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15.07.2019

Tags: China, KOL, Research, Innovation

Dr Dafang Zhong, director of Shanghai Center for Drug Metabolism and Pharmacokinetics Research at the Shanghai Institute of Materia Medica, Chinese Academy of Sciences, shares his professional career within the DMPK space, as well as the important work that the Center has done in contributing to the growth and development of the nascent Chinese innovative pharmaceutical industry, having worked on around half of all locally-developed innovative drugs launched in China!

Dr Zhong, could you briefly introduce yourself and how you came to join the Shanghai Center for Drug Metabolism and Pharmacokinetics Research (the Center)?

I did my BSc and MSc at Shenyang Pharmaceutical University in China before pursuing a PhD in pharmaceutical chemistry at the University of Bonn in Germany. After my PhD, I spent four years at the Central Laboratory of German Pharmacists as a postdoc research fellow. with a focus on pharmacokinetics. In 1994, I returned to Shenyang Pharmaceutical University as a Professor in Pharmaceutical Sciences. In 2005, Shenyang Pharmaceutical University decided to relocate to a new site and my research group, including me, decided to move to Shanghai. We saw more opportunities to contribute to new drug R&D in Shanghai. Personally, I was also more interested in R&D than teaching.

Initially, the Center was only a branch laboratory under the Shanghai Institute of Materia Medica (SIMM). We received some support and funding from the Shanghai Science and Technology Commission to establish a platform offering public services to support new drug R&D. Now, we are financially independent of SIMM.

Today, we have 40 full-time employees and around 20 postgrad students working at the Center. We have also established a small lab in Suzhou where we transfer some projects of lower technical requirements.

Could you provide an overview of the services you offer to the industry?

To date, we have completed over 200 projects in preparation for submission to relevant regulatory agencies for IND-enabling studies. We provide technical and professional DMPK services including pre-clinical drug metabolism studies, ADME studies, and so on. In the area of DMPK specifically, Chinese companies are still not as experienced, which is why they need our services and expertise. Over the past 14 years, we have built a robust track record of success and experience in DMPK research for new drug R&D.

In addition, we have also collaborated with hospitals all over China to investigate clinical pharmacokinetics and metabolism.

The area where we are located in Shanghai, the Zhangjiang Hi-Tech Park, is the epicentre of new drug R&D in Shanghai and maybe even the whole of China, so we are in a great position. In addition to many Big Pharma MNCs like Novartis and Roche, other large Chinese companies embarking on innovative drug discovery and development, such as Jiangsu Hengrui, China’s largest pharma company, also have a presence here.

Thus far, ten of the compounds we have worked on have been launched in China as new drugs – representing about half of all innovative drugs in China! We are very proud of our contribution to this.

On your side, you returned to China in 1994. How have you seen the drug R&D environment develop over the past 25 years?

When I first returned to Shenyang in 1994, there was almost no innovative drug development in China. The two exceptions were imrecoxib, developed by Jiangsu Hengrui, and icotinib from

Zhejiang Betta. In fact, both companies had approached my team in Shenyang for collaboration in the DMPK studies for those drugs. In that sense, I am happy that we have contributed to the development of the Chinese pharma industry as early as the 1990s! Both these drugs were approved in China in 2011.

Certainly, over the past decade, the landscape has changed significantly. We recently produced a report on the Center for our Board of Directors. In 2007, we worked on only six innovative compounds. Since 2015, however, we have worked on over 20 innovative drug compounds every year. This is a very rapid increase.

The overall regulatory environment has kept pace with industry development as well. For instance, the National Medical Products Administration (NMPA) has accelerated its work in processing and approving clinical trials and drug applications. A number of different policies have also boosted the development of the industry, such as the generics quality and consistency evaluation (GQCE) policy implemented in 2015.

As a member of the State Pharmacopeia Commission of China, I drafted the first guidelines for bio-analytical methods validation in China, which were adopted in the 2015 edition. This was very timely as they came just in time to guide both regulators and industry players in their compliance with China’s GQCE policy.

I am happy to say that in the area of bio-analysis specifically, China has made huge progress in the past few years. I am also a co-founder of the China Bio-analysis Forum (CBF), which held its seventh annual meeting in Suzhou just last week, to boost further development of this area. Through the CBF, I have also visited our sister conferences in Europe and Japan, the European Bio-analysis Forum (EBF) and the Japan Bio-analysis Forum (JBF), respectively.

Just last week as well, the State Council of China released a state decree about the management of genetic resources. Previously, protocols of clinical studies conducted in China had to be submitted to the Council for examination and approval, which added at least two months to every clinical phase of new drug development. My colleagues and I have discussed this limitation with officials at the Ministry of Science and Technology several times. I am happy to see that this has since been improved. Now, the protocols of clinical studies do not need to be examined or approved, simply kept on record, which will further support the growth of the entire pharma industry in China.

How do you assess the current quality of innovation in Chinese-developed drugs?

The industry is improving greatly. In the beginning, the molecules might only have minor changes in the structure to break the patent. However, recently, we are seeing very exciting new developments. Last year, for instance, we worked on an anti-cancer drug developed by Jiangsu Hengrui called pyrotinib, which demonstrated much better efficacy than current drug combinations. China's Center for Drug Evaluation even said that they had never seen a drug with such an impressive efficacy before, and therefore accelerated its review. They received the New Drug Approval (NDA) before they had even finished Phase III clinical studies!

Another drug we worked on, now in Phase III studies, is an anti-coagulant, which shows the same efficacy within clinical studies as existing drugs at only a $1/15^{th}$ dose. That is very impressive.

New drug study in China is always in progress. Just as an example, five years ago, we only worked on small molecules. Now, biologics are in high demand and we have worked on many, as well as established a department for antibody drug analysis to support our sponsors.

With many experienced and trained experts returning from the U.S. and Europe, coupled with the increasing demand in China for innovative drugs due to an ageing population, I see a bright future for Chinese drug R&D in the future.

With the huge demand for pre-clinical expertise within the industry, does the Center face any issues with recruitment or retention?

Employees at the Center essentially have two roles: one with SIMM and one with the Center. For instance, I am the director of the Center here and also a research scientist at SIMM. Part of our responsibilities, therefore, includes supervising postgrad students. To date, I have supervised over 40 PhD students and over 70 MSc students – most of whom enter the pharma industry in China and even internationally. In that sense, we are actually building the future talent pipeline of the industry.

Postgrad students benefit a lot from our work with industry. Not only do they receive training in the fundamentals of working with our analytical instruments and our SOPs, they also receive a lot of exposure to industry studies, which gives them the knowledge and experience to select the right topic for their own theses. In general, students in our lab have a good track record when it comes to publications, with many papers published in reputable journals. This is because they are exposed to current industry research and have sources of potential thesis topics, not just based on scientific interests but also industry interests.

For the core team itself, we are relatively stable, especially compared to other labs. This is because we try to foster a stable environment of research, which has a very different atmosphere compared to industry research. This is what appeals to our researchers as well.

Looking ahead, what are your priorities for the Center?

We hope to maintain our current track record of completing over 20 pre-clinical DMPK studies for new drug compounds. We also hope to develop our capabilities in biologics as well in special techniques such as radioactive-labelled drug study. This is important to further serve the needs of the industry here. At the moment, for instance, I am aware of only three labs in the whole of China that can work on radioactive-labelled drugs.

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