Yuguang Wang â?? CEO, Maxinovel Pharmaceuticals, China

> I am at a stage where I have a different perspective, which allows me to conduct R&D in a different way â?? doing disruptive innovation

27.01.2020

Tags:

China, Biotech, Maxinovel, Research, Oncology, Innovation

Dr Yuguang Wang, CEO of Maxinovel Pharmaceuticals, recaps his three decades of industry experience across Big Pharma, biotech and CRO organizations in China and the US, his motivation to establish Maxinovel Pharmaceuticals as a global, semi-virtual biotech, and their mission to develop a pipeline of orally-active one-pill combination of immuno-oncology (IO) therapy, targeted therapy and chemotherapy in order to better serve cancer patients.

Dr Wang, could you start by introducing yourself and your motivations for establishing Maxinovel to our international audience?

I have always been fascinated by medicine. That curiosity inspired me to go to Shandong Medical University, now part of Shandong University, to study pharmacy. Subsequently, I went to the University of Kansas in the US to pursue a PhD in medicinal chemistry and drug design, before starting my career at Schering-Plough in the US in 1990.

Over my three decades of industry experience, I can list three major milestones. Firstly, working at first-line drug discovery in Schering-Plough, I discovered a drug, Vorapaxar, a thrombin receptor antagonist approved by the US FDA in 2014. Secondly, I managed drug discovery operations, both at Schering-Plough and at a Chinese CRO, Shanghai ChemPartner, with teams ranging from six or seven people to up to 600 people. When I was at ChemPartner, my research service team worked

side by side with clients from both Big Pharma and biotech companies worldwide. This gave me familiarity with both Big Pharma and biotech operations. Finally, I was part of the senior ChemPartner team working on their successful IPO listing on the NYSE in 2010.

Looking back, having worked in the various parts of the industry most relevant to drug R&D, I wanted to see if I could establish a biotech company myself! I had many ideas I wanted to explore, and I thought establishing Maxinovel would be the best way to do that, and so in March 2016, Maxinovel was founded.

Today, Maxinovel is a semi-virtual company with global operations: a pre-clinical laboratory in Shanghai, a biomarker and translational lab in Guangzhou; early-stage clinical operations in Sydney; and our US base for global operations in New Jersey, where I live. We generate and keep our IP in-house and we outsource all subsequent testing and proof-of-concept (POC) activities like biological, DMPK and toxicology work.

What is your vision and R&D strategy for Maxinovel?

Our vision is to develop a pipeline of orally-active one-pill combination of immuno-oncology (IO) therapy, targeted therapy and chemotherapy. This is driven by my research philosophy, which has guided me through the industry well over the past few decades. For me, drug discovery is the philosophical practice of combining artistic design with intuition. This is why drug discovery is so difficult. Some drugs succeed while many others fail.

Our R&D strategy is to focus on disruptive innovation in the most important field â?? oncology â?? with a research theory that is different from the crowd. For example, currently, the most important field is immuno-oncology, especially the inhibition of the PD-1/PD-L1 axis. The industry has crowded around antibody discovery. In China alone, there are more than a hundred companies doing PD-1/PD-L1 antibody discovery because of the great commercial successes of drugs like the anti-PD-1 antibody Keytruda and the anti-PD-L1 antibody Imfinzi. What should we do and how should we do it? I believe we should also be working in the field of the inhibition of the PD-1/PD-L1 axis because this is the Olympics in drug discovery. We need to participate â?? and win.

Once we made our decision, the next step is to do the disruptive work. To me, being disruptive means we cannot follow the herd in doing anti-PD-1/PD-L1 antibodies. We must find the problem and then look at the problem through a different angle. For PD-1/PD-L1 antibody drugs like the market leader, Keytruda, the major problem is the low treatment response rate of using these drugs as monotherapy. The current reasoning is that PD-L1 expression is low. Is this explanation right? Most people would think so but we have doubt. The PD-1/PD-L1 axis is an immune escape mechanism used by tumour cells â?? in that sense, PD-L1 is the villain â??protectingâ?? the cancer cells from being killed. Therefore, it is perplexing that Keytruda is somehow less effective when there is less PD-L1 â??protectingâ?? the cancer cells than when there is more PD-L1! Therefore, we think that there must be more reasons for the observed low treatment response rate. If we can formulate a new hypothesis, we can discover next-generation PD-1/PD-L1 inhibitors effective for both PD-L1-high and PD-L1-low tumours. The logic is simple: if a drug can defeat PD-L1-high tumours, when there are more â??villainsâ?? to fight, then it should also be able to defeat PD-L1-low tumours when there are fewer such â??villainsâ?? to fight.

With that exciting ambition in mind, how is your pipeline advancing?

We currently have seven ongoing projects, with the two most clinically advanced being MAX-1 and MAX-4. We out-licensed our seventh project in 2018 to another biotech for a total of USD 220 million. That was a first-in-class asset we decided to out-license because it was not in our focus area of oncology.

MAX-1 is our orally active next generation PD-1/PD-L1 project, which will start Phase I trial in Australia soon. As I mentioned before, we believe the next generation PD-1/L1 inhibitor should be effective on both PD-L1-high and PD-L1-low tumours. I am very happy to disclose here for the first time to the outside world that we have formulated a new hypothesis to guide our PD-1/PD-L1 inhibition project. We have successfully discovered a clinical candidate with superior efficacy over Keytruda in PD-L1-low humanized model. We will present our finding at the 2020 AACR in San Diego. In 2019 AACR, we reported that our clinical candidate has similar efficacy in PD-L1-high humanized model as Imfinzi. As you can see, our clinical candidate is effective in both PD-L1-high and PD-L1-low tumour models, using market-leading drugs, Keytruda and Imfinzi, as references. Now, we are on a clinical path to confirm our preclinical findings. It is very exciting.

What about your targeted therapy project, MAX-4?

MAX-4 is our targeted therapy project that is already in Phase I trial in Australia. It has also obtained Orphan Drug Designation from the US FDA. Like IO, targeted therapy is incredibly crowded, too. We need to participate â?? but with a different approach. While most people working on the kinase oncogene receptors such as EGFR, cMet and ALK, etc. we are focusing on kinase oncogene partners.

In our Phase 1 trial, genomic analysis of our first PR patient revealed the high expression of this oncogene partner protein. We subsequently carried out RNA-seq of 30 patient-derived cell lines treated with our clinical candidate. We found a great correlation between the treatment efficacy and the oncogene partner protein expression level. Furthermore, we conducted a HTS of 81 tumour cell lines and found p=0.0001 between the IC50s and the oncogene partner TPMs. I am very happy to say that analysis of the TCGA database revealed that more than 30 types of tumours have this oncogene partner protein expression with TPM> 5. We are progressing dose-escalation study in both blood and solid tumours.

What other exciting projects are you working on?

The next one I can share is our topical JAK inhibitor for autoimmune skin diseases like alopecia areata, atopic dermatitis and vitiligo. We plan to bring it into the clinic next year. This is also a big market but big players are focusing on oral solutions while we decided to use a topical formulation for better safety and long-term usage. Again, we are travelling on a different path from the crowd to achieve the same treatment goals.

With the booming biotech environment in China, how have you found the experience of building a biotech here?

I am incredibly excited to be in China because I think I can accomplish things here that I cannot do in Big Pharma companies in the US! We think differently from Big Pharma. Big Pharma companies are extremely risk-averse. If someone has identified a successful mechanism of action or target,

everyone else will follow. But if someone fails in that field, no one else dares to try again. This is understandable because they are large organizations, after all. For me, however, I run my own biotech company so I have the flexibility and capability to take risks.

The word â??researchâ?? already implies that you have to search over and over again â?? â??reâ?? + â??searchâ??. If you only try once, it is not research! In China, I am able to test theories that would be difficult to test in Big Pharma companies in the US. This has given us room to explore and hopefully, to establish ourselves as leaders of doing disruptive innovation.

The overall environment in China today is indeed very constructive for biotech R&D. With the talent pool comprising many overseas returnees, the positive regulatory environment and more active capital markets, the timing is great.

In general, I believe I am very lucky to be building Maxinovel now. We would not have been able to undertake the kind of research we are doing now several years ago. New technologies like next-generation sequencing (NGS) have enabled us to understand more about the individual patient. This has allowed us to relook at tumours and reclassify them based on their genetic makeup and mutations. In five more years, even more tools and technology would have been developed to help us better understand and develop cancer therapies.

Looking forward, what are your key priorities for Maxinovel?

Our strengths are in discovery and R&D. Commercialization is our weak spot thus far so we are very open to different types of commercial collaboration subject to further discussion with potential partners. We are looking at global markets, not just China, so we will definitely need support.

Secondly, like many biotech companies in China, we have an IPO on our minds. We plan to IPO within the next three years, either in New York or Hong Kong, once we have an asset in Phase II and good clinical data on the others.

I am also grateful to have already assembled a very strong team, including experienced veterans that have worked in top pharma companies in both the US and China for decades. Moving forward, however, especially considering our IPO plans, we need to fill the CMO, CBO and CFO positions with people possessing strong reputations within the investor community. This has not been our focus in the past three years as we wanted to concentrate on our preclinical development but now we are a clinical-stage company and we are preparing for an IPO. Since we are confident we have great science and disruptive innovation, we need good spokespeople to share those with investors.

On a final, more personal note, after nearly 30 years in the industry, what keeps you excited?

Curiosity and passion for science! As mentioned, I have always been curious and passionate about science, even as a child. 30 years into the industry, I think I am at a stage where I have a different perspective, which allows me to conduct R&D in a different way â?? doing disruptive innovation. There is also less pressure on me, so I can just focus on my passion for discovering new medicines to ultimately serve the needs of patients globally.

See more interviews