Stephen Yoo â?? CEO & CSO, STCube Pharmaceuticals

Immuno-oncology has revolutionized cancer therapy, but despite the huge success there has been in the area, there are still many unmet patient needs

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Stephen Yoo highlights the pioneering work that STCube Pharmaceuticals â?? a US subsidiary of Korean firm STCube â?? is undertaking in the immuno-oncology field, its three technology platforms, partnership approach, and his outlook for the companyâ??s future.

Can you introduce yourself and what brought you to STCube?

STCube is a public company in Korea, and STCube Pharmaceuticals is a subsidiary of STCube based in the US. I Although STCube is a Korean company, a lot of our R&D and clinical trials are based in the US, where I have spent a large part of my career.

I got my PhD in biochemistry and biophysics at Texas A&M University, and after several academic appointments, I worked at the National Cancer Institute (NCI). To summarize my career before I joined STCube, I was trained as a pure basic biochemist in the field of transcriptional regulation and protein biochemistry. I then encountered the field of DNA repair and recognized that the DNA repair pathway was key in repairing double strand breaks during radiation or chemotherapy. I was exposed to how we can target the DNA repair pathway biochemically to benefit cancer patients as part of radiation or chemotherapy.

While I was at the NCI, I had the opportunity to learn about the field of immuno-oncology. I saw how the immune system works with radiation, and that combining radiation with immunotherapy would be a good combination, especially ionizing radiation with immune checkpoint blockade. That was when my colleague Dr Jung, the president of STCube in Korea, and I decided to work together. Our goal from the beginning was to identify a novel immune checkpoint that can be induced **to enhance** the effects of chemotherapy and radiation. That is where our journey started.

There has been a lot of success in the field of immuno-oncology but there are still many unmet needs. How is STCube looking to address these?

Yes, immuno-oncology has revolutionized cancer therapy, but despite the huge success there has been in the area, there are still many unmet patient needs. We have a strong rationale, and we are aiming to achieve the goal that everyone is striving forâ?? to increase the response rate in patients who are refractory to PD-1/PD-L1 antibody therapy. We also aim to target tumours that are unresponsive to PD-1/PD-L1 antibody therapy, such as colon and pancreatic tumours. In summary, with our antibody we will be able to treat tumours where the PD-1 antibody has been ineffective or increase the response rate within the tumour where the response rate was limited.

STCube has three platforms. Can you describe these platforms and explain the rationale that led you to develop them?

STCube Pharmaceuticals was founded in 2013. At that time, we initially hypothesized that there might be more resistant tumours even with immune PD-1 or PDL-1 antibodies. During the past few years, we initially worked in collaboration with two prominent laboratories at MD Anderson Cancer Center where we developed the first platform, an RNAi based immune checkpoint discovery platform in vivo. As part of this effort, we used a potent stressor such as ionizing radiation to identify a novel immune checkpoint.

Our second platform has also been developed through collaboration with MD Anderson. We discovered that most of the immune checkpoints are glycosylated, which is essential for their function. Thus, our platform allowed us to develop glyco-specific antibodies that can exert maximal efficacy with minimal toxicity in the tumour microenvironment.

Our third platform is a functional assay platform that has been developed to characterize our glyco-specific antibodies in vitro and in vivo. Together, these platforms enabled us to dive into deeper mechanisms of action. Using these platforms, we first developed a best in class against PDL-1 and PD-1 antibodies, the results of which we published in Cancer Cell and Cancer Research. We hope to prove that our antibodies are better than some FDA-approved drugs.

Your antibody program STT-003 is in phase one clinical trials. Where are the trials taking place and how are they advancing?

The antibody program we call the STT-003 is currently in Phase one clinical trials in the US at MD Anderson, Mount Sinai and Yale Cancer Center, and in Korea at the Yonsei University Severance Hospital and the Korean University Anam Hospital.

We anticipate seeing some efficacy results during our Phase 1 clinical trials and we have been approved to recruit more patients. Currently the PD-1 antibody is the most successful immune checkpoint blockade, but a lot of patients who are treated with the PD-1 antibody are still refractory. When we recruit the patient as part of our Phase 1 clinical trials, we do not select them as such, but we anticipate most of our patients to be refractory to the PD-1/PD-L1 antibody therapy.

We are also recruiting patients with tumours that are unresponsive to the PD-1 antibody, such as colon and pancreatic tumours, but have undergone chemotherapy as part of their treatment. These two patient populations allow us to test our hypothesis without being selective during the recruitment process.

STCube Pharmaceuticals was selected as one of the 2021 Global Top 10 Immunotherapy Solution Companies by Pharma Tech Outlook. Can you tell us more about the award?

Our research is based on a strong foundation of knowledge, and we have put out publications in collaboration with MD Anderson. Also, we are very strong in our research and development areas using the platforms that were described earlier.

STCube Pharmaceuticalsâ?? novel immune checkpoint protein, BTN1A1, was presented at the AACR poster session. Can you outline your journey to identifying BTN1A1?

We screened and identified BTN1A1 as a stress-inducible immune checkpoint. We initially envisioned that when a tumour is in a high stress environment, it will elicit a very potent immune response. One of the mechanisms of a tumour to survive is to express the immune checkpoint to suppress the immune responses of the tumour microenvironment. As part of our screening platform, we used ionizing radiation to provide the most potent stressor to the tumour microenvironment, in the hopes that the tumour will express all the immune checkpoints they have. During screening, we used several of the known immune checkpoints, but also discovered a novel immune checkpoint which was stress induced.

In 2020, STCube Pharmaceuticals and Samsung Biologics announced a strategic agreement. What does the partnership consist of?

Samsung Biologics produces the cell line development for us, but the antibody development is all in-house and proprietary to STCube. That is the strength of the company; having a strong research base and the innovative development of our novel immune checkpoint.

Have you begun considering partnerships with big biopharma companies or will you do this once you start phase two clinical trials?

There are a number of ongoing discussions with big pharma, and we attended BIO22 where we met with several companies. Nothing is decided yet, but we want to partner so that we can move as quickly as possible to benefit the patients who are desperate for a new treatment.

Are you thinking of commercialising your platforms for external programs as a future source of revenue?

Our goal is to develop a drug, not to provide a platform. We are not talking about a small market or a niche area; the field of cancer treatment is a major area, and the immune checkpoint blockade has a big potential.

Is STCube looking at any other disease areas?

We may have some very interesting opportunities in the field of autoimmune disease, but this is not our focus today.

A lot of STCubeâ??s research has come out of the US. Would you consider your research to be Korean innovation?

What is important to us is not where the innovation comes from, but that it is innovation in the cancer treatment field. Asia is becoming more important, but we are keen on developing and expanding these indications wherever we can benefit cancer patients.

Is there anything else you would like to share with PharmaBoardroomâ??s audience?

I would like to say that we have piggybacked on the efforts of the giants who pioneered and opened new possibilities and new treatment options for patients in the immuno-oncology field. There is still a strong need to improve the current success rate, especially with the PD-1 antibody, and that is what everybody has been working on. . We have identified the novel immune checkpoint that we hope to incorporate into the standard of care, and we have accumulated ample evidence to demonstrate this. Moving forward, we have the opportunity to move our assets forward in a way that we will be able to improve the response rate where the PD-1 antibody is already working, but more importantly, in tumours where the PD-1 antibody therapy is not working at all.

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