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Transcenta's Xueming Qian outlines the new company's origins, the space it seeks to fill within the highly competitive Chinese oncology market, and where Chinese biotech stands globally in 2019.

Dr Qian, Transcenta was established in January 2019 from the merger of two biotech companies: your company, MabSpace Biosciences and HJB, founded by Jonathan Zhao. What brought both companies together?

There were a number of reasons for the merger. Ultimately, there needed to be a common value proposition for us to work together. Jonathan and I actually worked together at Amgen, one of the world's leading biotech companies. We both understand the necessary elements for developing, producing and commercializing a biotherapeutic drug, so we share the same value and standards, and knew we could work well together.

We were also motivated by a need for external development. MabSpace was a biotech company focused on the discovery and development of therapeutic molecules. We outsourced our CMC work to external service providers. However, this became a problem because it meant that we did not have full control over the speed of our pipeline development. While for our first-in-class molecules without a specific timeline, this might have been fine, for other more follower-type molecules, speed to market is everything. Competition in China today is fierce so the fastest companies enjoy

a significant first-mover advantage. Look at Junshi with their PD1 drug, for instance, which was the first domestically developed PD-L1 drug to launch in China. The slower a company is, the less value their assets have and the more challenges they start to face, such as with patient enrollment. Therefore, I decided it was important to possess our own CMC capabilities.

HJB's team was only a few years old when we merged but they had exceptional focus on and expertise in biologics process development and manufacturing. At the same time, they lacked discovery capabilities. Prior to the merger, they were reliant on in-licensing assets from other institutions and companies, which can be a very costly and time-consuming process.

The merger between the two companies was therefore very synergistic as both companies had highly complementary capabilities and focuses. Both Jonathan and I wanted to form a company that would have fully integrated capabilities and last a long time. The name 'Transcenta' reflects our mission to transcend what has already been accomplished by other companies and become a different type of biotech company altogether. Our aspiration is to develop medicine for the global market in accordance with international standards. Our focus is on innovative molecules, first-in-class molecules, next-generation manufacturing and process development.

How smooth has the integration process been?

We are already beginning to see the benefits of the merger. As an indication, filing an IND for an antibody-based drug usually takes 18 to 24 months and costs around USD 5 to 6 million. With our new capabilities, we can shorten this to as little as 12 to 15 months and reduce the costs by over 40 percent. Furthermore, we now have complete control over our data so our IP is fully protected.

We have also taken the opportunity to further complement our leadership team. For instance, we have brought on board a new Head of Research, Dr Yi Gu, who used to be VP of R&D at Ambrx in San Diego and also co-site head and Director of Translational Sciences at AstraZeneca's R&D center in Shanghai. We have also added two senior executives in clinical development, Dr Jason Huang as our head of Clinical Development and Dr Li Xu as our acting CMO. Dr Huang worked for many years in clinical development in multiple MNCs including BMS and Novartis, and also spent some time in a biotech company in China before joining us. Dr Xu is a well-regarded drug developer who worked in Merck, Pfizer and Jiangsu Hengrui, and delivered multiple products to the market, including Crizotinib and Apatinib in China.

Could you share more about your proprietary platform technology, the Immune Tolerance Breaking Technology?

This is the technology we use to discover and generate therapeutic candidates. Today, antibody generation is somewhat of a commodity business. However, anyone can generate an antibody. For an antibody to be valuable, however, there are three criteria: it needs to be efficacious, specific and safe; it needs to be manufacturable at low cost; and there needs to exist good freedom to operate using this antibody, meaning that the antibody does not infringe on any existing patent rights held by other companies. Otherwise, you might not be able to use it for global development.

The global freedom to operate criterion makes the situation very complicated. Western companies started working with biologics two to three decades ago so they have a lot more experience and history in this field. Many have learnt not only to patent their own therapeutic antibodies but also the epitopes these antibodies bind to. A very notable case of this was the lawsuit Amgen filed against Sanofi and Regeneron in 2016, where Amgen claimed that their patent protects not only the sequence of their PCSK9 inhibitor and the structure of their drug but also the epitope to which the drug binds. This legal battle is still ongoing today and highlights the kind of business risks that we also have to contend with. In developing our own antibodies, we sometimes need to find a different route to our final destination. For example, there are several potential functional spots a drug can target. Any particular drug might only target one of those spots. We can analyse the patents of existing drugs and identify other potential functional spots to hit.

It is also very important to screen drugs and our discovery team places a lot of emphasis on this. We actually found our flagship PD-L1 antibody after screening several dozen potent neutralizing antibodies. I did not want to work on an antibody similar to the dozens already in clinical trials, I wanted to find a differentiator! This is how we found our flagship pH-dependent PD-L1 antibody.

Oncology is a big focus for Transcenta. What are some of your flagship assets in this area?

Oncology is currently two-thirds of our existing clinical pipeline. At the moment, we are very excited about two programs.

The first is a PD-L1 immune checkpoint inhibitor but what differentiates ours is that it is probably the only pH-dependent PD-L1 antibody globally. With this unique pH-dependent binding property, we have demonstrated in the pre-clinical setting that this antibody can be recycled after it binds to

a tumour cell. This means that the antibody can remain in the tumour of the patient for a longer time, which means the drug can work for a longer time. Overall, we see that this antibody has excellent activity but much lower toxicity compared to other first-generation PD-L1 molecules. We are very excited about this drug. We are first looking to register this drug using a niche indication but this drug could also serve as a backbone for combination therapy with our other assets.

We also have a very competitive program where we aim to be second globally and first in China. It is a targeted therapy that can be used for multiple solid tumours like lung cancer, pancreatic cancer, gastric cancer and so on. We are very excited about this too and we aim to file our IND in both the US and China in early next year. We believe that this drug could be significantly better than the existing therapies on the market.

Beyond these two, we have around eight other oncology molecules focusing on different mechanisms that can either work alone or in combination with our other pipeline molecules.

Besides oncology, what other therapeutic areas does Transcenta work in?

In addition to oncology, we also have a presence in bone disorders. We have in-licensed their China rights for a Phase II compound from Eli Lilly and we have the option to gain global rights to this compound as well. With aging populations, osteoporosis and fractures are big problems and we hope to develop an impactful medicine here.

In addition to this, we also have a very innovative antibody-based pipeline in nephrology. Our main asset here targets IgA nephropathy, which makes up a large portion of patients with chronic kidney disease (CKD) in Asia. To put this in perspective, in Western countries, between 10 to 20 percent of CKD patients are due to IgA nephropathy but in Asia, the figure is around 40 percent. In China, around 100 million patients have varying degrees of CKD, a fifth of them have serious CKD, and a third of them are due to IgA nephropathy – thus, a very significant number of patients indeed. We feel that we have an obligation to develop agents that can prevent and treat these types of diseases in China. Also, competition is low in these two non-oncology areas.

Both these areas are aided by my previous experience at Amgen, where I used to focus on bone and renal diseases in drug discovery.

We are also exploring potential in-licensing options and have in fact hired a global consultancy to scan global portfolios to identify potential assets of interest to us. We are actually currently closing a new fundraising round and will allocate around 15 percent of the new investment to in-licensing.

Another 15 percent will be invested in developing our own pipeline, and over half will go towards our existing clinical and CMC activities. The remaining 20 percent will be spent on the operations side.

Working across these different therapeutic areas and with speed being of essence, how do you organize the company to foster productivity and accelerate speed to market?

Our goal is to file simultaneously in both the US and China. This means that we have to ensure we work towards the highest international standards. In addition, our entire pipeline is focused on innovation, with 60 percent being more follow-on innovations and the remaining 40 percent being first-in-class innovations. This is riskier than many other Chinese biotechs but we have a clear rationale for each program we develop. We also hope to identify partners for co-development of the higher-risk assets.

We believe that the target matters most when it comes to drug development. 70 percent of whether a drug works or not depends on target selection. The remaining 30 percent then includes the drug's properties, clinical trial design and so on.

To maintain productivity, we organize the company in a very cross-functional way. We actually have a project-based structure so each project has a team leader and then representatives from pre-clinical, CMC, clinical development, regulatory and so on. This is very efficient and ensures that the whole team is very reactive. Within the company, we also have a research review board, a CMC review board and a clinical review board. Every other week, I host a team meeting with senior staff to coordinate and strategize activities across the entire company. In some ways, we function much like a miniature Amgen!

Looking forward, we hope to launch our products by 2022-2023 so we will start to develop our commercial capabilities in 2021.

Transcenta already has a rather international presence with offices in China and the US. Could you share more about your global presence?

Suzhou is mainly our discovery, research and clinical base, and I spend half my time here, where I focus on product development, business development and investor meetings. Our Hangzhou facility is a process development and manufacturing facility. Our clinical teams are spread between

Suzhou, Shanghai and Beijing in China, and Princeton in the US. Our presence in Princeton keeps us close to the Big Pharma companies HQed there. We also have a business development office in Boston, which gives us presence within an innovative biotech ecosystem with a lot of cutting-edge technology. As a company, we invest a lot in new technology to enhance efficiency and lower costs so our Boston office also serves as a gateway for product and technology licensing and partnerships.

It is important to have offices in key hubs so that we can attract the best talents, who may not necessarily want to relocate. We also plan to open another office in Guangzhou.

On a more personal note, what have you learnt about being a CEO in the past few months leading Transcenta Group?

As the CEO, a lot of my focus is on team management. The most important part is having the right people. You must build a team that works well together and shares the same value proposition as the company. They should also have similar experience level and standards so they can understand each other. We are very lucky here and over the last several years and the last six months especially, have assembled one of the best biotech teams in China.

I try to create more opportunities for my team to bond with each other. By better understanding each other's concerns, difficulties and challenges, they will become more collaborative.

Once you have the right team, you need to create the right structure to empower them to make good decisions. I am a very detail-oriented person but once I identify the leader for a specific area, I set clear corporate goals and count on them to deliver. I think sometimes we have a tendency to underestimate people but I believe that if you give them the right goal and the right support, people usually exceed your expectations. For instance, I mentioned that we successfully reduced the IND filing time from 18-24 months to 12 months. I set the ambitious target of 12 months to motivate my team and they achieved it! This was very rewarding for the entire company.

Finally, we have also implemented a rewards system that links bonuses not only to individual performance but also team and company performance. This ensures that everyone is invested in the results of the team and the company.

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