Gideon Ho â?? Co-Founder & CEO, HistoIndex

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Dr Gideon Ho, co-founder and CEO of HistoIndex, shares the story of the companyâ??s establishment in 2010, their proprietary technology to provide the worldâ??s first stain-free AI-driven biopsy and tissue analysis focused on the diagnosis of fibrosis and cancer, and his thoughts on the Singaporean healthcare start-up ecosystem.

Gideon, could you please briefly introduce yourself and the motivation for establishing HistoIndex in 2010?

I have been involved in biophotonics since my undergraduate days. Biophotonics is the study of optical processes in biological systems â?? or, as I like to put it, the use of light in biology! I have a masterâ??s degree in Engineering and a PhD in Bioengineering. Upon my return to Singapore from the UK after my PhD, I started at the Institute of Biotechnology and Nanotechnology (IBN), working in research, before moving to the commercial arm of A*STAR, which essentially functions much like a technology transfer office. In this way, I moved from academia to research to commercialization, which subsequently led to the establishment of HistoIndex in 2010.

The idea of HistoIndex came from our work in IBN on the use of stain-free imaging and analysis in pathology. For the past approximately 150 years, biopsies have been taken and analyzed the same way: under the microscope by pathologists, who leverage several decades of experience and expertise in order to diagnose disease. However, this is intrinsically a very subjective approach to

diagnosis, which we realized represented an opportunity for Artificial Intelligence (AI).

We started work on this fifteen years ago, before AI became the buzzword it is today. We started by tackling what we saw as the underlying issue that needed to be resolved before AI technology could even be brought it. Let me explain. A standard lab workflow will first comprise of biopsies going through a staining process in order to be viewed under the microscope. But the results from staining could differ due to variation in reagent batch, staining protocol and the binding affinity of different stains, which brings along inconsistencies and variabilities â?? not ideal for AI or machine learning. Whenever we work with data, AI and machine learning, we use the saying â??rubbish in, rubbish outâ??. The consistency of the inputs to the AI platform is absolutely critical to obtaining a reliable and accurate data output. Therefore, we developed a stain-free technology based on the use of photonics. Biopsies and tissues are scanned â?? without staining â?? and all the information including the targeted endogenous biomarkers within the tissues were captured. This is the information that will be fed to the AI program and then the program produces data readouts that aid researchers, clinicians and physicians with diagnoses.

When we started the company in 2010, we focused more on equipment sales but about four years ago, we pivoted away from that into a fee-for-service business model, with drug development companies, research institutes, universities and hospitals as our clients.

To what extent does this technology represent a game-changer within the pharma or healthcare sectors?

We have standardized the biopsy and tissue analysis process, using AI to generate very consistent, objective and measurable data that is free from human subjectivity. Based on this, we are able to use this technology to help companies to augment their drug development processes starting from their in vitro and preclinical animal studies to clinical trials. Being able to fully quantify and analyze the results of a drug candidate on patient samples during clinical trials are essential for drug development. This would ultimately aid in the development and commercialization of novel therapies, delivering benefits to patients.

For this reason, we have established many partnerships with leading drug development companies. We are currently working with them on preclinical studies and also to enhance the endpoint readouts from their Phase 2 and 3 clinical trials for new drug candidates, specifically within the area of non-alcoholic steatohepatitis (NASH). We have published and presented over a hundred papers in liver diseases in the past decade. This is an area of significant unmet medical needs â?? even today, not a single NASH drug has been approved by the US FDA. Since we have been working in this space for the past decade and we have a novel technology platform, we are well-positioned to set the standard here in terms of the use of AI digital pathology for diagnosis. As we have started working in this space when drugs are still in the clinical stage, once drugs are approved and enter the market, we expect that our technology will continue to serve the clinical diagnosis needs of the NASH patients. From my perspective, I expect the first NASH drug approval to come â?? fingers crossed â?? sometime in 2023.

In ten years, you have built a global network of clients and collaborators. Could you highlight your current international presence?

Working in drug development, it is very natural for us to look at the US and Europe markets, since most of the drug developers are based there. Within Asia, in recent years, China has become a

significant player but the drug development sector there is still in its infancy.

In that sense, in the US and Europe, we tend to work more with the leading drug development companies on their drug R&D programs, while in Asia, we tend to work more with hospitals, universities and research institutes on clinical and translational research. Currently, more than 150 hospitals, universities, research institutes, CROs and drug development companies all over the world have benefited from our technology platform.

As you mentioned, AI has become somewhat of a buzzword, as has diagnostics, especially as a result of the COVID-19 pandemic. How do you assess the competitive landscape and HistoIndexâ??s position in it?

Certainly, many companies have ventured into AI, and there are start-ups using AI to advance drug development, including NASH. However, when it comes to biopsy analysis, as far as I know, all the companies built their AI model around stained tissues and use these algorithms to analyze the stained images. We are the only company that digitizes stain-free biopsies, using our proprietary biophotonics technology and platform for stain-free AI-based digital pathology. This is a huge differentiator.

COVID-19 has definitely increased the public awareness of the healthcare industry overall. A year ago, the general public would have never heard of PCR and serology tests but now they are discussing antibody versus antigen testing and so on.

COVID-19 has also thrown out some prevalent industry assumptions or conceptions. We can see that COVID-19 vaccine and drug development timelines were dramatically shortened. What used to take years to do could be done in basically less than a year. This goes to show that if there is a problem urgent enough and people are willing to invest the resources, time and effort, we can find solutions very quickly. As the saying goes, a rising tide raises all ships. We have benefited from this increased awareness even though we do not work in the COVID-19 space.

How has the company been funded over the past decade?

We were spun out of A*STAR, so in the early stages we had some grant support from A*STAR and SPRING Singapore (now known as Enterprise Singapore) to kickstart the testing and validation of the platform technology. Just like any start-up, we subsequently received angel funding, corporate, institutional funding and so on.

As a truly homegrown start-up, how do you assess the environment in Singapore more broadly when it comes to innovative healthcare start-ups?

I think we have to acknowledge that Singapore is not like the US when it comes healthcare innovation. We are still young. I actually see HistoIndex as having grown up with the Singaporean healthcare innovation ecosystem. When we started ten years ago, Singapore was also just beginning to invest in its biotech and medtech ecosystem. The only funding available then was early-stage funding. Then as the ecosystem grew, public support evolved, the start-ups â?? like HistoIndex â?? also grew. Today, there are many growth-stage medtech companies in Singapore, and the government is also more aware of how to support them, how to build new start-ups, how to

bring in mentors and angel investors, and so on. Everything is coming together, and I am sure the ecosystem will continue to evolve along with the companies within the ecosystem, so I am very positive about the outlook of Singaporean healthcare innovation.

Even though other cities in the region have also started investing in healthcare, biotech, medtech and so on, I still think Singapore is the best place for a start-up like us. In Singapore, you can do business with the US and Europe, as well as China and Asia more broadly, without having to deal with geopolitical considerations. Singapore also tops globally when it comes to competitive economy, education, IP protection, smart cities, governance and quality of living. There are many advantages to building a start-up here.

That being said, one of the challenges is that Singapore is a small country, with a small talent pool. How has HistoIndex dealt with this?

That is true. The expertise here in biomedical sciences on the commercial side is still not very developed, so we do have to source globally. HistoIndex works with a very global team and before COVID-19, it was actually challenging to bring the necessary talent we needed into Singapore because of work passes and visas restrictions. However, since COVID-19, this challenge has been mitigated somewhat since remote working has become the norm. Telecommuting is the default for us right now, with the only caveat being my staff needing to take a lot more night calls. I myself spend most of my time in the US or Europe, so I actually have not seen my staff from other departments face-to-face for over a year now.

Looking forward, what do you hope to achieve for HistoIndex in the medium term?

I mentioned that I expect â?? hope â?? there will be a NASH drug approved in 2023. In line with that, we are working towards having our NASH clinical diagnostic platform approved by the FDA around that time too, so that it might become a new industry standard for NASH tissue diagnostics. In addition, we also want to branch from liver diseases into oncology, particularly breast cancer, which has recently overtaken lung cancer as the top cancer diagnosis in the world. We have been presenting and publishing many papers in cancer, so that is our mid-term plan as well. We want to help cancer patients access the right drugs for their specific types of cancer.

Finally, coming from the research and academic side of the industry, how do you balance between your CEO duties now and your research focus?

Everything in the healthcare sector strives on evidence-based medicine, including our business where ultimately you will need to be able to explain the science behind the technology, including the AI. My priority is to drive the emphasis on the science while working with my business development team to advance the commercialization of it. My personal view is that first and foremost, the technology must be tested and validated repeatedly with reproducible results over multiple studies before building a business around it. In spite of me saying that, I believe the entire process could be expedited as seen recently with the vaccine development for COVID-19. Fundamentally, your science has to work first before you can start to sell it.

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