Zhengyu Yuan – President & CEO, MicuRx

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Dr. Zhengyu Yuan, president & CEO of MicuRx, shares the story of how MicuRx was founded in 2007 to develop new and innovative antimicrobial drugs; their flagship product, contezolid, which recently concluded Phase III trials in China; and their future plans for an IPO.

Dr. Yuan, could you please introduce MicuRx to our international audience?

MicuRx was established in 2007 by my partner, Mikhail (Mike) Gordeev (currently EVP and CSO) and myself. When we started, we had nothing but a business plan and some ideas for new molecules on paper. In 2008, the team finally identified our first clinical candidate, then named MRX-1, and today, the generic name is contezolid. We have finished Phase II trials for contezolid in the US and Phase III pivotal trials in China, and expect to submit the NDA in China in the next two months. This also marks the rare occasion when a novel drug would file for NDA in China before the US!

MicuRx focuses on antimicrobial resistance (AMR). We selected this area by chance – but MicuRx is actually not our first biotech company in this area.

Both Mike and I initially used to work at Affymax, a technology company focused on chemistry, where we developed new technologies to accelerate the drug discovery process. However, we

realized that technology is still only technology, and true value creation only comes from actually discovering and developing the final drug candidate. Therefore, we decided to leave Affymax –with our boss then, Eric Gorden – to establish a new company Versicor in 1996. We assessed which therapeutic areas were most suitable for our specific technological expertise, and we decided on AMR because we initially thought the drug discovery process would be more straightforward. Of course, we found out quickly enough that there is no such thing as a straightforward drug discovery process! Despite the challenges, AMR is also a very rewarding area because there are critical unmet medical needs, and we can clearly see the benefits our drugs could provide to patients. Eventually, after getting two of drug candidates to NDA in US, the company, which was renamed as Vicuron Pharmaceuticals, was acquired by Pfizer for USD 1.9 billion in 2005.

Mike and I saw more opportunities in this space, and we thought there was so much more to be done, particularly within the discovery space. We could see that – in 2005 – more biotechs were focused on in-licensing rather than creation. We wanted to do the opposite: to discover and develop novel compounds. Therefore, we founded MicuRx in 2007.

Having been around for 12 years now, and as one of the first biotechs to base itself in both the US and China, what is your perspective on the current changes within the Chinese biotech environment?

Even when we started in 2007, we thought it was important to be present both in the US and China, since these two countries could offer complementary advantages. It also reflected the international nature of our team, since Mike is originally from Russia, and I am originally from Shanghai, before we both went to the US to study and work. In 2007, China’s drug discovery and development industry was still in its infancy, and there was no critical mass, so it was very challenging. However, MicuRx could draw on its very experienced team, based in the US, to guide our operations in China. The positives about China, on the other hand, were the size of its market – both current and future – and the presence of young talents, who could do a lot of work with greater cost efficiency, if supervised well. Therefore, we combined US experience and Chinese infrastructure to accelerate the entire drug discovery process. The remaining challenge we saw in China was the regulatory hurdles, but we thought those could be mitigated subsequently as we enter the clinic and raise more resources.

The recent developments in China, like everything else, have pros and cons. On one hand, we have many more talents, a much better industry infrastructure, and much friendlier and more forward-

thinking regulatory agencies. All these make drug discovery and development easier in China. On the other hand, costs have gone up and competition for financial and clinical resources keeps increasing. For instance, it is now more challenging to maintain the same quality standards in terms of clinical operation. But these are simply the growing pains of a maturing industry.

Could you tell us more about your flagship product, contezolid?

Contezolid is a drug belonging to the oxazolidinone class of molecules. Within this class there is an existing blockbuster drug on the market, linezolid or Zyvox currently marketed by Pfizer which was launched in 2000 in US, and 2007 in China. This is a very effective drug for multi-drug resistant (MDR) Gram-positive bacterial infections, including Methicillin-resistant *staphylococcus aureus* (MRSA) and Vancomycin-resistant *Enterococci* (VRE). These bacteria have been termed 'superbugs' due to their significant resistance to most of the existing antibiotics. In hospitals especially, the resistance rates are very high.

When linezolid was launched, it was exciting because, compared with another older drug vancomycin, linezolid was available both intravenously and orally with very good tissue distribution, and was effective against many different types of Gram-positive bacterial infections without nephrotoxicity commonly seen in vancomycin. However, linezolid also has some problems with toxicity, specifically bone marrow toxicity, which limits its use to a large extent clinically. For infections with no alternatives, for example, drug-resistant tuberculosis, it is still prescribed but around 70 percent of patients will eventually develop bone marrow toxicity related side effects and around 30 percent will develop neuropathy, sometimes even losing their eyesight.

Therefore, almost as soon as linezolid was launched, the market wanted to have a second-generation version of the drug that was safer. In 2008, we identified contezolid, a compound we soon proof that was as efficacious as linezolid but overcome the bone marrow toxicity. The development of contezolid in China has been designated as a "Significant New Drugs Development Special Project", and contezolid has also been granted QIDP designation and Fast Track status by the US FDA. We are now very excited to have completed Phase III trial in China and expect to file for NDA in China soon. It has been a long 12-year journey but we consider ourselves lucky to even complete it because after all, most biotech companies do not even make it to the end.

Having completed the clinical development process, what are your plans for contezolid's commercialization?

Our product is much easier and safer to use than the existing drugs on the market so we certainly hope that we will gain significant market share. We would also need to price this drug based on the right pharmaco-economics principles, so that it is affordable for patients while still reflecting the therapeutic value of this novel compound.

Considering that contezolid will be a drug for hospital market mainly in China, we are still evaluating the best approach for commercialization. Probably it is best for us to leverage another company's existing network. We are looking for a strategic partner that not only has a strong hospital sales network, experience and infrastructure, but also understands the importance of medical education. As a novel drug, contezolid has its own unique medical benefits. Our team will be able to explain and emphasize the drug's medical advantages and benefits, and to address the likely concerns over the use of a novel drug from physicians and patients.

For the US and other international markets, we would still have to wait a few years. As a biotech, out-licensing is always a possibility but not the only one. Phase III trials are very expensive but at the moment, if we can raise enough money to conduct Phase III trials in key global markets, we will do it ourselves since the risk is relatively low now. We just need to collect the clinical data. Our team has successfully filed for NDAs in the US before so we are experienced. Nevertheless, we will consider all options when the moment comes.

What are MicuRx's IPO plans?

We had planned to be listed in Hong Kong last year, and now we might have one more option to be listed on Shanghai's STAR Board. We are evaluating all possible options. For MicuRx, the purpose is to raise sufficient funds for clinical development and to generate good return for our investors eventually. We will keep focusing on the fundamental value of our portfolio and assets and create value through inventions not by playing the markets. I believe that the market will eventually recognize it.

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