

Interview with Le Sun, , AbMax

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You spent two decades in the US as an academic, executive, and entrepreneur, and then left to return to China and found AbMax. What's the story behind how you came back to China ?

I first went to the US in 1986 to pursue the American Dream. At that time, China was comparatively backward. We were amazed at highways – even basic infrastructure was a marvel ! I wanted to learn the exciting science and technology, as a graduate student, and later worked in private industry. In terms of innovation, the US was the centre, and even today, innovation is led by the US. During my time I climbed up the corporate ladder. I worked for a reagent research company first, and was exposed to the cutting edge of science, high-quality publications, and so on. My Ph.D supervisor Gordon was very important in my life. He was a pioneer in cell culture, monoclonal antibody drugs, a member of the National Academy of the US. He was the first, way back in the 1980s, who suggested to use monoclonal antibodies in the treatment of cancer. He and Mendelson wrote a paper on the subject, however, later on, when he noticed there were more people dying of starvation than cancer, he switched the focus of his research ! However, the monoclonal antibody he made in research in the drug became Erbitux. He was interested in not just publications, but in finding a cure for human disease, and while it is stimulating to work at a research company and help scientists with high quality published papers, it's still far away from a hospital bed. In 2000, I decided along with my Ph.D supervisor and two other friends to start a company called A&G Pharmaceutical in Baltimore, to develop therapeutic and diagnostic treatments for breast cancer, also provide service to Big Pharma – J&J, Pfizer, Boehringer Ingelheim, and also the National Cancer Institutes and others. We tried to develop an antibody drug for cancer, and realized the type of cancer in the US and China were very different. In developed countries, breast cancer and prostate cancers are leading killers for women and men, and lung cancers predominate for both. At the time in China, it was more stomach and liver cancers, which count in the millions of cases, yet amount to only a few thousand cases in the year in the US, because of their relation to infectious diseases, like Hepatitis B&C and other viruses. Being away from the country, we wanted still to do something. And having seen Herceptin's successful launch in 1997, with more in the pipeline, we also saw a change in the Chinese pharmaceutical industry. There wasn't much respect for IP before 2000, but there was a transition based on the realization that successful price-only competition cannot last long. The Chinese government started talking about IP protection, with some pressure from the west, and some internal. Then they began to put it in regulations when researchers apply for grants – the government suddenly began to ask if scientists had the IP rights, and this made a huge difference. Before it was just a matter of money and market access – and now they want to know if you have IP rights ! In 2004, there was another transition when the industry realized that genomics would not solve all their problems. However, if you have an antibody, you have a drug. Authorities realized that antibodies are something China can do, and catch up fast. At the time there were only 10 antibody drugs on the market, compared with many thousands of small molecules !

The Chinese government was willing to invest money, and there were many "sea-turtles" already coming back. In terms of my personal life, the American Dream – a house, three cars, etc. – was already realized, so I was ready to take the risk and return.

Staying for a moment on the sea-turtle story – how did the Chinese government support your return ? We read about macro support, but what about on an individual level ?

In 2004, when I returned, we didn't expect any government support, because it's very much a "burn and catch" in biotech – there may be a slim chance at success. At that time, I licensed a patent of a monoclonal antibody from my PhD supervisor. It's against the same target but a different antibody patent, and we had the idea to use an antibody-drug conjugate. Now, it's a proven concept, but back then it was pioneering and was really ahead of its time. It had 100 times potency of the antibody itself. Antibody drugs, as you know, are very expensive. It's beautiful for pharmaceutical companies, who sell \$9 billion a year, but for the patient, costs can rise upwards of \$30,000 per year. That's way beyond the reach of a normal Chinese citizen, and is of course not covered by medical insurance. The main reason is manufacturing expense – but this new method allowed annual dosages of just 15mg, instead of 1g, because it was much more potent. The cost of the treatment would therefore drop significantly. We got RMB100,000 from the government as part of a package to attract sea-turtles – but on our side we put in about RMB5 million. For two years we struggled because Chinese VC was also not there for biotech. Chinese VCs were more into real estate development, a sector that is more tangible and with quicker returns than biotech. Chinese biotech and pharmaceutical companies were also more disconnected at that time. Pharmaceuticals were in small molecule drugs and TCM – not really protein drugs. This is different from the West, where the system is much more streamlined. Academic institutions file a patent, then small biotech companies come in to work together and make an antibody. Then they humanize it, do some more work, and go to bigger pharma, as my former company had done with MedImmune. They decide which treatments it's appropriate for, and work on it some more, and spend more money to co-develop it past Phase 1. Then a Pfizer, Roche, or Genentech comes in and takes it past Phase 3. Chinese pharma is different, and especially back then was focused mainly on generics. They had the mindset of "No Phase 3, no talk !" and the small biotechs would respond that they don't have the RMB1 billion to take it there ! This is what we called the "Yangtze River" between academics, small biotechs, and pharmaceuticals. A Chinese scientist may publish in Science and Nature and think, "We're wonderful," and the Chinese pharmaceutical companies say merely : "Show me your Phase 3 data !" In the US, we have the gap bridged. In 2006, Lei Ting, a pioneer and visionary, and the government came together to acknowledge that Chinese pharmaceutical companies did not have the resources to copy Pfizer, J&J, and so on. The Chinese Academy doesn't have the resources to match the NIH to innovate new drugs to a Phase 3. The question naturally arose of how to catch up. They then found ABO, and conglomerated a group of companies that could occupy their own niche at every step, with AbMax's in monoclonal antibody production.

How would you define AbMax's specific role in that value chain ?

To use an IT metaphor, AbMax produces the software, and other companies mass-produce the compact discs ! AbMax is the stepping stone for drug development. Companies no longer have to build this capacity internally, and using companies like AbMax is the most cost-effective and fast way. Our clients may have already learned from Big Pharma that even with money, building up the capacity takes time. You need the HR, and technology, and it takes time. But with AbMax, you can have results almost overnight.

This brings us to an important point : can you elaborate on AbMax's speed, as the world record holder in monoclonal antibody production ?

Crunching the numbers is not hard. If there are \$9 billion in sales a year, every day counts. And it goes without saying that there are huge gains if you are the first-to-market. Everybody is rushing to be the first. The first gets a major share, and everyone who comes after divides a smaller and smaller share of the pie. Speed to market is critical to drug companies. Often, if competitive intelligence shows another company ahead in the development cycle, they will cancel the project entirely. AbMax can reduce the time for a monoclonal antibody from 180 days to 46 days – this is a big difference.

The same forces are at work in academia. The first publishes in Science and Nature, and the second publishes in the second tier journals, and so on. It's the same situation for grants. The first gets a grant, and more and more money comes in a positive feedback loop. For this reason, it makes clear sense to use AbMax, the fastest in the world.

This brings up a natural question : where's the disconnect between the current market and one in which everyone uses AbMax ?

AbMax was begun with RMB1.5 million in startup capital. It's a small amount of money. We had to buy the equipment, raw material from the US – which costs 60% more here than in the US – and also to build up a team. It's not so easy to take the technology and come here. It takes time to adapt to the Chinese environment in terms of technology. Our belief is, we want to be not only the fastest but also the highest quality. AbMax spent at least two years doing teambuilding. Of course, despite these humble beginnings the company has great prospects for growth.

Antibodies can be used in many ways : diagnosis, therapeutics, basic research, etc., depending on the requirements. The antibody-antigen relationship is like a key and lock. You have to ask what the key is for. Does it open just one door, or does it open the whole floor ? AbMax had to come up with a customized game plan and come out with the good result. In China, we often joke that there's the Audi, and the Auto – and the price is a 20 fold difference ! They are both cars, but they have different purposes. AbMax must, on one hand, build up technology, and at the same time build a technical support team to understand the customers' needs. Our competitors have an average of 25% success – for every four projects, one will be successful. At AbMax, we count a 90% success rate. Of 100 projects last year, 90 of them have a good result. We want to be the best first, before we become the largest. This is our culture defined. Some companies want to be Wal-Mart. We are AbMax. Max in quality. The culture we foster here is that our speed attracts, but the quality retains.

That's a clear value proposition. How important is the international market to AbMax ?

In the beginning we did many roadshows with ABO – Europe, US, Japan, South Korea, Hong Kong, etc. – and for the first two years, international orders or MNC orders originating in China accounted for upwards of 80% of turnover. Now, this figure is around 10%. After 2009 the international orders changed and dropped significantly. This forced us to evaluate other areas and regions and began to look inwards to China. We found a huge demand for antibodies from academia, which have many grants. In the first five years of the 2000s, the government invested much money in hardware and world-class laboratories. After that phase, they had already bought everything they could, and now they need to produce. The Chinese government changed their tack, and adopted the stance that innovation has to come from the industry. Innovation used to be led by academia, and now it has to be led by industry and driven by the market, and this suddenly gave the industry a huge boost of cash. But once they got the money they had to produce the results. The Chinese government is very results-oriented. This is much different than the US government. They talk about translational medicines, and they have SBIR, but it's only for small companies. They have no funding for large companies. We suddenly had bigger customers from Chinese pharmaceutical and biotech companies, which now account for some 80% of AbMax's business.

With A&G, you had big blue-chip companies like J&J, Pfizer, and Boehringer Ingelheim. Now that MNCs are a smaller portion of AbMax's portfolio - where do you want to bring it ?

Big Pharma is on a clear trend of outsourcing and closing R&D centres in the US. However, my view is that they still want to the old way of doing business, but they have translocated the internal R&D facilities externally. They still want a one-stop R&D service, and are now forcing companies, like the big CRO WuXi, to become what they used to be, experts in small molecule design and production, middle scale production, preclinical studies - everything ! Wuxi spends a lot of money building up such capacity, but it's important to note that the reason Big Pharma failed in productivity is because they became big and decisions took too long to make. Now with outsourcing they're forcing their best CROs to become huge and slow just as the Big Pharma companies used to be !

Real innovation in biotech comes from small companies, and small companies are always founded by someone with special skill - otherwise, he will never attract the money to start the company. This means that in a specific area, the small company may have the best skillset. Once companies merge and grow larger, the high quality people leave and want to start their own companies !

What's at the top of your priority list here at AbMax?

AbMax is best in the mouse monoclonal generation today. Now we must ask ourselves : Why not become the biggest ? We are hiring more sales and marketing people to market our service, to go to more meetings and trade shows. That's our one business priority. At the same time, because monoclonal antibody drugs are so hot, and because the antibodies we generate still need to be humanized, in China we have much work to do in this regard. Our customers have begged us to provide this service, and we see it as a major extension of our business. Last year AbMax hired a VP who has Big Pharma experience at BMS and BioDuro, and he has come onboard to help us build this platform.

What would you expect us to see if we returned to AbMax in five to ten years ?

AbMax will be an innovation-driven company. More and more companies in academia are willing to share IP with us, and we will mature, although as a pure CRO there's a limitation. Particularly in the country, at a national level, you cannot be a CRO or CMO for people all the time in the long-term, it's not sustainable business. President Hu Jintao just announced that by 2020 China wants to be an innovative country, not just a CMO.

In biotech, one notable success story in collaboration with Chinese academics to produce innovation is in creating the vaccine for the head foot and mouth virus, known as the EV71 virus. In 2008 there was an outbreak, and arranged by BPBC myself, the Director of the Beijing Biological Institution and the Deputy Director of the Chinese CDC Biology Institution, all came together to see if there is something we could do about this problem. We didn't have any government support, but we were willing to put our own money in and do something about it. We realized it's a problem that is not going to go away.

In the end, we didn't exchange money, but we exchanged resources. AbMax made a neutralization monoclonal antibody in 35 days, came up with an assay kit, used to measure the viral protection. This began in May 2008. In 2010, the vaccine was already in Phase 1 clinical trials - that's a record. Later we found out that Singapore and Taiwan had been working on the vaccine since 1997 ! And now, our vaccine is already in Phase 3. Normally drugs take 10-14 years. And vaccines are much more difficult to develop because of the focus on safety. In cancer drugs, the patient is already dying, so side effects are excused. You administer a vaccine to healthy two year old children, and there could be impacts up to 60 or 70 years later !

As a result of this collaboration between a service company, academic institution, and drug company, and the risk-sharing and IP-sharing that occurred, we have now filed patents for the antibody and the vaccine, and published a paper jointly with the Chinese CDC. AbMax also has the EV71 kits available in the market, and is the only company in the whole world to do so. Overall, this is just one successful story of biotech in China, but I'm very optimistic about Chinese biotech. Many companies do "me-too" biogenerics and biosimilars. But the second wave is already beginning, of "me-better" from the big Chinese biotech pioneers. Based on the work they give to AbMax, we can see "me-first" is coming as well. We have already made some patent filings for professors from Fudan University and Peking University on the monoclonal antibody we generated for them.

Looking to the future, to launch a biosimilar in the antibody space in China can cost as little as \$20 million. Many Chinese company have that in their pockets, and much more. The problem is that the hurdles are higher than for small molecules. There are many GMP facilities to make small molecules, but to produce protein antibody requires a big facility that costs upwards of \$200m in greenfield investment. But with CROs under the ABO model, while we can't lower the hurdle, we can build many stepping stones, so that companies don't have to spend so much to build a facility, only to find out that their product fails. They can just contract out the work. They don't have to hire someone with a RMB 1 million salary and spend \$2 million to set up an antibody generation core facility. They can just come to AbMax, spend RMB 200,000, and get the same results. Better than that, we only ask 50% of the RMB 200,000 up-front ; the rest is paid upon success. And AbMax can deliver in 60 days. It takes a lawyer longer to negotiate basic agreements ! And AbMax's clients keep all the rights. We are fee-for-service ; we have no rights, the customer retains them all. As an independent third party, we are obliged to show all our laboratory notes, another advantage over other research arrangements. The bottom line is that what used to cost \$2 million now costs RMB 200,000. And companies can take the remainder of that money and invest it in many new projects.

Going forward, we don't want to be viewed as a pure service provider. Pure money transactions are not the best " money cannot buy everything, as the success of the EV71 project proves. There's no secret. It's just a matter of opening up to each other. AbMax will shift from being viewed as a Contract Research Organization to a Collaborative Research Organization, and doing so will be win-win for everyone.

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