Hung-Kai Kevin Chen – Co-Founder & CEO, Elixiron

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Dr Hung-Kai Kevin Chen, co-founder and CEO of Elixiron Immunotherapeutics, an innovative rising biotech focused on immunotherapeutic solutions, describes the company's unique approach to developing new treatment methods for two disease areas with massive unmet medical need: hard-to-treat cancer and

chronic hepatitis B. Dr Chen goes on to share his vision for using reverse-translation research and an immunology approach to position Elixiron into one of Taiwan's rising stars in biotech.

How has your diverse research and industry experience prepared you to lead your own innovative biotech company?

I studied and was trained in Taiwan, getting both my MS and PhD from National Yang-Ming University. Early in my career, I decided I wanted to pursue a path that would lead me to develop new treatments for the patients rather than follow a path of a clinical practitioner. After getting my PhD in immunology, I travelled to the US to do my post-doctorate fellowship where I became involved in research for the treatment of neurodegenerative diseases. Later on, I joined Gladstone Institutes as an assistant investigator at the Center for Translational Research. I have always been very interested in developing the ability to translate my own research into potential new drugs to treat patients with unmet medical needs.

At Gladstone Institutes, we collaborated with Merck Research Laboratories to develop structural modulators of apolipoprotein E4 for the treatment of Alzheimer's disease. I realized that the training I had up until then was not enough to develop new drugs. Therefore, I decided to join the industry and learn about drug development from scratch by leading several projects with GlaxoSmithKline for treatments of neurological and immunological diseases.

When I returned to Taiwan, I was shocked to realize that although the academic and research environment is strong, translation is a real challenge here. As a trained medical doctor working in the industry, I can bring my experience in translational medicine to bridge the translation gap and address the issue of high failure rates in drug development from the preclinical stage to human clinical trials. Therefore, at Elixiron, we leverage the power of human translation to guide drug discovery, starting from clinical observations in patients to identify pathogenic mechanisms and translating backwards for target validation – which we call the "reverse-translation" model.

What is Elixiron's strategy to identify and develop new therapeutic solutions?

"Begin with the end" is our strategy. Every project in Elixiron starts with an examination of a real-world problem in patients from which we then determine the disease-causing mechanisms and potential therapeutic approaches. This approach could dramatically improve translatability from bench to bedside because patients in the clinic are where our drug discovery process starts.

Elixiron co-founder Dr Muh-Hwa Yang is a physician-scientist specialized in medical oncology and the other co-founder Dr. Cheng-Lung Ku is a clinical immunologist studying human autoimmune and infectious diseases. Their translational work laid the foundation of the company.

How would you describe Elixiron's approach to immuno-oncology?

The fundamental principle of immuno-oncology is that cancers exploit specific immunosuppressive mechanisms to evade the host immune system. Therefore, therapies which counteract such mechanisms of immune evasion can effectively elicit anti-tumour immunity. Based on our own translational studies, we have identified specific immunosuppressive pathways that have taken place in the tumour microenvironment of hard-to-treat cancers. By targeting these immunosuppressive pathways, our candidate drugs in development can potentially harness the full power of the immune system to fight cancer.

How does Elixiron's solution differ from the existing immunotherapies on the market?

In the immuno-oncology industry, immune checkpoint inhibitors like anti-PD-1/PD-L1 are highly discussed topics. In China alone, there are over 100 companies developing similar checkpoint inhibitors. Despite their initial success, many cancer patients are still resistant to treatments of current checkpoint inhibitors. In addition, cancer metastasis accounts for most cancer deaths. Therefore, we decided to go beyond PD-1 to develop the next generation of cancer immunotherapy to address the unmet medical needs.

In a microscopic view, tumour types that are relatively responsive to checkpoint inhibitors like melanoma or lung cancers are often infiltrated with T lymphocytes, thereby termed as immunologically "hot" tumours. On the other hand, the microenvironment of so-called "cold tumours" is extremely immunosuppressive, driven by the M2 type tumour-associated macrophages, which prevent the entry of T cells and become refractory to anti-PD-1 immunotherapy.

Elixiron's co-founder, Dr Yang, has recently discovered that metastatic tumours have a relatively "cold" and immunosuppressive microenvironment in which the tumour-associated macrophages adopt a predominantly M2-phenotype. In addition, these macrophages secrete specific immunosuppressive cytokines to drive immune resistance and cancer metastasis. Based on these findings, we focused on the development of novel immunotherapeutics to counteract such immunosuppressive mechanisms in order to reinvigorate the immune system for the treatment of cold tumours and control of cancer metastasis.

Our lead product, EI-1071, is a kinase inhibitor of Colony Stimulating Factor 1 Receptor (CSF-1R), ready to kick off its clinical development in the next six months. In addition, we have several therapeutic antibodies in preclinical development. Elixiron is operated by an elite group of R&D professionals led by Dr Daw-Tsun Shih, a seasoned industry veteran from Big Pharma.

Elixiron is also developing an immunological approach for the treatment of the hepatitis B virus (HBV). Tell us more about this side of the company.

We actually view chronic hepatitis B virus (HBV) infection as an immunological disease like we do cancers. HBV induces virus-specific immunosuppression to maintain a chronic infection reminiscent of immune evasion occurring in cancers. From our own translational studies, we have identified a

specific immunosuppressive pathway that is highly upregulated in patients with chronic HBV infection. Accordingly, we are developing a pathway-specific immunotherapy to restore anti-HBV immunity which holds therapeutic promise for a long-term HBV functional cure.

What approach have you identified to take on the task of developing Elixiron's innovation pipeline?

We have been rather successful in raising capital financing to support R&D activities. Elixiron is well equipped with a professional team of diverse expertise from preclinical discovery to clinical development. With the unique translational approach, we are committed to translating scientific innovation into therapeutic development, thereby driving rapid business growth. We aim to bring our major preclinical assets up to clinical proof-of-concept stage and then work with big pharmas for their late-stage development and commercialization.

What objectives do you aim to achieve within the upcoming future to develop Elixiron as a strong biotech player?

In five years, I expect Elixiron to be positioned as a rising star in the biotechnology area particularly when it comes to immunotherapeutics. By that time, Elixiron will have at least two promising immunotherapeutics in clinical trials for cancer and chronic hepatitis B. Our innovative products have received positive feedback from potential partners, including big pharma. We'll continue to build momentum and expand our global footprint.

What are the strengths of Taiwan for setting up a biotech company?

We are blessed to have the support of a high-quality and very affordable healthcare system enabling us to leverage the power of translational medicine to drive therapeutic innovation. In fact, I am proud to say that Taiwan is one of the best places for translational research. The physicians and scientists here are well-trained up to Western standards and the infrastructure system operates in a relatively transparent and cost-effective way.

The challenge is the lack of interdisciplinary knowledge and collaborative mindset when it comes to translating research. Many biomedical researchers are still accustomed to traditional research models limited to their own areas of expertise. By combining all the pieces together and creating

synergies, we can build a productive value chain of the biotech industry.

One message I would like to deliver to the industry and government of Taiwan is that attracting talent, especially those with work experience in global pharmaceutical companies, is the key to growth in the biotech industry. Reform of grant policy may be needed to encourage collaborations between academic researchers, physicians and the industry. Translational research should be an important focus from the start where physicians and scientists are able to think on a larger, more cross-functional scale.

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