Interview: Lu Xianping – Chairman and CEO, ChipScreen BioSciences, China

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09.07.2018

Tags:

China, ChipScreen, Biotech, Shenzhen, Innovation

Dr. Lu Xianping is the founder and now Chairman and CEO of one of China’s few truly innovative biotech companies, ChipScreen BioSciences Co. In this exciting interview, he shares the long journey towards the commercialization of their first cancer drug, Chidamide, launched in China in 2015, ad now awaiting market approval in Japan and the US; incisive comments on the state of the Chinese biopharma innovation environment; as well as his hopes to build ChipScreen into the next Genentech of China!

Dr. Lu, could you please introduce ChipScreen to our international audience?

ChipScreen is probably the only truly innovative, vertically integrated biopharma company in China. I would not hesitate to call ourselves exceptional – we have been acknowledged to be the innovators of the first modern-day Chinese drug!

Our name comes from the chemical genomics-based technology we have developed as a drug screening tool. We conduct experiments to generate huge datasets, and subsequently use algorithms to construct modeling systems that can predict what type of molecules would have the most successful profile for a particular disease, e.g. such as a better safety profile in terms of molecular toxicology and pharmacology. What this platform allows us to do is to focus only on first-in-class or best-in-class molecules. We are not after ‘me-too’ drugs.

I am originally from Chengdu city in Sichuan province but did my PhD in Peking University Medical College and subsequently went to the US for my postgraduate fellowship in the University of California San Diego (UCSD) and subsequently worked there for many years. When I returned 18 years ago, my team and I decided to establish our company in Shenzhen because we found it to be a very beautiful city with a vibrant immigrant culture, reminiscent of California in the US. This is why we decided to bring our technology, our funds and our team here. This initial environment really supported our money-losing but innovative R&D effort.

Today, our HQ remains here, we have a large R&D center and GMP facility in Shenzhen as well as in Chengdu, Beijing has our clinical research operations, and Shanghai hosts our oncology and diabetes sales and marketing business. Beijing and Shanghai still drives our medical, sales and marketing efforts as that is where the KOLs and the people with multinational experience tend to congregate. We have just over 350 employees, with about 110 focusing on R&D.

I am extremely proud that after 12 years of R&D, our first product, Chidamide, was launched in 2015. This was a huge milestone for the company. Chidamide is scheduling to submit NDA in Japan next year and phase III in US too by our partner. If work goes well, that would make us the first Chinese-discovered and developed innovative drug to receive approval in a highly regulated country like Japan – ever!

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Could you tell us more about your first product, Chidamide, and what differentiates it?

Chidamide is a novel subtype selective HDAC inhibitor acting as an epigenetic modulator – it is the third in this area in the whole world, and the only subtype selective inhibitor in the world. Previously approved inhibitors have been pan-inhibitors, inhibiting 18 subtypes. We only inhibit four different subtypes, which generates a totally different mechanism of action. When our results were published 10 years ago, it was not initially recognized because people doubted that such innovation could come from a Chinese company. Today, we have been widely cited in reviews and articles by researchers and companies in the world have developed other compounds in this class. I am very proud that we are now acknowledged globally as the pioneer of this class of compounds. As an indication, in the American Chemical Society (ACS) 2017’s annual medicinal chemistry review, Chidamide was selected to feature on the front and back cover as a case history study. Chidamide is the first non-FDA approved drug to be selected for this purpose, because it is not just a first-in-class but also best-in-class compound.

Chidamide was first approved for NHL T lymphoma, and it appears to have the best effect of all the treatments globally in this catagory. This year, we hope to add an indication in breast cancer, as we have achieved a positive pivotal Phase III end point result recently. While breast cancer is a crowded field, we are specifically targeting metastatic, drug-resistant cases, where not many options are left. We should be submitting our supplementary NDA next month and hopefully it will be approved this year. We are also looking at certain types of lung cancer as well as other blood cancers, where initial data shows that it is extremely effective in patients with specific mutations.

Another great benefit of Chidamide as an orally available drug is that it reduces hospitalization costs as patients can take it home!

Currently, Chidamide is in phase II trials in the US, where our partner has managed to establish great results in combination with PD-1 treatments. We hope to launch phase III trials soon. In Japan, we received orphan drug designation in 2016, and we aim to file our NDA there next year.

What other innovations and clinical programs are you investing in?

As a company, ChipScreen focuses on four specialty areas: oncology, metabolic disease, autoimmune and endocrinology.

Our second product is a new generation of insulin sensitizer for T2D, a non-TZD type that used to be the best-selling anti-diabetes drug from Big Pharma companies like Takeda, Lilly and GSK, with peak sales of over USD 6.5 billion. However, side effects eventually caused doctors to drop the prescription. Ours is a PPAR pan agonists with moderate transcription activity and a different mode of action. We have finished the largest ever pivotal trial in China with more than 1,300 patients across over 60 centers, and demonstrated significantly reduced side effects. We are looking to have this product approved next year.

We also have CS2164, a new oncology drug in phase IIa, a novel small molecule targeting three different signaling pathways: chronic inflammation (CSF1R), mitosis (Aurora B) and angiogenesis (VEGFRs). We are moving into phase II in liver cancer as well as advancing on a couple of other indications to see which has the most potential.

We will also file an IND soon in China with a compound that has shown significant pre-clinical activity against a variety of auto-immune disease in many model systems, as well as in cancer, where we can take a small molecule approach in the area of immuno-oncology by changing the micro-environment to either control side effects or make the treatment more effective. These are our three most promising clinical programs.

We are also exploring products for nonalcoholic steatohepatitis (NASH). With our diabetes compound, for instance, we intend to start certain exploratory studies to see if we can help NASH patients, and we also have two other pre-clinical programs with different targets on NASH. We hope to combine this with our diabetes product to help late-stage NASH patients.

The Chinese biotech industry is really still in its infancy and as you said, ChipScreen is by far and large the leader here. How do you see the opportunities for ChipScreen as the industry matures?

As a profit-making company, we are now able to self-finance our various R&D programs. But organic growth alone will not be enough for us. The China Securities Regulatory Commission recently released new guidelines to allow truly innovative companies, especially companies ready to support the Chinese national innovation vision, to be listed on mainland stock exchanges even if they are not yet profitable. There are many factors behind this, not least the decision of the Hong Kong Stock Exchange to allow pre-revenues biotech companies to list as long as they meet certain criteria, and the recent US-Chinese trade war's impact on ZTE, the Chinese telecom company. It is clear that biotech has become one of the industries the Chinese government considers extremely strategic.

ChipScreen has been homegrown since the very beginning. At the beginning, we struggled to find refinancing. But over the past decade, we have grown with our investors very closely; we have not

even been able to accept new investors because our existing investors have not wanted to exit! This reflects their confidence in the company and the management team. However, we do recognize that our current investors are more focused on supporting early-stage biotech companies. Now that we have a product on the market and we are looking to the next phase of growth, an IPO will enable us to attract investors with more of a commercial development focus and positioning.

With the Chinese capital markets now opening to us, the final obstacle for innovative companies like us has been removed. We certainly plan to list within this or next year, and with the diversified financial resources that will bring, we are able to take our company to the next level – globally.

Innovation has always been a hot topic – sometimes a sore point – for Chinese companies. Now that the Chinese government has made the healthcare and life sciences a strategic national priority, what are the opportunities and challenges for companies here?

When ChipScreen started, doing innovative research and development was extremely difficult. From discovery to clinical, we have to deal not only with the lack of infrastructure but the lack of tradition. After all, there is nothing we can copy. In any case, innovation cannot be copied. In addition, there was barely any government funding available then. The public funding situation has changed a lot in the past five years, so much so that I do see a bit of a bubble forming. Even a newly established company with just an idea but no products can somehow be valued at CNY 500 million.

Money is also just one part of the equation. There are now so many overseas Chinese returning to China to establish new companies that I have confidence China will make some huge breakthroughs in this industry in the next ten years. But the challenge today is that many Chinese scientists are only focused on making quick money in hot areas, looking at the short term. I hope this mentality changes, because otherwise, the bubble will burst one day and companies will realize that their products are not truly globally competitive.

The Greater Bay Area is often compared to Silicon Valley. I would say there is still a major difference in the culture of innovation between the two. Unfortunately, many Chinese companies claim that they are innovative but in reality what they are doing is imitation.

Nevertheless, the Chinese pharma market is booming. China has one of the largest populations in the world and it is rapidly aging. When he was sharing his Healthy China 2030 vision at 2016, Chairman Xi actually used a phrase that was similarly said first by us on national TV on 2015: “???????????” – innovative medicines that people can afford! If you have a population of 1.3 billion people and you offer free public healthcare, you have to be very realistic about how you are going to afford this. It is clear we cannot afford the prices of US-made drugs for 1.3 billion people.

How can we provide comparable good medication at an affordable price? Only by promoting Chinese innovation. For instance, Chidamide was launched in China first at a price one-tenth of a similar drug used in the US and our drug has much better efficacy, fewer side effects and more convenience!

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Finally, true innovation has to occur in an environment with free speech and free thinking. ChipScreen has managed to foster this within the company. Chinese people are genuinely working very hard to catch up to Western standards and achievements in this field. But innovation requires free thinking and speech – these are non-negotiable.

What kind of partners will ChipScreen be looking for to advance its further development?

Our first product was out-licensed to a US company specializing in developing Chinese products on the global market. Two years ago, it was sub-licensed to Eisai for part of Asia region, which, as you know, is one of the top 50 pharma companies globally. We now have a second product soon to be approved, which means we are looking to establish similar partnerships, perhaps with other pharma companies along The Belt and Road. This will certainly help to bring Chinese innovation more global and is in line with the national strategy of the country.

Today we only focus on small molecules but other fields like antibodies and new therapeutic technologies like cell therapy are certainly on our radar.

I personally really like the story of Genentech – as one of the first innovative biotech company in the world! Many of our partners and collaborators have referred to ChipScreen as the Genentech of China! Of course Genentech was eventually acquired by Roche. Perhaps ChipScreen could have a different story eventually!

Final message?

I hope people with certain values – will seize the current opportunities – the government has policy to promote new economies, and certain talents, you have all three things together to promote innovation. But I hope fervently that these people can return to basic and translational science, and not just chase after hot money.

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