CEO, Hua Medicine



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Unlike many of its Chinese biotech peers with broad portfolios, Hua Medicine has focused intensively on developing a single product, dorzagliatin, for diabetes. As CEO Li Chen notes, this strategic concentration has allowed Hua Medicine to pioneer in homeostasis control modulation and address specific unmet medical needs in diabetes treatment, distinguishing them in a competitive market. In a wide-ranging conversation, he also notes how the evolution in China's regulatory landscape has benefited the company, and how strategic partnerships - notably with Bayer - are taking Hua Medicine to the next level.

How do you assess the current stage of China biotech development and the appetite of institutional investors?

It’s been quite a journey. Over the last three years, we’ve observed a significant downturn in the financial cycle globally, which naturally impacted the financial and stock markets. From last year onwards, we’ve seen a sharp decline in overall investment in China’s biotech sector. In fact, we’re now back to investment levels similar to those of 2015. This trend is evident across various publications and investor communities. There’s now a sense of questioning whether innovation in China, and its value both domestically and globally, represents a future opportunity. It’s worth recalling that in 2018, many Chinese startups were licensing products from overseas, conducting

rapid development, and subsequently launching them in China with hopes of successful commercialization.

With a population of 1.4 billion, there's certainly a perception that if a product exists elsewhere, it can be replicated and catered to the Chinese market. For instance, if there's a successful product like PD-1, the mindset is often, "Let's develop our own PD-1." This has led to a wave of biotech startups focusing on replicating or translating global innovation and building multiple product pipelines. Unlike Hua Medicine, which started with one proprietary project and gradually launched its product in the area of diabetes.

Looking back, it's easy to see the allure of pursuing multiple targets when there was a lucrative market. What did Hua Medicine do differently?

In our case, for instance, we've been focused on one product since 2010, particularly in the diabetes area. While the hype was palpable, we recognized a critical turning point. We pondered whether building a portfolio of products was the way forward, alongside the desire to bring a product to market. However, true biotech isn't about managing portfolios like big pharma does. It's about addressing unmet medical needs where there's a clinical void that larger pharmaceutical companies haven't tapped into or failed to address. So, we've stayed committed to diabetes, refining our approach to homeostasis control modulation. By utilizing fixed biosensors within the body, we aim to restore homeostasis. Our research has advanced to the point where we're not just regulating insulin but also GLP-1.

Instead of going down the conventional route of GLP-1 receptor agonists, we've developed dorzagliatin, which addresses the dysfunction of GLP-1 secretion in obese diabetes patients. Our data and publications, such as those in Nature Communications, support this approach. It's all about pushing the boundaries of what's possible.

It seems that one aspect often overlooked is the influence of Big Pharma in determining what constitutes innovation. How does this factor into your product development strategy where the typical path for diabetes is GLP-1?

The sway of Big Pharma in defining innovation is substantial. While PD-1 and CAR-T were once the center of attention in cancer immunotherapy, the shift towards ADC now highlights the evolving landscape of therapeutic technologies. Take GLP-1 therapy, for instance. While it's currently in the

limelight, it’s worth noting that the first generation of GLP-1 receptor agonists was introduced as far back as 2005. Initially, it involved twice-daily injections, which was far from ideal. Then came the advancements—once-daily injectables, followed by once-weekly options, marking the third generation of GLP-1 receptor agonists. Over the past two decades, we’ve witnessed a transformation in the approach to diabetes treatment. Considering that insulin had been around for a century with only four generations developed, the pace of innovation is now accelerating. At Hua Medicine, after launching our first-generation dorzagliatin in China, we’ve already embarked on developing the second generation—once-daily oral formulations.

We are proud to say Hua Medicine’s product was launched in China in 2022 as the globally first-in-class dorzagliatin and overcoming what was viewed as the standard of care for diabetes.

How has the regulatory landscape in China progressed, particularly regarding IND approvals, and how has that impacted your development journey?

Back in 2012, IND approvals were a lengthy process, taking up to eighteen months. However, recent regulatory announcements indicate a significant improvement, with approval times potentially shortened to just 30 days. For our GKA project, it took eight months for approval, during which we completed 18 clinical studies, four of which were conducted in the US. Utilizing US centers allowed us to conduct certain studies in parallel with those in China, enhancing efficiency. By comparing data from the US and China, we can better tailor our development efforts to address specific diabetes-related issues in China during phase three trials.

One challenge in the China market is predicting demand and pricing. Were your market predictions for 2022 similar to the current reality? How important can having a foreign partner with greater commercial reach and negotiation power be?

We filed the NDA in 2021, but I began seeking partners for commercialization in China before phase III completed. By August 2020, we had partnered with Bayer for commercialization. While multinational companies like Bayer bring extensive experience, it’s not necessarily about better negotiation. In fact, Bayer greatly benefited from our negotiations with regulators and the National Reimbursement Drug List (NRDL), securing a favorable deal for our drug. Our product entered the NRDL at a price 46% around higher than Januvia’s a DPP-4 inhibitor, a significant achievement considering the competitive landscape. DPP-4 inhibitors focus on GLP-1 degradation in lean

individuals contrasts with our approach, which targets GLP-1 secretion in obese individuals with diabetes, making our drug more effective in certain populations.

What role have health technology assessment and data played in allowing dorzagliatin to achieve reimbursement in China?

We've developed pharmacoeconomic models for our drug dorzagliatin, comparing it with existing anti-diabetic therapies. Our drug notably improves beta cell function, delays disease progression, and reduces blood glucose fluctuation. Interestingly, the American Diabetes Association's new guideline emphasizes improving the time in range (TIR) rather than just lowering blood glucose levels. Our drug has shown a significant increase in TIR, with some patients achieving drug-free remission for up to a year. We've gathered clinical data and continue to follow up with real-world evidence, showing remarkable results, such as patients remaining drug-free for six years. These insights are novel and have garnered attention from regulators, showcasing the unique impact of our drug within the Chinese healthcare system.

With your product now on the China market, what do you see as the next steps?

Our focus remains on expanding the indications for our therapy rather than becoming commercial sellers. We're exploring the potential to extend beyond diabetes treatment, such as preventing memory loss. Our research suggests that optimizing glucose homeostasis could have broader implications for neurological and immunological balance. For instance, our second-generation GKA has shown potential in restoring GLP-1 secretion in obese type 2 diabetes patients, a novel finding that distinguishes it from existing GLP-1 therapies. We aim to leverage our unique mechanism of action to develop even better therapies, drawing inspiration from the evolution of GLP-1 treatments over the years.

Moving forward, we're exploring personalized diabetes care, utilizing algorithms developed by Hua Medicine. These algorithms allow us to sub-classify type 2 diabetes into six categories, enabling personalized treatment regimens tailored to each patient's needs. While this approach holds great promise, it does require close collaboration with clinicians who need to be well-versed in the various treatment options available. Our goal is to work with clinicians to implement personalized diabetes care and expand our reach into markets like the US, particularly focusing on diabetic kidney disease (DKD).

Given your partnership with Bayer in China for commercialization of your asset and their significant presence globally, why hasn't this partnership expanded into other global markets?

While Bayer is an excellent partner for the diabetes market in China, they currently don't have a diabetes business in Europe or the US. However, when considering our drug's potential impact on kidney disease, there's an opportunity for collaboration beyond diabetes. Our drug addresses blood glucose fluctuation, a major contributor to kidney disease, and it can be used in late-stage kidney patients as it's not excreted through the kidneys. This unique property positions us well to target the niche market of nephrology in the US, where there's a clear demand for alternatives to insulin, which can exacerbate kidney issues due to blood glucose fluctuations. So, rather than broadening into the general diabetes market, our focus is on addressing specific medical needs where our drug can make a significant impact.

You recently filed an FDA IND for your second-generation of dorzagliatin. Given the need for substantial capital to advance further, what are your expectations regarding financing?

Our FDA IND filing for second generation dorzagliatin occurred just before last Christmas, making it a relatively recent development. As for financing, Hua Medicine is in a favorable position with approximately 1.4 billion RMB, equivalent to around 200 to 300 million dollars, as a cash reserve. Additionally, our company generates revenue annually from sales of our first asset here in China, which is an important aspect to highlight, as it dispels the misconception that companies like ours are financially strapped. With this financial stability and ongoing revenue generation, we're well-equipped to fund our proof-of-concept study in the US.

Do you anticipate the geopolitical tensions between your country and US affecting scientific collaboration?

Diabetes is a global concern, and my US colleagues are just as eager for advancements in treatment as anyone else. The desire for effective diabetes medications, improved beta cell function, and the possibility of remission is universal. Despite any geopolitical tensions, we remain open to collaboration opportunities in the US. In fact, we're currently in discussions with various

players in the diabetes field, exploring potential partnerships for our second-generation drug. With the rising focus on diabetes and obesity worldwide, particularly in the pharmaceutical industry, there's significant interest in developing assets in this area. For example, even companies like Sanofi, traditionally strong in diabetes, may be now looking into obesity medications due to investor "pressure". This dynamic landscape presents opportunities for innovative treatments like ours to make a significant impact.

Has the increased global interest in diabetes and obesity altered the discussions that Hua Medicines is having with stakeholders?

The increased interest in obesity medications has opened up new opportunities for us. While our primary focus remains on diabetes, we're exploring avenues to expand our product's reach. One key strategy is to target niche markets where we can quickly establish proof of concept. In particular, we see great potential in addressing diabetes-related kidney disease, where there's high demand and limited effective treatments beyond insulin. Additionally, our drug has shown promise in combination therapies, enhancing the efficacy of existing treatments while reducing their side effects.

Looking ahead, we're also considering longer-term possibilities, such as conducting real-world studies in China to explore indications like cognition impairment and diabetes prevention. In fact, discussions with healthcare professionals in China have highlighted the significant overlap between diabetes and memory loss patients, indicating a potential avenue for further research and collaboration.

While some may prioritize addressing non-alcoholic steatohepatitis (NASH) over central nervous system disorders, our focus remains on leveraging our unique technology platform. Our expertise in enzyme allosteric modulation allows us to explore various avenues, from enhancing insulin sensitivity to treating rare genetic disorders in children. With computational tools and AI, we're well-equipped to stay focused and drive innovation in diabetes and related areas.

What is your long-term vision for Hua Medicine? Do you aim to become a full-fledged pharmaceutical company, or is there an exit strategy in mind?

Our vision for Hua Medicine is guided by our motto "Winning for the Future 2030," which serves as a constant reminder of our long-term goals. We've already achieved the milestone of going from

zero to one, transitioning from theory to having a medicine in the homeostasis area with dorzagliatin, our globally first-in-class product.

Looking ahead, we aim to pursue a “one to ten” strategy in three dimensions. Firstly, we want to expand our market presence from China to the world, entering ten additional markets through partnerships or other means. Secondly, in terms of our product pipeline, we see opportunities to develop second-generation treatments, fixed-dose combinations with existing therapies, and explore new indications. Finally, we plan to delve deeper into personalized medicine, focusing on specific disease areas where we can leverage our unique advantages. By 2030, we aim to complete this journey and achieve our vision.

As a final message, given this very particular moment we are living through, what would you like to say to our global biotech and big pharma audience?

To the global biotech and big pharma leaders, I want to convey that innovation in biotech is real and significant in China. Among all, Hua Medicine is a testament to this, representing a biotech company that has successfully developed a globally first-in-class therapy, on a global scale from basic science to clinical therapy.

Moreover, the younger generation of talent in China is driving innovation forward. Many of the individuals I hired from overseas to build Roche R&D center are now CEOs of their own companies, leading innovation in biotech hubs across China.

While it’s true that some companies may struggle or even close, it’s part of the natural cycle of growth and innovation. What’s crucial is that the Chinese government has recognized the importance of investing in biotech innovation. For the first time, innovation drug development has been explicitly mentioned in national documents, signifying its importance.

In Shanghai, the Pudong area has been designated as a deeper reform zone, with plans to develop a new pricing system that supports innovation. The shift in China’s approach to biotech and pharmaceuticals signals a recognition by the central government of the need to foster innovation in these sectors as drivers of economic growth. While historically reliant on overseas generics, Chinese companies are now increasingly capable of managing their own generic drug production. With a population of 1.4 billion requiring basic care, there’s a growing emphasis on improving manufacturing capabilities and developing biosimilars domestically. It is expected, by the industry, that the government’s upcoming innovation drug development plan is poised to reshape the industry, leading to changes in pricing, market dynamics, and commercialization pathways in

China. This transformation is drawing the attention of major players, recognizing that China is poised to become a major player in biotech innovation and are eager to be a part of this exciting journey.

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