Qinghua Wang – CEO & Founder, Innogen, China



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The rate of diabetes in China has exploded: the number of diabetic patients has surpassed 100 million and is expected to increase to 150 million by 2040. Dr Qinghua Wang, founder and CEO of Innogen, returned to China in 2014 with the hope of tackling this disease with Diabegone, an innovative first-in-class drug.

Dr Wang, after so many years in the field of diabetes, could you start by introducing the diabetes market and your role in it?

The discovery of insulin dates back almost 100 years. In 1921, at the University of Toronto, Frederick Banting and Charles Best were the first ones to extract traces of insulin, which to their surprise, could reduce blood sugar levels. In 1922, Elizabeth Hughes, a type 1 diabetic patient, was the first American patient to be treated successfully with insulin. At that point, people believed insulin could cure diabetes. By 1923, the discovery was already awarded a Nobel Prize. The translation from research to medicine was extremely fast.

We now know that insulin is a good therapy, which has saved the lives of countless diabetic patients – but, it is not a cure. Diabetes is one of the leading causes of death, among cancer and cardiovascular complications. The incidence of diabetes is increasing steadily as people become more and more obese. To put it into perspective, ten years ago, one percent of the Chinese population suffered from diabetes; today, the number has increased to more than 10 percent.

There are two main international societies focused on diabetes: American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD). Their last annual meeting was held in Barcelona, which I attended and where I also presented my work. These associations support research in the field of diabetes and are currently promoting glucagon-like peptide-1 (GLP-1) receptor agonist as the first-line treatment for type 2 diabetes, in place of insulin.

Insulin reduces blood glucose levels at a cost. The hormone can cause weight gain (three to five kg per year), which in turn causes cardiovascular complications. On a more severe note, insulin can also cause fatal hypoglycaemia. On the other hand, the GLP-1 receptor agonist drug actually exerts beneficial effects: it can reduce body weight and help the heart and kidney.

Insulin injections is the only therapy for type 1 diabetes and it is not the best therapy for type 2 diabetes. There is actually a larger population of patients suffering from type 2 diabetes than type 1. This is why the research being carried out by Innogen on the GLP-1 receptor agonist is so vital. My motivation lies behind the need for developing more efficient drugs for diabetes. I first chose to focus on diabetes after doing an internship in a hospital where I fully grasped the morbidity and mortality effects of diabetes.

Could you also tell us about your background?

I began my medical training in a school in Shanghai and then, continued my studies in Biochemistry in Antwerp. Next, I completed a PhD specializing on insulin action and insulin signalling transduction. I have, therefore, been dedicated to this field for more than 30 years. After my PhD, I continued as a postdoc, again focusing on diabetes and glucose transport, at the University of Toronto. I also spent some time understanding how the brain is involved in the regulation of glucose levels in the body. My final postdoc was on physiology. By 2000, I became an independent researcher and Assistant Professor in the same department where insulin was discovered almost 100 years ago! My laboratory was based in Saint Michael’s hospital – it is affiliated to the University of Toronto. Dr Mladen Vranic, Dr Best’s own postdoc fellow, was my mentor for many years during my time in Toronto.

In total, I have been working as a clinician-scientist for 20 years. My research is focused on finding the cause of diabetes and metabolic diseases. We are working on translational medicine. This means we are not solely interested in doing research for publications or for achieving grants. We are interested in translating it into medicine! We want our discoveries to be useful to patients. Innogen has 10 patents, covering both China and the rest of the world, aimed at helping diabetic

patients.

The reason I came back to China in 2014 was that my parents were getting old. I left my hometown for more than 20 years, and it was time to prioritize my family. I also see great potential in Shanghai for translational research, so I resigned my position in Toronto and became fully invested in China.

These last few years, I have been lecturing in Fudan University and the endocrinology division in Huashan Hospital. This means I have the medical resources to continue my research and develop, what I like to call, my translational medical platform. This platform is the basis for the creation of Innogen. I flipped the platform and built a company from it. It focuses on trying to push drug candidates into the market.

Innogen's leading product is Diabegone, an injection for type 2 diabetes that is now undergoing clinical trials. How will it change the life of patients?

Diabegone is a GLP-1 receptor agonist. Glucagon's function is to raise glucose levels. For example, when people are fasting at night, glucagon maintains blood glucose levels required to support the brain. GLP-1 is very similar in sequence to the peptide glucagon, hence the name, but with an opposite role.

GLP-1 stimulates insulin secretion, which in turn reduces blood glucose levels, and promotes the proliferation of pancreatic beta cells. Furthermore, GLP-1 is also favourable to the liver as it prevents the development of hypoglycaemia.

What is the advantage of Diabegone over existing products?

The first GLP-1 receptor agonist drug was approved by the US FDA in 2005. At that time, the agonist was obtained from an animal. Immunologist Dr Gerald Prud'homme, one of my colleagues in Toronto, was surprised at the FDA's approval – because introducing an animal protein into a human body causes the immune system to react. I, on the other hand, was not surprised. One might suffer from minor side-effects but the disease is still being treated. In addition, the FDA opened the door to the development of GLP-1 drugs and stimulated many scientists to collaborate.

The half-life of the native GLP-1 is only one minute. In the earlier days, people were stranded in bed receiving a constant infusion of GLP-1. There was a clear need for a long-lasting GLP-1 receptor

agonist. We contributed largely to the field by developing a long-lasting recombinant fusion protein – that requires a single injection per week or longer.

There are currently six GLP-1 drugs – from both animal and human origin, as well as with long and short lasting effects. Eli Lilly developed a weekly formulation of GLP-1 receptor agonist Dulaglutide. Moreover, Novo Nordisk is developing an oral version of Semaglutide, a GLP-1 based treatment for type II diabetes. The third one is ours: Supaglutide (Diabegone). We are behind clinical trials, compared to the MNCs, but we are moving very efficiently through clinical trials.

When do you plan to commercialize Diabegone?

In 2015, we started Innogen, and began by developing a drug for pre-clinical studies in animals. Here, we studied the efficacy, toxicity and pharmacology kinetics, while adhering to CMC standards. We filed for IND in 2017. By June 2018, we got the approval with no corrections, allowing us to begin clinical trials immediately. By the end of 2018, we were already performing Phase I studies. In June 2019, we finished Phase I studies and we are now planning on starting Phase II studies. We expect to commercialize in two or three years.

Diabegone is one of your products, but not the only one in your pipeline. Could you share some of the other projects you are currently developing?

Diabegone is our flagship product. We do, however, have a number of ongoing pipeline projects. We are developing first-in-class drug candidates for type 1 and 2 diabetes, obesity and diabetes complications – like diabetic kidney disease, heart disease, and liver disease. They are all in different stages, some have finished phase I studies, and most are in pre-clinical studies.

What is the competition like in China among MNCs and local companies?

Last year’s sales for GLP-1 drug were more than 9 billion USD. 85 percent of these sales are attributed to drugs that are from human origin and that have long-lasting effects. The remaining 15 percent is attributed to drugs from animal origin and that have short-lasting effects. We are developing an innovative first-in-class drug that is in a good position to compete against existing ones. We offer higher quality and potency, as well as a broader safety window. Importantly, our CMC production is very efficient.

In addition to this, we see that you have developed a drug design technology platform. Can you tell us more about it?

We have established a mammalian expression system using gene engineering recombinant protein production technique to produce therapeutic proteins in large quantities. With this system, we can produce most proteins at a high quality, high yield and low cost! This platform is not only suitable for the production of proteins that target metabolic diseases – but it can also produce drugs for cancer, cardiovascular diseases and neurological complications. However, we specialize in diabetes and metabolic diseases.

Another hot topic is biotech investment in China. How have investors here responded to Innogen?

Investors want to invest in the right place and we are the right place. We have a very strong and persistent capability for innovation. Diabegone is somehow behind other first-in-line products for diabetes that are being developed by big MNCs. Nonetheless, we are still in a very good position to collaborate with investors that are looking for innovation. Innogen’s outstanding and continuous innovative ability is undoubtedly its cornerstone for realizing its ultimate goal of becoming a leader in the field of diabetic metabolic diseases.

IPO is also on the back of our minds, but it is not necessary for now. There are a few companies doing an IPO in Hong Kong. Some are succeeding, others are not. We want to make sure we are ready when we take the step.

Innogen is defined as an international pharmaceutical manufacturing and R&D company. What is your internationalization strategy?

We do have an internationalization plan. Diabegone is patented in China and the US. Our CMC production and drug production meets the standards of both FDA and NMDA.

Innogen is first committed to China, where we aim to help patients and generate a significant market value. Nonetheless, China provides a good environment to bridge local companies into the Western world. It is clear that the US has the largest drug market and China, the second. In the future, we will aim to focus on the US. We will not establish a facility there because it is not cost-

efficient. We will instead make use of CROs.

What do you plan to achieve in the next 5 years?

In the next five years, Innogen will be a leader in diabetes. In addition, Diabegone, the first long-lasting human origin diabetes drug in China, will be in the market. We have an advantage because we are introducing quality and safety into our products at a competitive price. We also aim to have three or four more products in the market.

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