Byoung S. Kwon, CEO â?? Eutilex

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Eutilexâ??s CEO, Byoung S. Kwon, outlines the companyâ??s approach to cancer research, including its antibodies and CAR-T-centred pipeline and focus on unmet needs. He also explains recent partnerships in China.

Can you introduce yourself briefly and tell us what made you decide to go into the bio venture field and found Eutilex?

Approximately 10 years ago, I was developing a T-cell therapy clinical trial in the lab at the National Cancer Centre in Korea. While working on the development of this immuno-oncology drug, I realised that a research lab requires a huge amount of money to participate in clinical trials, while a company can be more efficient. This is the reason why I decided to create Eutilex. I founded Eutilex the T-cell therapy went into clinical trials, so we were able to have our initial public offering (IPO) just three years after starting the company. We are currently conducting multiple clinical trials globally with several more in the final stages of preparation to start clinical trials.

Can you tell us more about how Eutilex started with T-cell therapeutics?

I have a scientific background in T-cell biology. I have forty years of experience in the field of clinical research. Early in my career, I discovered that there are two concepts for cancer treatment: selective activation and selective suppression. These concepts mean that you can suppress or activate the whole immune system for therapeutic purposes. My research theme or goal was to be able to activate the T-cells in order to kill cancer. The T-cells require 2 signals to get activated: the first signal is through T-cell antigen receptors (TCR) and the second signal is through co-stimulation factors.

My theme for immunology research is selective inhibition and selective suppression. I had to find a way to handle the immune system selectively and through my preliminary research, I realised that this co-stimulation is not the only key for therapeutic activation of our immune system. Therefore, this concept led me to discover the activation signals such as the 4-1BB (CD137) antibody. In other words, triggering 4-1BB leads to the antigen-specific activation of T-cells. This is referred to as a selective activation concept: when cancer cells trigger the immune system, the T-cells triggered by cancer cells are on the surface of 4-1BB. Once you give a signal through 4-1BB, then you activate only the T-cells specific to cancer. This results in a safe but effective way to kill cancer cells through the bodyâ??s natural immune system.

Throughout my research career, I found 4-1BB for the first time and characterized how this 4-1BB works. This is how we developed T-cell therapeutics and the support 4-1BB signals used for our CAR-T cell therapeutics.

Today the company has a pipeline focused on antibodies and CAR-T. Can you tell us more about Eutilexâ??s platform technologies?

Eutilex has developed four platform technologies, each with multiple pipelines.

Our first platform technology is co-stimulatory molecule technology, which is called antibody therapy. Co-stimulatory molecule technology encompasses every version of co-stimulation that contains antibody pipelines targeting various immune checkpoint activators and inhibitors. There are two well-known immune checkpoint inhibitors: PD-1 and PD-L1. Similarly, 4-1BB is a well-known immune checkpoint activator and it is a lead antibody in our platform. As I mentioned, I discovered 4-1BB in 1989. Our 4-1BB antibody is called EU101 and is in clinical trials in the USA, in Korea, and in China. Our next antibody is called EU103 and is set to begin clinical trials in the first quarter of 2023.

Our second platform technology is our proprietary T-cell therapy using 4-1BB. We extract T-cells that respond to a specific cancer antigen and culture them. Our first T-cell therapy pipeline is called EU204, also known as EBViNT. In our T-cell therapy clinical trials for cancers, we also have other pipelines such as WTiNT.

Our third platform is our CAR-T therapy. Our lead CAR-T product is EU307(GPC3-IL18) for solid cancers like liver cancer. We are currently preparing to file our investigational new drug (IND) application for CAR-T therapy this year. Our other CAR-T pipelines include EU301 for hematologic cancers, and EU309 for glioblastoma multiforme (GBM), brain cancer.

Finally, our fourth platform is our allogenic T-cell therapy. The first product will be in clinical trials during the third quarter of 2023, at which time we hope to commercialise an off-the-shelf T-cell product.

Eutilex has a lot of different platforms with different simulation methods. Is there any common denominator?

Different methods are ideal because drug development is an evolutionary process. You cannot perfect a drug in one-shot, you continuously have to improve and correct the deficiencies. So, you need a denominator that simulates the human system closely, or as much as possible.

Therefore, all these different therapeutic platforms are based upon how we can handle these T-cells to attack cancer, and then how we can manage, modify or improve the cancer microenvironment. For example, our CAR-T can stand alone, but we also have the flexibility to have our product combine with other pipelines, such as our antibody therapeutics.

Going back to your question, most pipelines currently are based on 4-1BB where we have expertise, so I can say that 4-1BB is a common denominator.

Some of these solutions are probably not going to be first-line therapies, so it may be more difficult to reach the market. Does Eutilex focus only on their scientific aspect?

When we develop a therapeutic, we strategically select those cancer areas with high unmet needs. So, for example, hepatocellular carcinoma, or liver cancer, has a very high incidence in China, in Korea, and in South America. Because of this disease incidence, many companies, including Eutilex, are now working on liver cancer. It is the reason why there are a lot of hospitals in Korea waiting for us to launch a trial for liver cancer.

Eutilex is taking the approach of unmet needs that perhaps other western companies will not take. Can you tell us more about the clinical trials for liver cancer specifically?

We are going to file with the Korean Food and Drug Administration (FDA) and once we get approval, we will start the clinical trials for liver cancer. There are a lot of things we have to take into consideration because this is a solid cancer in the liver. We need to know where toxicity can be a problem and we need to study the hepatic arteries.

However, EU307â??s target, GPC3, is overexpressed in liver cancer cells and is not present in normal cells, so EU307 shows no toxicity because it only attacks the liver cancer cells. And, significantly, EU307 has already proven efficacy in killing liver cancer cells.

How is Eutilex financing its portfolio? Is Eutilex commercialising part of the platform to third parties?

We do not have much of a problem with the financial aspect thanks to strong support from the market. Therefore, we have collected enough capital to conduct our trials. Additionally, we have had success licensing out our antibody therapies, which helps bring in capital for our trials.

Eutilex recently signed an agreement with OBiO Technology in China. What are your thoughts on this collaboration?

We have licensed out antibodies to China, but the Chinese market is difficult. China is known as the country with the highest number of cancer patients for many of our pipelines. For example, EBViNT is associated with cancers such as gastric cancers or nasopharyngeal carcinomas (NPC). China has a higher number of these patients than the rest of the world. EBViNT is our best product, and we wanted to work with OBiO because they are equipped with what we were looking for, such as a good manufacturing practice (GMP) facility where we can produce T-cell receptor (TCR-T) cells and CAR-T cells. The contract manufacturing organisation (CMO) companies in China have experience in recruiting patients and they have a close relationship with the Chinese FDA. Therefore, we decided to collaborate in various ways.

Is a joint venture the most suitable way to ensure intellectual property (IP) protection of these technologies in a country like China?

We are establishing a joint venture because we have connections with companies in China and some of those companies have a good understanding of the business in China. Although we always must be careful with IP protection, IP protection in China is much more secure than even five or ten years ago.

Autologous and allogeneic transplants are set to reshape the entire industry. Can you tell us more about your allogeneic programs since you are also experimenting with allogeneic manufacturing? What has been your experience so far?

Allogeneic technology has been in development for a long time. There are many good ways to edit genes and limit rejection through gene editing. Currently, our differentiation scheme is T-cell-derived induced pluripotent stem (IPS). This is the differentiation process where some of the gene editing process is completed. Eutilex uses a different approach to replace certain T-cell antigen receptors that we target. Currently, we are progressing in natural allogeneic T-cells, but are also developing allogeneic CAR T-cell therapies.

What does Eutilex aim to achieve in the years ahead?

We are currently focused on clinical trials: ongoing T-cell therapy and antibody therapy trials. At the beginning of next year, we are launching our new CAR-T clinical trial, EU307, and we hope that it will go smoothly. We always expect to face some issues but hopefully no major problems. Our goal is to cure cancer without toxicity. This is what inspires our research team to move forward in this direction.

Will your strategy for curing cancer without toxicity be Eutilexâ??s commercialised therapy, or will you look for a big pharma partner to bring this to the market?

We will do as much as we can on our own, but we may also look for big pharma companies, or collaborators for commercialisation.

We have had some preliminary discussions with pharma companies, but also with research collaborators. For example, we have alliances with large hospitals in Europe and in the US, since

they also build their own GMP facilities for CAR-T or T-cell set up. Thus, we hope our collaborators will help promote our product in the commercial market, not only through financial means but through their logistics or networks.

To conclude, what would be your message to those who are unaware of the scientific developments taking place in Korea?

Much of my career was spent in the USA. When I came back to Korea, I told the Korean FDA personnel that we all have the same goals, which is to provide new drugs to patients. The lives of our patients are our top priority. Developing new drugs has nothing to do with money; saving human lives is all that truly matters. Patients require the help of a regulatory agency, and I am not the only one that has pushed the Korean FDA for reforms. Thus, the conservative regulatory environment in Korea has been changing to match the countryâ??s high level of innovation. There are many companies like Eutilex that are pushing drug development in Korea in a way that other countries may be unaware of. I hope multinational companies will pay attention because they can help small companies in Korea by providing these novel drugs to the patients as quickly as possible.

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