Shun Luo â?? Chairman, Founder and CEO, Thousand Oaks Biopharmaceuticals, China

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02.07.2019

Tags:

China, CMO, CDMO, Thousand Oaks, Manufacturing

Dr Shun Luo, chairman, founder and CEO of Thousand Oaks Biopharmaceuticals, shares the companyâ??s vision to deliver more accessible and affordable biologics to patients globally by lowering the cost of goods manufactured (COGM) per gram of recombinant protein; the paradigm-shifting technology and processes Thousand Oaks Biopharmaceuticals is innovating as an integrated chemistry, manufacturing and controls (CMC) bio-manufacturer; the dry powder cell culture media facility they are building; and the strength and extensive global experience of his leadership team at Thousand Oaks Biopharmaceuticals.

Dr Luo, could you share your reason for returning to China in 2010 to establish your first company, Jianshun Biosciences (JSB)?

This decision was the result of the combination of the development of the Chinese pharmaceutical industry as well as my personal industry experience. I returned to China from the US at the end of 2010 because I could see the transformation of the Chinese economy from a labor- and natural resources-intensive economy to a more high-tech economy focusing on areas like IT, AI and of course, biotech. The Chinese biopharma industry started to take off between 2008 and 2010.

I can still remember, in the 30 years I had been away from China, I returned thrice: once in 1998 when I was invited back to Shanghai to visit Zhangjiang Hi-Tech Park by the Shanghai municipal government. Back then, it was still farmlands and the government officials were explaining their vision for Shanghai to develop into an international metropolitan city leading on the world stage. It was difficult to imagine what this vision meant for Shanghai back then! The next time I returned was 2005, and by then, Shanghai had revamped itself. I remember the first impression of Shanghai leaving Pudong International Airport and marvelling at the well-organized and clean highways taking you into the city, the politeness and friendliness of various service attendant and so on. Shanghai has really transformed itself in the past 20 years, not just in terms of infrastructure but also the human factor.

Drawing on my professional experience, I spent 25 years working in biologics â?? starting from 1993 and with Serono, Genentech, Amgen and others, to name just a few. My specialty was in cell culture technology, particularly media development and media commercialization, and I became very familiar with both the technical and business processes at a reasonably high level. When I returned to China in 2010, this was an area that the Chinese biopharma lacked. Up until then, serum-free media in China was completely supplied by American life sciences companies, but the quality and efficacy of those media were not as strong as those developed within biopharma companies themselves. Having come from biopharma companies like Genentech and Amgen, I was confident that I could bring better solutions in serum-free media to the Chinese industry.

Cell culture technology is the core for bio-manufacturing, not only recombinant proteins but any biologicals, including vaccines as well as gene and cell therapies! This is why I decided to seize the opportunity to return to China and establish JS Biosciences to become the leading player in China in cell culture technology development and commercialization, with a focus in serum-free and chemically defined media.

Subsequently, you established a second company, Thousand Oaks Biopharmaceuticals, in 2017. What was the strategic rationale behind this, how do the two companies and their capabilities complement each other?

The Chinese regulatory environment started to change at the beginning of 2015, as the now-National Medical Products Administration (NMPA â?? the Chinese FDA) started to implement reforms in line with international standards. These have all been positive changes for the entire industry. Particularly for us as developers of raw materials, serum-free media and cell culture technology, it is good that China has aligned with and become compliant with international standards.

In the meantime, many innovative biotech start-ups emerged and a staggering amount of capital was injected into the business. As I reflect, the whole industry needed to be more efficient. Realistically, not every company will survive all the way from start-up to commercialization. They need a lot of help and support along the way.

At this point, I realized I had two options: I could easily start a biotech company myself or I could stay on the service side. Ten years of my career were spent in discovery work where I discovered many interesting molecules. At the same time, I realized that I was well-positioned to develop a highly specialized focus based on current industry needs. Around 2014 or 2015, I could see the whole biologics industry was evolving to go down the same path as small molecules in terms of manufacturing. Today, very few small molecules are actually manufactured by the pharma companies themselves; they are all outsourced to contract manufacturers. This will happen to biologics as well â?? and is already happening. Commercial manufacturing will become more highly specialized, leaving biotech companies to focus the drug discovery and development. Previously, I was very involved in process development and had learnt an incredible amount about global bio-manufacturing strategies from industry pioneers like Patrick Yang, then EVP of Product Operations, and Ann L. Lee, then SVP and Global Head of Pharma Technical Development, both at Genentech.

Therefore, I decided to establish Thousand Oaks Biopharmaceutical in March 2017 focusing solely on CMC bio-manufacturing. As you might guess, I chose the name â??Thousand Oaksâ?? because the founding team all used to work at Amgen! With JS Bio, we already had a strong foundation in the best quality raw materials so it was straightforward to transition the business into a fully-fledged CDMO business. We can now offer a platform for companies from critical raw materials all the way through to biologics manufacturing.

With this strong focus on your core area of expertise, what are some new technologies and capabilities Thousand Oaks Biopharmaceuticals can offer to your clients?

Our approach is science-based innovation with a lot of technology integration. Our CDMO business has the ultimate goal to increase globally the accessibility and affordability of biologics for patients. How do we measure this? It is very simple: we want to reduce the cost of goods manufactured (COGM) per gram of recombinant protein.

Firstly, we have a strategic partnership in JYSS Bio-engineering, a Hangzhou-based disposable bioreactor technology company with their own innovative IP for disposables. I am very excited about this because this is genuinely disruptive technology! It increases efficiency as well as reduces costs. We already have a couple of ongoing projects with clients in Europe and the US, and these are going very well. We have had the technology evaluated in Singapore as well, and we are seeing great interest from India as well. There are also companies in Europe and the US that are interested in collaborating with us on this technology specifically.

This means that now Thousand Oaks Biopharmaceuticals can manufacture the cell culture media, the disposable bioreactors and all the consumables then integrate this as a platform into our CDMO business. Of course, we offer an open platform based on our customer needs, we do not require them to use our disposable bioreactors nor disposables nor raw materials if they prefer their own

platform. I like to say that we are taking the Dell PC approach, not the Apple approach!

Secondly, continuous manufacturing and continuous processes are very important trends in the bio-manufacturing industry. But I believe if companies only take the traditional approach then they will not advance very fast. We have to innovate and think outside the box. It is almost like a paradigm shift. This is why we want to develop something truly innovative by combining upstream and downstream processes!

Finally, we are also in the process of establishing our second dry powder cell culture media facility, which will be the largest dry powder media manufacturing facility globally â?? and this will be almost fully automated! This is a huge accomplishment that will really position us as a global leader in this space. Previously, I was R&D Head of JRH Biosciences (later acquired by Sigma-Aldrich), for the industryâ??s leading dry powder media company, and our manufacturing head now is also from JRH Biosciences.

How have these new technologies been accepted by your clients? Are they receptive so far?

On the cell culture media side, our technology has been widely accepted because we have proven that our cell culture media can increase productivity many-fold compared to commercial cell culture media from the major multinational companies.

In terms of the disposable equipment, we see that around 50 percent of our clients are open to being early adopters, particularly for new development projects. They are willing to evaluate the potential benefits. Around 30 percent are cautious about moving forward and the remaining 20 percent are closed, comprising usually more traditional companies.

In terms of our use of Artificial Intelligence (AI) in the dry powder cell culture media facility, I believe this will be well-received. We hear a lot about the opportunities and challenges of AI replacing human activities. I spent 18 months with Beckman Coulterâ??s Automation division, so I have a very good grasp of the role of automation. There are many benefits we can see. Firstly, by eliminating the human factor from the manufacturing process, we remove human emotion, error or judgment from the process. We can run the processes around the clock without stopping for holidays or other events. In addition, none of the proprietary formulations or other information run the risk of being exposed or shared. With automation we can run high-throughput processes to increase efficiency. For all these reasons, I am very excited about our new facility and what it can deliver to our clients!

In the US and even in Europe, very often biotech companies focus on the clinical development of their products, with CMC manufacturing relegated to second place in terms of importance. How do Chinese biotech and pharma companies see the importance of CMC manufacturing?

CMC is the bottleneck for most biotechs in China. Most of the overseas returnees that are driving Chinaâ??s biopharma industry development are not familiar with the commercial segment of the business. Most of them would have worked in research, but fewer in commercial processes, and even fewer in manufacturing.

However, manufacturing is a critical factor for biotech success. Looking at the global industry, global biotech leaders like Genentech and Amgen actually invested a lot of resources into process manufacturing from a very early stage. They focused on developing manufacturing as a core

competency, and largely because of that strategic decision, these biotech companies grew into global industry players. Small and new biotech companies may believe that their focus should be to develop innovative products to generate commercial value. However, at the end of the day, if you cannot manufacture your products, they cannot reach the market, your patients do not benefit and the company will not have commercial value.

From my previous experience at Genentech, I can share this story about the launch of LucentisÂ®. It was approved by the US FDA on 30 June 2006 and that very same day, 11 million doses were shipped out to patients. This was due to Pat Youngâ??s global manufacturing strategy and the companyâ??s focus on manufacturing processes and supply chain. This is a big contributor to LucentisÂ®â??s first-year sales of USD 2.3 billion. Having that global manufacturing network was absolutely essential!

With China now modifying its Market Authorization Holdership (MAH) system, it is prime time for CMOs and CDMOs to grow within the Chinese market but this is also a sector that is dominated by large players like Boehringer Ingelheim, Lonza and WuXi AppTec. What do you see as the competitive advantage of Thousand Oaks Biopharmaceuticals?

We differentiate ourselves by focusing on having an integrated CMC bio-manufacturing. Many of the local Chinese CMOs are weak. By contrast, Thousand Oaks Biopharmaceuticals has a top-notch CMC bio-manufacturing team with extensive experience in manufacturing. For instance, our Head of Manufacturing is Steven Lee, previously VP at BMS overseeing their entire biologics development before he left to lead A-Bio Pharma, the first biologics CMO, in Singapore. It was under his leadership that BMS launched OrenciaÂ®, acknowledged to be one of the most difficult biologics to manufacture. We have 11 more people in our core leadership team bringing significant manufacturing experience from top five global biopharmaceutical and life science companies.

Of course, I have mentioned my own track record at a number of globally leading companies. In fact, Amgenâ??s bio-manufacturing facility in Singapore uses the core technology that my department helped to develop while I was with Amgen. It was also my track record that convinced all these industry leaders to come join Thousand Oaks Biopharmaceuticals in our mission to make high-quality biologic therapeutics more affordable and accessible. These people are all my colleagues and partners for the past 30 years. Today, we are all inspired by that dream of achieving global affordability and accessibility of biologics for humankind.

With Thousand Oak Biopharmaceuticals capabilities and experience, undoubtedly the larger players on the market would be interested in collaboration or even outright acquisition. What is your personal vision for the company?

Indeed, three major global players have approached us regarding a potential acquisition. However, our focus is to become a global CMC bio-manufacturing player and an industry leader. We want to displace the existing leaders as quickly as possible and I believe with our innovative technology, business model and globally experienced talented team, we can achieve this.

At the 2019 J.P.Morgan Healthcare Conference, I explained that Thousand Oaks Biopharmaceuticals is looking to serve patients globally, not just Chinese patients. If we can bring the COGM down for biologics then this will deliver huge affordability and accessibility to the entire global industry for the benefit of patients and humankind.

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