Hardy Chan – Chairman and President, Allianz Pharmascience, Taiwan

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Dr Hardy Chan shares the story of how he came out of retirement to lead Allianz Pharmascience; an up-and-coming biotech which aims to meet the unmet medical needs of rare disease patients, particularly in Asia. Dr Chan delves deep into the innovative

science behind the company's pipeline and shares the patient-first commitment of the venture.

Please begin by introducing yourself and how you came to lead Allianz Pharmascience.

As the co-founder of ScinoPharm, I was well connected with Uni-President Enterprises Corp. – the major shareholder of the company. The group had a biotech investment venture that seeded a number of companies, one of which was working on the degradation of androgen receptors. The company had been going on for quite a while. It came to a time to evaluate its long-term viability. At the time, I had just retired from ScinoPharm. After visiting the company, I was intrigued by what they had to offer, so in an agreement with Uni-President, I agreed to reorganize the company and transfer the key intellectual assets back to Taiwan.

What fascinated me the most about the company was a collaboration it had with a well-known international opinion leader at the National Institutes of Health in the field of neurodegenerative diseases. Their jointly published paper revealed the potential of Nrf2 activators in treating several neurodegenerative diseases, especially those linked to aberrant protein aggregation. ALS, SBMA

and SCAs, as well as Parkinson's, Huntington's, and even Alzheimer's disease, all to some degree share that commonality.

What were your initial priorities upon taking on the role of chairman and president of Allianz?

Once I was charged with running Allianz, the reorganized new company, I decided not to set up in-house laboratories as we recognized that we lacked the resources and more importantly, the technical expertise to cover all required scientific fields. However, thanks to my previous experience and networking within the local scientific community, I was able to gather the best researchers in the various areas to work with Allianz on a contract basis, essentially establishing a network of virtual laboratories. We have entered into 20 plus contracts with the most prestigious investigators in Taiwan.

Taiwanese researchers often have the right level of experience with sufficient resources but could use more relevant projects to work on. Coming together, witnessing the enthusiasm of professors in Taiwan joining force with Allianz in combating the most desperate medical needs of rare disease patients has just been a wonderful experience. All in all, I started Allianz as a personal dream to improve the lives of patients who would otherwise have virtually no hope. This has been the most wonderful chapter of my life.

How does your other company Helios Bioelectronics fit into the operations of Allianz?

Thus far in development, our compounds have been working marvellously in animal models – but of course, this is a different story from human use. Therefore, I had to consider the question of how our clinical trials should best be conducted and monitored. In short, is our drug working and providing clinical benefits? One of Helios Bioelectronics' projects, a company I started with two Taiwanese academicians, is to try to explore a so-called microRNA expression profiling concept (3-D landscapes) to measure both drug- and symptom relief-related miRNA changes. If the utility of such an approach is proved useful in some of Allianz's upcoming clinical trials, the same approach could be applied to other clinical trials as well. Personally, I am most intrigued by the psychiatric space.

Helios' approach took advantage of the combined strengths of Taiwan semiconductor industry as well as the basic biological research prowess of the island.

Your three pipeline compounds ALZ001, ALZ002, and ALZ003 are all in different stages of their development. Can you walk us through Allianz's pipeline?

All three of our pipeline candidates use the same mechanism of action. ALZ compounds are modulators of redox homeostasis to treat diseases across the areas of neurodegenerative diseases, inflammatory disorders, and cancers. ALZ001 has indications for chronic inflammation in skin disorders such as acne vulgaris, psoriasis, and keloid – one of which passed and the rest to be in phase II trials. ALZ002 is our compound with indications in neurodegenerative diseases – Huntington's disease, spinal and bulbar muscular atrophy (SBMA), and spinocerebellar ataxia (SCA) type two and three – all of which are rare diseases and the first two indications having orphan drug designation by the FDA, with SBMA set to enter phase I this summer. Finally, ALZ003 has an indication for treating glioblastoma multiforme, the most aggressive malignant brain tumour arising from glial cells.

Reactive oxygen species (ROS) levels are very high in cancer cells. Different levels of increased ROS can result in either cell repair or cell death. This maintenance is called redox homeostasis. Using our drug to induce high levels of ROS production in cancer cells, ALZ003 causes damage within cancer cells by altering ubiquitin-proteasome systems and mitochondrial functions. Looking at the function of mitochondria in neurodegenerative diseases, we see that the function of operation has been slowed down compared to cancer cells. Recently, experimental evidence indicates that pharmacological Nrf2 activation is beneficial in counteracting many of the pathological processes in neurodegenerative diseases through the increase of antioxidant capacity, mitochondrial biogenesis, and possibly, the clearance of misfolded proteins by proteasomal degradation. Through collaboration, we have been able to see that our drugs are able to improve the function of mitochondria in genetic defective cells and activate the heat shock protein response to facilitate correct folding of polyQ-expanded proteins. Our preliminary results show that ALZ002 significantly improves the behaviour in mouse models with Huntington's disease and type 2 spinocerebellar ataxia (SCA).

What is your strategy to continue the development of Allianz's pipeline?

In the treatment of orphan diseases in Taiwan, they are often waiting for the US to develop drugs and complete trials before bringing new products to the market. Our strategy in Allianz is to submit our compounds to the FDA for approval then bring part of the trial to Taiwan. As I mentioned

earlier, we have already obtained orphan drug designations for SBMA and Huntington's disease.

After conducting phase I trials we are aiming to partner with special interest groups to help organize and participate in global clinical trials. At the end of the day, big pharma is needed for this level of development, but I am not driven by the goal of reaching later stage trials and licensing out the compounds – I want to be able to retain marketing rights in Allianz so as to best serve the Asian population.

What is the level of medical need for rare disease in the region?

Asia, particularly Japan, has a large population of SBMA patients while Huntington's disease is primarily a Western disease. In these diseases, the occurrence is increasing while the age of diagnosis is getting younger, therefore, if Allianz's drugs can even slow down the progression of the diseases this would be a very significant advance in treating these rare diseases. This is why Allianz is not just a business, but a passion.

What is the role of biotechs like Allianz in the pan-Asian ambition to treat patients within the region?

We must recognize that in Asia orphan diseases are being neglected because of social stigmas. It is very challenging to openly get people excited about the development of these drugs. Asia in many ways is advancing – many stakeholders are working on PD-1 and immunotherapies, so they do not need any more scientists in the area. In the US, orphan drug prices are in the range of six figures, so in Allianz, we are trying to explore if we can offer something more reasonable to these patients. Someone needs to take care of this population and as we are not under severe pressure, Allianz can be the one to deliver this hope to rare disease patients. With the use of ICT and biomedicine, we are merging all these capabilities which in the past were never brought together for the sake of developing an impactful solution. Even if we can help just a few patients, in the end, it will all be worthwhile.

Looking forward, what are your current priorities for developing Allianz's pipeline?

Our first priority in Allianz is for neurodegenerative disorders. As a small company, we must focus our efforts, therefore in cancer, we would like to have an early-stage industry partner. In skin

disease, we have already passed phase II trials for acne vulgaris, so we invite collaborators to explore working with us in this area.

As a seasoned expert, what advice can you offer on arranging a successful marriage between the business and science sides of biotechnology?

During my time in the US, I often wore two hats, directing both R&D and business development. I was fortunate enough to have this unique experience early on in my career that many people often do not have the chance to get. Subsequently, when I cofounded ScinoPharm it was not an easy venture and we had to go out and work very hard to raise money. Nevertheless, this taught me how to manage people, capital resources, and customers. Being faced with the responsibility of failure, I had to develop a blind optimism that requires the ability to negotiate win-win situations.

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