

Interview | Enhancing Market Position in the Synthetic Biology Industry to Promote High End Biologically Manufactured Alternatives—A Dialogue with Cathay Biotech Inc. Chairman Liu Xiucan

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Directors & Boards

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--Liu Xiucan

高端访谈 | 提高合成生物产业话语权 推动高端替代——对话凯赛生物董事长刘修才



At 20 years old, Liu Xiucan, born and raised in a small town in Anhui Province, was admitted to China University of Science and Technology to study modern chemistry following the resuming of China's national college entrance exams in 1977. Twelve years later, he went to study in the United States where he earned a doctoral degree in biochemistry and continued to work as a researcher from 1991 to June 1994.

As chance would have it, Mr. Liu, a scientist by training, changed his career path because of a seminar. At the seminar, a Mr. Zhang Qixian predicted that China, the world's largest oil importer and consumer, would import 80% of its oil by 2030 and that the energy and environmental challenges would be largely solved if chemical products were manufactured using biological instead of chemical manufacturing in his report on the future of China's biochemical industry.

At that time, Reform and Opening up in China was a draw for many overseas Chinese students. Mr. Liu, inspired by the report, joined the wave. He quitted from Sandoz Inc. in 1994 and decided to start his own business back in China. Mr. Zhang, who presented the report, became Liu's business partner.

However, starting a business was never easy. With little funding to build his own factory, Mr. Liu started off by buying and optimizing homegrown biochemical technologies and then sold them abroad. He acquired six technologies in three years, transferred four of them and thus gained the startup capital. His acquisitions included five strains of long-chain dicarboxylic acids from the Institute of Microbiology, Chinese Academy of Sciences at RMB 2.5 million yuan, which would turn into cash cows with mass production. Mr. Liu founded Cathay Biotech Inc. in Zhongguancun in 1997.

Back then, Mr. Liu found few investors or believers in what he called "a biological alternative to chemical production", as bio-based production was yet to emerge in mainland China.

"When I visited DuPont in 1998, I was told that bio-based methods cannot compete with chemical production. And our initial efforts at biological manufacturing were met with doubts -- how could corn be turned into nylon?" Many years later, Mr. Liu could still vividly recall the difficulties of the company's early days when he even had to take up a sales role after decades in the research lab.

However, the efforts paid off. Mr. Liu's company received \$26 million in the first round of capital raising in 2006, led by BioVeda Capital, the world's first venture capital fund specializing in China's life sciences sector. In November the same year, Cathay Biotech Inc. raised \$52 million in the second round from investors including Goldman Sachs and China Renaissance Capital Investment

Inc. In 2007, it raised \$135.42 million in the third round, which was followed by another \$73 million a year later.

Cathay Biotech Inc.'s IPO application with the US Securities and Exchange Commission was submitted in 2011. That was a "cold winter" for Chinese companies looking to list on U.S. exchanges. "The valuation given by overseas investors was so low -- we were aiming for over \$15 per share, but their number was less than \$5." Mr. Liu was forced to withdraw the application to avoid excessive underpricing.

And wait he would. It was nine years later when his company was listed on the Science and Technology Innovation Board of Shanghai Stock Exchange under the stock code 688065 on August 12, 2020.

For Mr. Liu, the IPO was just a step along the journey. He was mindful of the company's performance and future direction, as well as the expectations of investors.

Cathay Biotech Inc. recently announced its agreement with the Management Committee of the Shanxi Transition and Comprehensive Reform Demonstration Zone. According to the agreement, the two parties would jointly develop a Shanxi Synthetic Biological Industry Ecological Park (hereinafter referred to as the Industrial Park), with the company or its subsidiary contributing RMB 4.01 billion yuan. Cathay Biotech Inc.'s investments in the Industrial Park would include a 2.4-million-ton corn deep processing project, a biological phenylenediamine project with an annual production capacity of 500000 tons, a biological polyamide project with an annual production capacity of 900000 tons and a biological long chain dicarboxylic acid project with an annual production capacity of 80,000 tons.

Mr. Liu and Cathay Biotech Inc. set out again.

Directors & Boards: Would you share your story in terms of leading the company to become the first in industrial implementation of synthetic biology and break through foreign technological monopoly? What is your deepest reflection?

Liu Xiucan: I decided to give it a try out of a scientist's curiosity and love for challenge. Having visited all the labs in the world that used biological methods, I concluded that the challenge of replacing chemical methods with biological ones did not lie in material transformation, but in purification: Production with biological materials resulted in impurities, which would be bad for polymerization. Therefore, bio-based manufacturing did not work then.

The reason for impurities was the amazing complexity and diversity of organisms. Organisms can be ingredients for chemical materials which cannot be synthesized through chemical methods and which feature superior properties. But on the other hand, their metabolites can compromise product yields--After all, people did not know every detail about the transformation from corn to polyamides. Improving purity could mean higher costs, making biological manufacturing much more expensive than a comparable chemical method.

However, having done a lot of research on the mechanism of oil-water mixing at the molecular level when working on carcinogenic drugs for a US company, I had theoretical knowledge about how structures coalesced or broke down. I thought, from a technical point of view, I could solve the purification challenge.

I invented a filter technology that only allowed long chain dicarboxylic acids to pass through--anything bigger or smaller than these were not allowed. That was my simple solution for a complex problem, at a low cost. It turned out to be more successful than I had thought.

***Directors & Boards:* There are often huge gaps between innovation, industrial-scale production and market expansion. How have you managed to bridge those gaps?**

Liu Xiucan: We at Cathay Biotech Inc. have focused on synthetic biology, including lab research, scale-up and manufacturing since the founding of the company more than 20 years ago. We have great R&D results in areas including synthetic biology, cell engineering, biochemistry, polymer materials and engineering. We are now a world-renowned R&D platform for biological manufacturing theories and practices, and the only company with the full set of technologies from lab to factory and successful commercialization.

Exploring the production of Vitamin C through biological methods was a project we did for the Chinese government. Back then China only produced 5% of the world's Vitamin C, at a loss. We managed to reduce the production cost by more than 50% in less than two years. With the introduction of biological methods, made-in-China Vitamin C soon replaced alternatives produced using chemical methods. I was greatly inspired by the results. I thought that with the industrial implementation of Vitamin C production, biological methods were proved to be feasible alternatives to chemical ones and that they could be applied to more products.

Cathay Biotech Inc. adheres to a R&D-driven strategy, with theoretical research into and industrial implementation of biological manufacturing as two focuses. Our R&D efforts are linked to market trends and manufacturing practices so that our technological directions are effectively guided by market demands.

As I used to work in the lab, I knew little about business. So I went to a good friend who did, and persuaded him to join the team. Still, we had a lot of trouble due to our lack of business knowledge. Paul Caswell, one of our engineers was also sent out to do sales pitches. He knocked on doors here and there. Finally, he told me the DuPont business cards he had received could cover a wall in his room. Yet he did not manage to sell a kilogram of product. I ended up having to go out and sell the products myself. As no one else had tried biological manufacturing before, many didn't believe this small company called Cathay Biotech Inc. could make it.

We still need to overcome significant commercial barriers for product promotion and application. But fortunately, with our perseverance and frequent interactions with prospective clients, we have achieved breakthroughs in sales.

Directors & Boards: What do you think is the future high ground and what is the key to future innovation in the synthetic biology industry?

Liu Xiucui: Synthetic biology is a branch of biological science that has newly emerged in the 21st century. It has also been one of the most rapidly developing interdisciplinary topics in recent years, integrating science and engineering. Contrary to traditional biology, which dissects living organisms to study their internal structures, synthetic biology builds components from the most basic elements.

Synthetic biotechnology makes it possible to assemble materials efficiently and in vivo with the help of the metabolic system of organisms which have been genetically edited. Though this technology is used in fields such as biomaterials, biofuels, and biomedicine, it is not acceptable to everyone.

In the early days, we tried to sell our products to DuPont. They did not trust us, doubting how many more years we could survive. And they did not think we were doing it at a low cost. Things are quite different now—we have become well established and are blazing our way forward. But we still face obstacles in commercialization. For example, we have produced polymers and explored their applications. Our products can be cheaper alternatives for materials used in the automobile sector, yet automakers have their doubts on safety grounds. Overcoming such obstacles requires time and also applicable quality standards.

In fact, bio-based polyamide, with applications in high-end textile, electronics and electrical appliances, automotive lightweight technology, etc., is a trillion-yuan market. In recent decades, major breakthroughs in gene sequencing and gene editing technologies have led to the birth of synthetic biology as a new discipline. Looking forward, materials needed by mankind will be produced in a more efficient and environmentally friendly way, disrupting the traditional

chemical industry. At the same time, synthetic biology will become the greatest industry, like the information technology in the current era.

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Directors & Boards: Why did you choose to invest in Shanxi?

Liu Xiucan: The partnership began by serendipity. In 2015, our fledgling company received RMB 830 million yuan in financing from Lu'an Chemical Group, a Shanxi-based company to expand our monomers and bio-based polyamide project. Lu'an Chemical Group didn't know much about our synthetic biology business, but as they got to know us better, they not only became a shareholder, but also invited us to invest in Shanxi. It is rare for a local government to see synthetic biology as a potentially major industry.

Shanxi's modernization drive has been a major reason for our decision to invest in the province. According to our agreement, Cathay Biotech Inc. will invest in key projects within the Shanxi Synthetic Biological Industry Ecological Park, including biotechnological production of long chain dicarboxylic acids, bio-pentanediamine, and bio-polyamide and the development of a R&D center for synthetic biology.

We are thankful for leaders at all levels in Shanxi Province for their trust and support, and for granting us the opportunity to become the first in the world to take synthetic biology to large scale industrial plant implementation. We will bring our R&D achievements accumulated over 20 years to the platform. Utilizing the favorable conditions, we will work with the government and develop a world-class synthetic biomaterials industrial park.

Directors & Boards: As a leading entrepreneur, what role do you think the chairman plays in the company? How to elevate synthetic biology to an industrial scale?

Liu Xiucan: Cathay Biotech Inc. currently has four core technologies: synthetic biological technology for developing microbial metabolic pathway and efficient engineered bacteria, microbial metabolism regulation and efficient microbial transformation, isolation and purification of the biotransformation / fermentation system, and polymerization and its downstream applications. The R&D team consists of talents in synthetic biology, cell engineering, biochemistry, polymer materials, engineering, among other disciplines, and has applied for nearly 400 patents in this field, of which more than 90 have been officially licensed.

I always think that there are two necessary conditions to grow the synthetic biology business big. First, you have to be influential in this industry—that is to say you must have scale. Second, you must be able to generate huge profits. A factory making 500 million yuan a year is a big business by the standard of a small county in Shandong Province and a huge success for its co-founders. But it is still not significant industry-wide or nation-wide.

Cathay Biotech Inc. is the only major tech company that have developed multiple products on its R&D platform with synthetic biology approach. I think the company's future direction is to focus on the polyamide industry chain. Bio-based polyamide and its monomer bio-pentanediamine products are important components of the industry chain and will be central to our research and investment efforts.

As chairman of the company, my goal is to elevate synthetic biology to an industrial scale so that it can solve China's dependence on imported oil, especially on high-end oil products.

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