Henry Yau – Managing Director and Honorary Assistant Professor, The University of Hong Kong Clinical Trials Centre (HKU-CTC)

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Henry Yau, MD and Honorary Assistant Professor at the University of Hong Kong Clinical Trials Centre (HKU-CTC) discusses the center's development, the diverse range of services it offers, and the clinical trials environment in Hong Kong.

Having been with the organization since nearly the beginning from 2000, how have you seen the Center develop in the past two decades?

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Having been established in 1998, we will celebrate our 20th anniversary next year. While it has been a very journey for HKU-CTC, progress has been encouraging and I am very pleased with where the Center is today.

From a tiny team of only three to four people in 1998 offering mainly administration support services, we have since grown to a fully-fledged organization with over 50 full-time employees acting as a one-stop center for facilitating all kinds of clinical trials. Over the past 19 years, we have facilitated more than 1,200 clinical trials. Currently, we are coordinating around 430 ongoing studies, of which around 280 are industry-sponsored and the other 150-odd are investigator-initiated. We are certainly the largest clinical trials center in Hong Kong.

We conduct all sorts of clinical studies in terms of clinical trial phases and disease areas but in line with international trends, we have seen a surge in the number of oncology, cardiology and hepatology clinical trials. Since the setting up of our Phase 1 Center in 2014, we are now starting to conduct more and more phase 1 and clinical pharmacology trials, especially in the most popular areas like cancers, hepatitis, cardiovascular and immunological diseases. We expect this trend to continue. Many of such studies finally led to high-impact publications in international scientific journals and even contributed to the launch of new treatments and new healthcare strategies.

Our success is even more laudable when one considers our unique financial model: we are in essence self-financed despite falling under The University of Hong Kong (HKU). When our Center was set up, we received seed funding from HKU's Medical Faculty with a time frame of three years to test our performance and financial model. After three years, if we were able to perform and to survive on our own, we would be allowed to run as a self-sustaining unit that can invest our income into our own operation and development. We are therefore the only self-financed clinical trials center of such a scale in the region. Now only three of our employees are financed by the university; everyone else is employed using other financial resources solicited by CTC. This meant that we have had to grow our center on a very financially sustainable basis. If we had been reliant on university funding, we would not have been able to reach our current size owing to the university's limited resources.

You have undertaken the role of Managing Director for five years from 2012. What are some of your Center's main achievements during that time?

Thanks to the direction and support of the HKU Medical Faculty, Queen Mary Hospital (QMH) and CTC's Committee of Management (COM), in particular the former Faculty Dean, Professor Lee Sum-ping; the current

Faculty Dean, Professor Gabriel Leung; QMH's Hospital Chief Executive, Dr. Luk Che-chung; the COM Chairman, Professor Karen Lam; and CTC's Chief Director, Professor Lau Yu-lung, and with the joint effort of the entire HKU-CTC team, we have implemented a strategic plan aimed at promoting the successful and sustainable development of the Center. A main focus has been to expand the scope of our services through growing our team. Since 2012, the headcount has increased by about 100 percent in line with the expansion of our activities.

Our Site Management Organization (SMO) team was reengineered to provide more comprehensive and professional site management services, for clinical studies conducted at QMH and other hospitals. Our Contract Research Organization (CRO) arm also expanded substantially. In particular, it launched its electronic data capture service, which allows the extension of data management services to cover clinical studies conducted outside Hong Kong. I will elaborate more on these developments later on.

With the strong support of the Food and Health Bureau (FHB) of the Hong Kong SAR government and QMH, we built a Phase 1 Centre and a Pharmacokinetics Laboratory. They are dedicated, state-of-the-art clinical research facilities specifically designed for conducting phase 1 and clinical pharmacology trials. I am glad that the Phase 1 Centre has quickly obtained wide recognition by the industry and has also been accredited by the China Food and Drug Administration (CFDA) since July 2016, in addition to the other 13 accredited clinical specialties in QMH.

Very significantly, the expansion of our service offerings also meant that we were able to support more investigator-initiated studies. In the early days, we focused mainly on industry-sponsored studies. In the last five years, we specifically expanded our services to support investigator-initiated studies, which has enabled some of our investigators to conceive larger, multinational, multi-center studies where previously they might have only considered conducting small-scale studies. For instance, we are now helping one professor to run an investigator-initiated nephrology drug trial involving over 10 centers across seven countries in Asia in addition to Hong Kong. This sort of complex projects used to be very challenging because investigators may not have the full management expertise or enough capacity to implement all required tasks such as contractual negotiations, quality management, setting up of electronic data systems and data management, as well as statistical analysis and reporting.

On a broader scope, we spent a significant amount of effort in improving the clinical research environment of Hong Kong. In order to help harmonize the standards for clinical research ethics review and oversight, during 2013-14, we led the development of a new standard operating procedure template for research ethics committees and successfully received acceptance by all six research ethics committees under the public healthcare system in Hong Kong, including not only HKU but also the Hospital Authority (HA) and another medical school. We also authored a book called "Clinical Research Management and Compliance at Study Sites" for the HA, and the "Guideline on Ethics Oversight and Scientific Evaluation of Phase 1 Clinical Trials" for Hong Kong.

Can you elaborate on the full scope of services that you offer now?

We position ourselves as a professional clinical research management organization helping our investigators to run their clinical trials, whether investigator-initiated or industry-sponsored. This means that we want to be a one-stop shop offering all the professional services across the entire clinical development pipeline. For example, if a pharma company has a new drug compound and want to conduct clinical trials in Hong Kong, even if they do not have any presence here, we are able to provide them all the necessary services. All they need to provide is the drug compound and the funding.

To do this, we structure our operational staff into two teams: the SMO team and the CRO team. The SMO is responsible for working with our investigators and we are rather unique in providing multidimensional and comprehensive support to them. For instance, we can help them compile ethics review applications, negotiate financial and legal details and even write up the necessary contracts. We have an electronic project budgeting and payment management platform that has been developed entirely in-house to go through a protocol, price

every single requirement and produce a budget tailored to the specific trial set-up. We also have our own contract template that we offer to sponsors. This template can then be customized and archived for that specific company, which eliminates the need to renegotiate new contracts for subsequent clinical trials run by the same company. Having worked with over 200 sponsors in the industry, including the top global pharma and medical device companies, we have an extensive library of contracts that we can draw upon. This means that unless there are significant regulatory changes, it only takes less than an hour to prepare a contract for a new clinical trial with a company we have worked with before, versus the weeks or months it can sometimes take. During the entire period of a study, the SMO team works continuously and closely with our investigators to provide the required support like investigational drug management, biological specimen management, study document management, logistics coordination and safety reporting.

In terms of the CRO team, we are also unique in that despite being a university unit, we have managed to develop a CRO team that provides services on par with professional CROs, from protocol to regulatory affairs, project management to monitoring, and data management to statistical analysis, and so on. This team supports the sponsors and helps to manage their clinical trials. The SMO team and the CRO team therefore work together in parallel to ensure the smooth conduct of clinical trials.

Our Phase 1 Centre commenced full operation in 2014. With a professional team consisting of clinical, scientific and operational professionals working in collaboration with our strong SMO and CRO teams, HKU-CTC is fully capable of undertaking various types of phase 1 and clinical pharmacology trials – whether in patients or healthy volunteers. To facilitate communication with our volunteers, we have also established a Volunteer Resource Centre (VRC).

Since 2012, we have also developed a training program focusing on Good Clinical Practice (GCP) and clinical study operation – called PRACTISE® – because we realized that a lot of the existing clinical trials training programs did not bring satisfactory learning outcomes to the participants as those programs usually only regurgitated the regulatory provisions without much digestion of the information. What is special about our program is that in addition to the featured lectures, we also offer interactive sessions where participants break into groups to discuss real cases. This makes the course much more engaging and effective for participants. We offer this course in English, Mandarin and Cantonese and it has proven very popular not only in Hong Kong but internationally, from Asia to Middle East and North Africa, including places like the Chinese mainland, Taiwan, Vietnam, Egypt and the UAE. Another testament to its success is that we have even seen interest from large pharma companies, where typically, it is pharma companies that will train hospitals in the running of clinical trials! To encourage continuous learning by clinical research personnel, we also contributed to the development of TRREE (Training and Resources in Research Ethics Evaluation) – an international, non-profit e-learning platform initiated from Switzerland for training and learning human research ethics and GCP.

What are some flagship projects HKU-CTC have supported?

We now run both industry-sponsored and investigator-initiated trials on various therapeutic areas. There are too many notable projects for me to enumerate but in terms of scale, the largest project we have run was a pediatric vaccine trial run by the now-Chief Director of the Center, Professor Lau Yu-lung. It saw some 1,200 participants across Hong Kong, which is the largest ever for an industry-sponsored vaccine trial in Hong Kong. As the principal investigator, Professor Lau successfully networked with a number of hospitals in order to establish a large catchment area for the study.

We have also run clinical trials for proprietary Chinese medicine, with a notable one being a large study on Parkinson's disease, involving 160 patients across six hospitals. Our Center provided the full spectrum of services for the trial. We have also managed medical device trials, with an exciting one being a trial for an innovative implantable device as an adjunct care for stroke patients, coming from an Israeli company. We were responsible for project management and monitoring of the trial for centers in Hong Kong. For the moment, we are collaborating with a Hong Kong pharma company in planning for a phase 1 trial on a novel biological drug targeting cancer treatment, and also a local medical device company in designing a first-in-human trial for its innovative device for diagnosis of gastrointestinal diseases.

Having been well-established for nearly two decades now, we have also built an international reputation. For instance, we are in the process of providing data management services to a research team in Denmark and they are so satisfied with our services that they are proposing that we assist them in the conduct of a multinational, multi-center study in Nordic countries because we are deemed the best non-profit organization that managed to provide the high standard and cost-effective solutions they required.

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In the region, we have also proactively sought collaboration in mainland China. Around two years ago, there was a period of turmoil in the Chinese clinical trials landscape because the CFDA issued a notice in July 2015 requiring all companies that had submitted drug marketing approval applications to self-inspect and re-examine their clinical trials data. If they were not confident that the data met CFDA requirements, they were given a short grace period to withdraw their applications. Otherwise, if the CFDA found any issues in their applications, severe penalties could be imposed. This naturally caused a huge storm in China and 86 percent of submitted applications were withdrawn. Chinese hospitals and centers then began to look for good management models to help with maintaining the quality of their clinical research in a cost-effective manner. This is when we entered into our first official collaboration on clinical trial organization management with a leading hospital in the Guizhou province.

With such breadth in services and scope, how do you ensure that your employees are trained to the highest standards?

People is a priority for us. As a self-financed entity under a non-profit academic organization, we are unable to compete with industry or even the public sector when it comes to financial remuneration. This means that our employment model needs to rely on non-financial incentives. We seek to attract people with a strong passion to do something unique and of value to society. While this value may be rather intangible, it is something that is clearly differentiable from the commercial setting. For instance, we provide our staff with opportunities to participate in key decision-making processes, to understand the implications and value of their work, and to influence the development of the larger organization. This contrasts sharply with the work in a commercial CRO, where they may be relegated only to routine and tedious monitoring work.

Having evolved into a mid-sized organization, we are going to place more emphasis on our middle and senior management training and succession. In September this year, we will launch our first Leadership Development Program to proactively grow our next generation of leaders. While our key management personnel are still in their golden age, leadership development is a decades-long process so it is important to start building that pipeline early. This program will include many opportunities for participants to expose themselves to new experiences through job rotation programs and external placement schemes. As a founding member of the International Clinical Trial Center Network (ICN), we have access to other top-tier clinical trials centers globally such as those under Harvard University, University of Cambridge, University of Zurich and Kyoto University.

On a daily basis as well, the senior management spends a significant amount of time interacting with our employees through group and one-to-one meetings in order to understand their career development, expectations and concerns. This is rather resource-intensive but we believe it brings a lot of value to our organization. We are already considering the third generation of leaders, because you cannot have the second generation without the third generation supporting them from below!

More broadly speaking, how attractive is the clinical trials environment in Hong Kong?

Hong Kong is actually a heaven for the conduct of clinical trials because we have world-renowned medical schools and investigators, a good public healthcare system, and highly educated patients, as well as our leading HKU-CTC! This is a small city with an extremely high population density, where people have access to high quality public healthcare services supported by one centralized electronic clinical management system. This means that our investigators can also have the possibility of getting access to over seven million people and their

medical data and records for research purpose.

Unfortunately, there are also challenges preventing Hong Kong from realizing her full potential in this area. The HA was established as a healthcare organization primarily to provide healthcare services to the Hong Kong society. While it professes to be built on the three pillars of service, education and research, in reality, the priority on research is not the highest; conventional wisdom has been that it is really up to the two medical schools to focus on education and research.

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As academic institutions, both universities are naturally focused on the provision of medical education and professional training, and professors do run their own research. But to fully unleash the potential value of clinical research in Hong Kong, I believe the HA and the Hong Kong SAR government can be more proactive in creating a more research-friendly environment. For example, the HA does not currently have a dedicated unit focused on facilitating the entire clinical research process across the 42 public hospitals/institutions and over 100 out-patient clinics that it manages, keeping updated on local and international norms and trends, and synchronizing all the relevant processes. Doctors and other medical professionals, particularly those outside the two designated teaching hospitals, are not incentivized to conduct clinical trials. As HA employees, all they have to do is serve patients. Admirably, many doctors do have the passion and drive to conduct clinical trials in order to advance medical research but this is something they have to fit into their already hectic schedules. Furthermore, the highly valuable medical data collected into the HA's clinical management system has been under-utilized in research because the system was not designed with an aim of facilitating research. If a unified platform can be established to integrate Hong Kong's clinical research capabilities and streamline the entire value chain for development of novel drugs, devices and other medicinal products and methods, I have no doubt that Hong Kong will become the best city for clinical development and even big data research in medicine in the region.

A final message for our international audience?

Clinical research is an essential step for translating laboratory research and discoveries into clinical use. The ultimate goal is to advance human healthcare – for the benefits of patients and every single one of us. HKU-CTC is a dynamic organization constituted of high caliber and energetic professionals passionate in contributing to this goal. While the Center has grown a lot in the past two decades, I still see us at the early stage of development because there is still so much to do.

Fortunately we are not alone. To move forward, we will leverage Hong Kong's advantages as the world city of Asia and tighten our collaboration with partners around the world, in particular in supporting more large-scale, multinational, multi-center studies, with a special focus on prevalent diseases in Asia. We are going to invest significant effort in fostering collaboration with mainland Chinese institutions as there is a huge potential there for new drug, device and healthcare development. In the next one to two years, we also plan to do a lot of internal reinforcement in order to strengthen the Center and pave the way for the next phase of rapid growth – in terms of scale, service scope, geographical coverage and global impact.

We welcome collaboration with academic institutions, research organizations and the industry. If you are looking for a highly capable, professional, reliable and ethical partner in clinical development in Asia, HKU-CTC is where you should not miss!