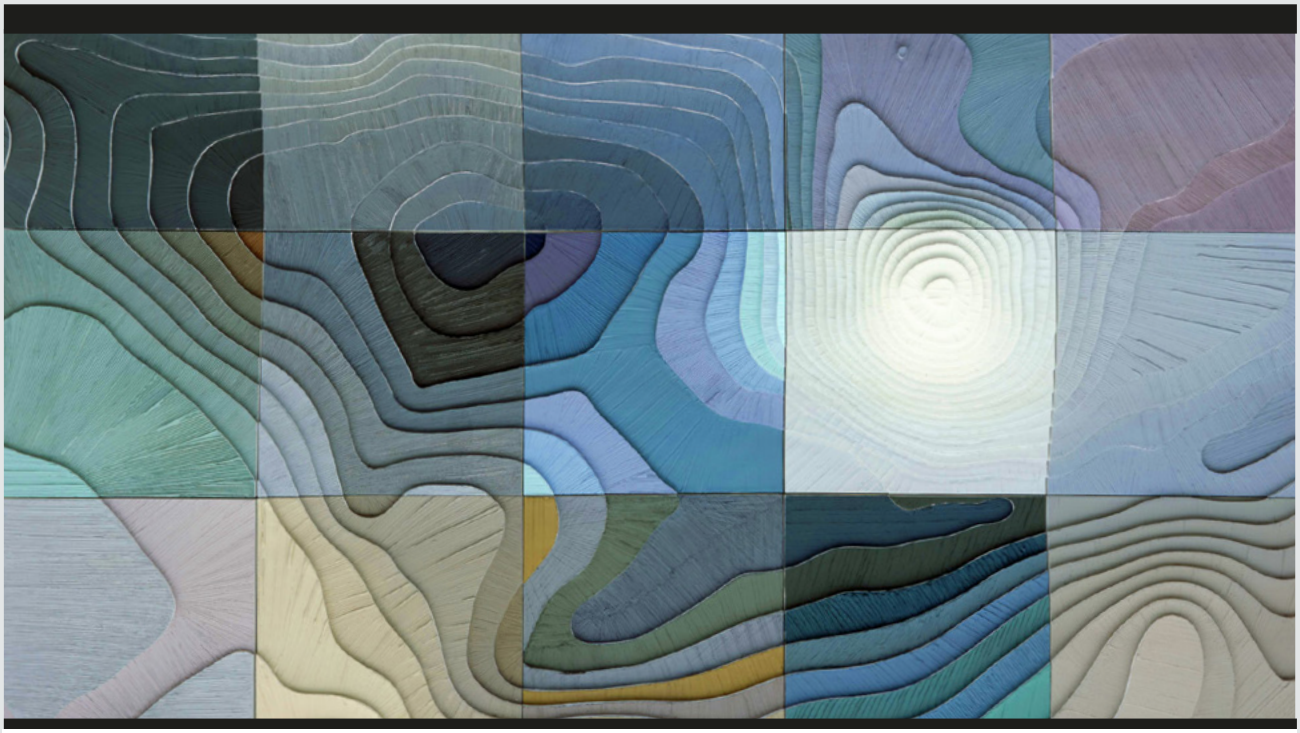
PHARMA BOARDROOM

InFocus Precision Medicine



ASIA

JULY 2020

Contents

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DISCOVERING PRECISION MEDICINE . . .

Precision medicine is very much in vogue today but it remains an extremely broad, even nebulous concept within the industry with as many definitions as there are practitioners. Nevertheless, at its core, all would agree that precision medicine is a rapidly evolving field characterized by the use of modern molecular diagnostic tools to 'personalize' the entire patient journey as much as possible, across preventative health, diagnosis, treatment and recovery, with the ultimate goal of maximizing therapeutic outcomes.

As our understanding of pathogenesis advances in tandem with biomedical technology, the stakeholder ecosystem implicated in the pursuit of precision medicine continues to grow. Genomic sequencing, biomarker identifications, Big Data analytics, AI and bioinformatics, companion diagnostics, electronic health records – it seems the goalposts for the 'achievement' of precision medicine keep moving the more we advance.

Countries across the world have invested colossal resources into this emerging field, most notably the US Precision Medicine Initiative (PMI) in 2015 and China's competing national precision medicine strategy, unrolled a year later in 2016. Today, it is estimated that around 40 countries have unveiled their own versions of a precision medicine initiative, motivated by a cascade of concerns including rapidly aging populations across many regions, increasingly unsustainable healthcare expenditures, and the rising prevalence of non-communicable disease. Astute industry observers have likened this global competition to the 21st century's space race.

Nevertheless, the most ardent advocate of precision medicine envisions a future where precision medicine is so integrated into healthcare systems that it is simply seen as the standard practice of medicine. It is patently obvious that precision medicine goes far beyond any single technology platform or therapeutic modality but rather entails paradigm shifts across the entire healthcare landscape. Such a transformative change is perhaps best viewed as an ultramarathon instead of a revolution.

...IN ASIA

With the contemporary inception of precision medicine often attributed to the initiation of the Human Genome Project in 1990, the US has been the birthplace of many of the fundamental technologies now used in the practice of precision medicine, most notably next-generation sequencing (NGS), as well as many of the leading therapeutics in this space. However, over the past couple of decades, waves of US-educated Asian researchers, scientists and academics have brought these novel processes and technologies home to Asia, and more recently, began to improve on them.

Asian and Western healthcare markets undoubtedly differ significantly across a number of characteristics, including genetic composition, disease prevalence and progression, healthcare infrastructures, socio-economic levels, and technological readiness, to name just a few. The Asian region also possesses a much higher heterogeneity. For all these myriad reasons, the precision medicine landscape in Asia is variegated.

Nevertheless, different Asian markets have seized various opportunities to leverage their specific strengths to accelerate certain aspects of development within precision medicine, with many governments seeing it – rightly – as the new frontier not only in healthcare development but also in socioeconomic development. As the adage goes, health is wealth.

While many hurdles still remain in terms of the advancement of precision medicine in Asia, particularly in terms of overall awareness, level of funding particularly in diagnostics, a persistent siloed approach, and an overcrowding of small companies scattered across the region, the dynamism in the region is undeniable. As a promising sign of the future, regional collaborations are also coalescing as Asian countries increasingly realize and seek to draw upon each other's complementary advantages.

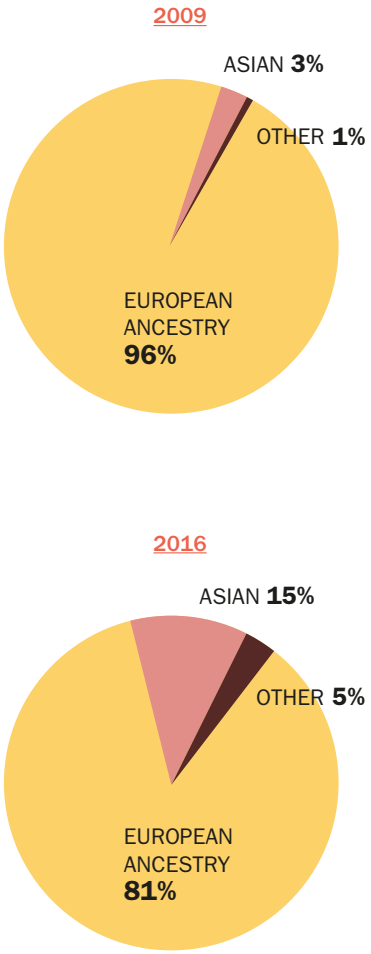
This report will take a first look at some technology frontrunners, specifically the industrialized economics of South Korea, Taiwan and Hong Kong, to highlight particular hotspots of innovations within the field of precision medicine, from molecular diagnostics; to cancer precision therapeutics; to cell and gene therapies; and to the next frontier of science, microbiome research, to showcase how companies in Asia are taking up the mantle of addressing the urgently unmet medical needs on their own turf.

RECLAIMING OUR GENETIC DESTINY

The completion of the Human Genome Project (HGP) in April 2003 with the publication of the first human genome sequence is probably one of the most significant landmarks in humanity's quest for knowledge, costing USD three billion across 13 years. But even after nearly two decades, we have barely scratched the surface of the genomic wealth contained within our DNA, but concerted efforts continue to collect, analyze and utilize genomic data.

However, one glaring weakness is this field today is the severe lack of diversity in the overall genomic data landscape. Through the HGP itself involved scientists from six countries including Japan and China, the five main sites that sequenced the majority of the human genome were based in the US and the UK. Despite efforts like the Human Genome Diversity Project and the 1000 Genomes Project, today, it is estimated that the vast majority of genomic data collected and deployed in studies globally come from people of European ancestry. Indeed, genomic data from Asian populations – which broadly represents two-thirds of the world population – only comprises 15 percent of all available genomic data globally. Admittedly, this has increased from a woeful three percent in 2009 but the gap remains huge.

PERSISTENT BIAS IN GENOME-WIDE ASSOCIATION STUDIES (GWAS)



Despite the increase in Asian representation, a large gap still remains in the availability of Asian genomic data.

Given the fundamental importance of genomic data to the advent of precision medicine, this weakness puts Asia on the back foot when it comes to developing and deploying personalized therapies for patients. The problem is even more urgent as a growing body of research has emerged demonstrating that disease prevalence, presentation and prognosis can be markedly different between Caucasian and Asian populations. There are observable and often significant differences in aspects like standard clinical practice, pharmacokinetics, as well as, crucially, the presence of specific disease biomarkers. For instance, researchers have found that across all drugs approved in Japan from 2001 to 2009, the doses approved for use in the West were higher in 32 percent of drugs across all therapeutic classes compared to the doses approved in Japan. This means that not only might precision therapeutics developed globally be less effective in Asian populations, they may also simply be less relevant by virtue of the fact that they do not necessarily address the most pressing healthcare concerns in the region. Even when they do, the need for bridging clinical trials to ensure compatibility and efficacy in Asian populations often lengthens the drug development and approval windows for global therapeutics.

Of course, the Asian region itself – comprising 48 countries, by the UN's count – is impressively heterogenous. In the past couple of years, many Asian governments, having recognized the transformative potential of precision medicine, have launched national and regional programs to remedy this oversight, as well as more generally advance their own capabilities in this groundbreaking field. China, of course, announced its own precision medicine initiative in 2015, a couple of months after the US Precision Medicine Initiative was announced by then-President Barack Obama, pledging a staggering USD 9 billion by 2030. Singapore launched a National Precision Medicine Programme in 2019. More regionally, the GenomeAsia100K initiative is a non-profit consortium launched in 2018, which seeks to sequence the DNA of 100,000 people across Asia. Reference genome datasets have been created by the Koreans, the Japanese and the Chinese, and large biobanks like the BioBank Japan and the China Kadoorie Biobank have also been established.

ONLY
15%
OF ALL AVAILABLE GENOMIC DATA GLOBALLY CORRESPONDS TO ASIAN POPULATIONS

Efforts are also being made to tackle the Asian characteristics of different diseases. For instance, Japan's National Cancer Center has cooperated with over 200 medical institutions and pharma companies on LC-SCRUM, a nationwide genetic screening project that has screened treatment target genes in over 7,000 lung cancer patients since 2013, contributing to the development of novel therapeutics in Japan. All these are crucial efforts if Asia hopes to reclaim its genetic destiny and truly advance the progress of precision medicine for patients in the region.

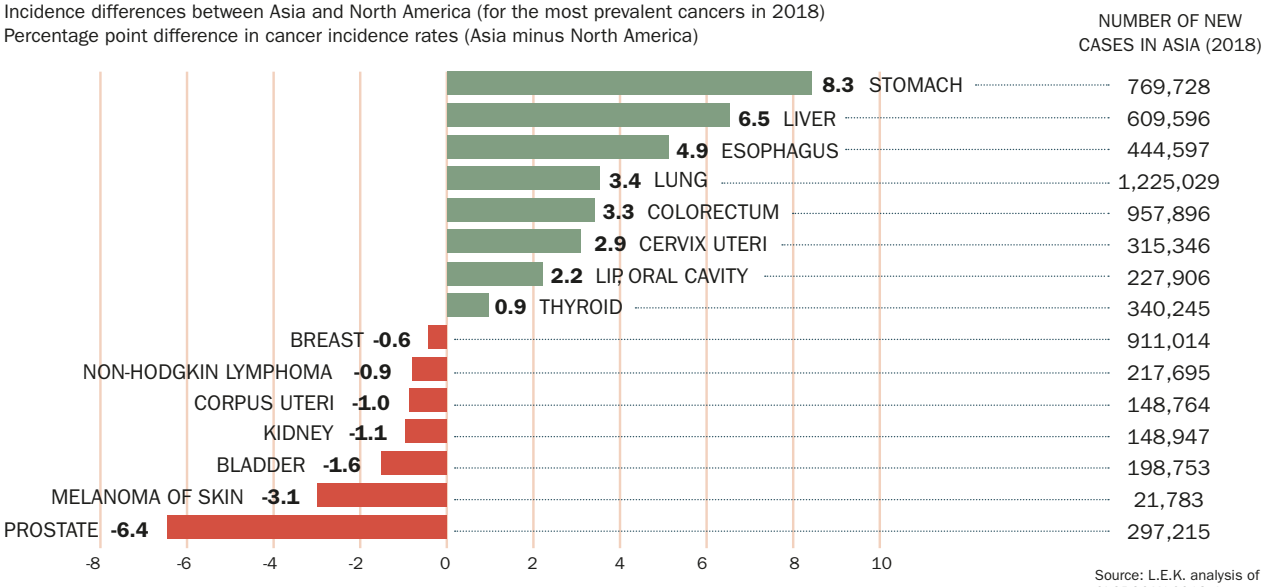
ETHNIC DIFFERENCES ACROSS DISEASE

CANCER

Cancer, with its strong genetic component, has understandably benefited most from precision medicine approaches, which makes it even more important for stakeholders to understand and appreciate the variation in cancer prevalence between Asian and Western populations. Notably, gastrointestinal cancers are far more common in Asian populations but very few resources have historically been dedicated to R&D in these areas. Even in globally common cancers like lung cancer, there are differences in terms of the causative underlying mutations. For instance, lung cancer patients from Japan, China and Southeast Asia are known to have a higher incidence of epidermal growth factor receptor (EGFR) mutation. In 2017, the Asia Early Phase Oncology Drug Development Consortium, comprising Japan, China, Taiwan, Singapore and South Korea, was formed to reconcile the disconnect between global cancer R&D priorities and Asian unmet needs.

PERCENTAGE POINT DIFFERENCE IN DISEASE INCIDENCE FOR THE MOST PREVALENT CANCERS IN ASIAN AND NORTH AMERICAN POPULATIONS

Incidence differences between Asia and North America (for the most prevalent cancers in 2018)
Percentage point difference in cancer incidence rates (Asia minus North America)

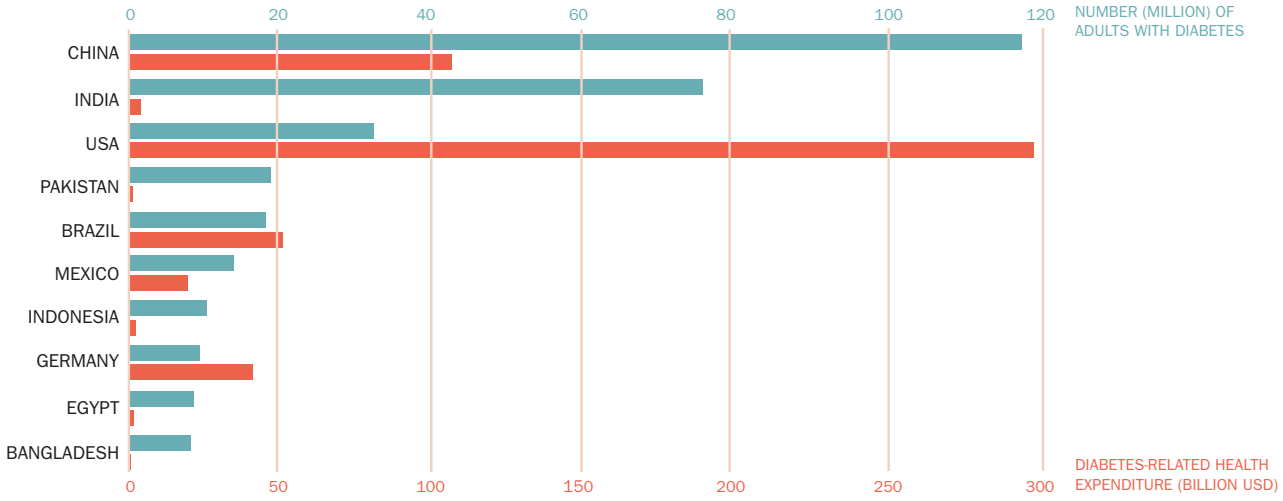


Source: L.E.K. analysis of GLOBOCAN 2018 data

DIABETES

Shockingly, over 60 percent of the global diabetic population reside in Asia, with nearly half in China and India combined. While the cause is not yet well-understood, studies have established that the average Asian diabetic is leaner compared to his Caucasian counterpart, leading to the epithet "the lean diabetic". Asian diabetics also tend to be younger – the largest group of diabetics in Asia is people aged between 40 and 59, compared to people aged over 60 in Europe – and more insulin-resistant. As they tend to develop diabetes at younger ages, they also face higher risks of long-term diabetic complications as well as more severe comorbidities over a longer period of time. Some countries like Japan and Taiwan have introduced urine glucose screening programs to diagnose cases of childhood diabetes in an effort to tackle the disease early.

TOP 10 COUNTRIES WITH DIABETES (20-79 YEARS) AND THEIR HEALTH EXPENDITURE, 2019

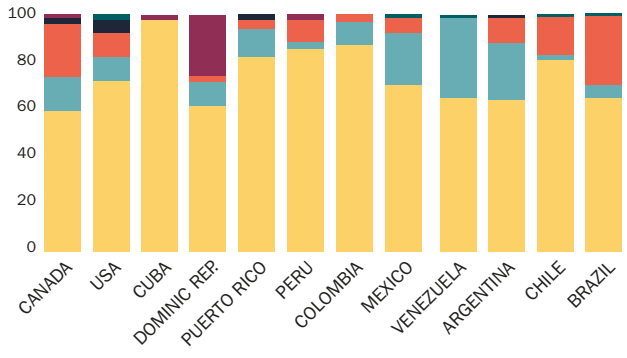


Source: International Diabetes Federation Atlas 2019

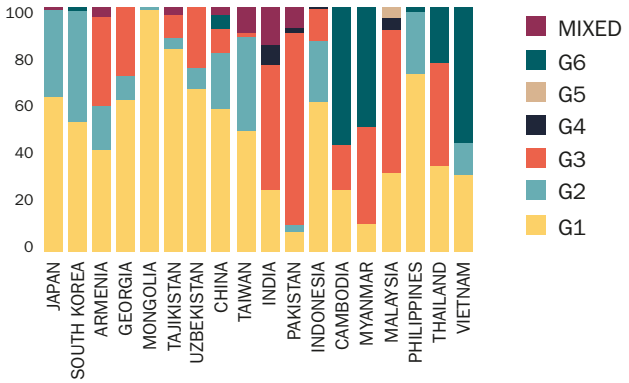
HEPATITIS C VIRUS (HCV)

Infectious diseases, though without a genetic basis, can also benefit from precision medicine approaches. HCV is currently classified into seven different genotypes based on its viral genome sequence, and their prevalence varies significantly across different regions. Genotypes 1 and 3 are common worldwide but in Asia, genotypes 2 and 6 are also fairly common – though there is also significant variation across the different Asian countries. Genotypes 2 and 3 are around three times more likely to respond to combination interferon + ribavirin therapies compared to genotype 1.

ANTI-HEPATITIS C VIRUS GENOTYPE DISTRIBUTION IN AMERICA



ANTI-HEPATITIS C GENOTYPE DISTRIBUTION IN ASIA



Molecular Diagnostics

Molecular diagnostics are the cavalry of precision medicine, facilitating the assessment and evaluation of patients' health at the most fundamental level. Not only to be used at the beginning of the patient journey, the value of leveraging precision diagnostic tools throughout the patient journey to monitor treatment efficacy and control disease progression is increasingly evident. Particularly in light of the COVID-19 pandemic, the transformative impact of effective and efficient diagnostic tools on global healthcare systems cannot be understated.

While North America has nearly half of the global molecular diagnostics market, perhaps surprisingly, the Asia-Pacific region is home to more molecular diagnostic firms than either the US or Europe, consisting of 40 percent of the market in terms of quantity. The region also represents the fastest-growing market for molecular diagnostics. With lower barriers to entry than pharmaceutical development, Asian companies, particularly those based in more technologically advanced markets like South Korea, Taiwan and Hong Kong, have proven adept at innovating new molecular diagnostic tools for disease prevention, diagnosis and management.

However, the typically high costs of these diagnostic tools impede their widespread adoption, particularly across less developed countries in the region. In addition, the reimbursement landscape for diagnostics is also patchy as many public and private insurers remain slow to view diagnostic tests as a necessary expense within already burgeoning healthcare expenditures. In addition, the successful usage of companion diagnostics also requires the existence of a fairly sophisticated healthcare infrastructure as well as proper training for physicians and pathologists. While the molecular diagnostics industry itself is booming in the region, companies still have to fight the uphill battle of advocating for the integration of molecular diagnostics within the broader healthcare systems.

Dr Johnsee Lee, chairman of the Taiwan Bio Industry Organization since 2010, is perhaps one of the most recognizable faces within the Taiwanese biotech industry as well as a staunch supporter of the overall Taiwanese high-tech industrial ecosystem, having previously been the president of the Industrial Technology Research Institute (ITRI) and the chairman of the Development Center of Biotechnology (DCB). He is also the founder and CEO of two diagnostic companies, Personal Genomics and Quark Biosciences. In 2019, he successfully brought the world's largest biotech event to Taiwan, jointly organizing the BIO Asia-Taiwan International Conference and Exhibition with the US-based global association, Biotechnology Innovation Organization (BIO). The event was a huge success, hosting over 2,000 one-to-one partnering sessions.

However, with the ongoing COVID-19 situation, the BIO Asia-Taiwan conference has had to move online, much like most other industry events this year. He elaborates, "generally speaking, most sectors of the economy – especially the transportation, food & beverage sector – have seen a significant reduction in activity and consumption, and accordingly, there has been a negative impact on the Taiwanese economy." Nevertheless, he points out the silver lining to holding the conference virtually. "It would save us a lot of expenses in terms of eliminating the need for physical venue and travelling costs, and we are subsequently investing these resources on various

Johnsee Lee
chairman, Taiwan Bio Industry Organization

> "the pandemic has also encouraged regulators around the world to be more flexible and change their approaches to managing regulatory processes. Many companies have been able to bring their products to market in a shorter span of time"

digital and virtual conferencing tools to prepare online content as well as filming capabilities."

Taiwan has been heralded as one of the models for its response to the COVID-19 pandemic. Despite its proximity to mainland China, a highly coordinated and effective national response including the integration of its national health insurance database and its immigration and customs database, the use of real-time alerts and other technology-based tracking measures, as well as a highly compliant population, meant that the territory has thus far managed to keep the number of confirmed cases under 500 and just seven deaths out of nearly 24 million citizens (as of June 30).

Beyond the public response, the Taiwanese biomedical and life sciences industry has also rallied forces, with Dr Lee amongst those leading the charge to combat COVID-19. He supplies, "as Chairman of Taiwan BIO, we are also trying to mobilize our members to coordinate responses to the COVID-19 situation. For instance, we have one team focusing on diagnostics. Some of our members work on reagents, some on assays, some on instruments – so by bringing them together, we can work on developing and offering a total diagnostic solution to institutions in Taiwan as well as globally. The short-term goal is to offer a better supply of the necessary COVID-19 diagnostic tests."

In addition to diagnostics, he adds, "we have another team working on R&D, comprising both academic and research institutions as well as vaccines and drug development companies. There are many different projects in progress."

Another crucial aspect is regulatory cooperation. On this, Dr Lee shares, "we are working with the Taiwanese government to accelerate regulatory approval processes. Unlike in the US, Taiwan did not have any Emergency Use Authorization frameworks, but following our advocacy, on 26 March 2020, the Taiwanese government issued a new regulation for the emergency use of necessary healthcare innovation to combat COVID-19." He highlights, "already, one company has been approved under this new regulation. This is a positive step."

Looking more broadly, he opines, "the pandemic has also encouraged regulators around the world to be more flexible and change their approaches to managing regulatory processes. Many companies have been able to bring their products to market in a shorter span of time."

For Taiwan, he is also convinced that this global crisis brings invaluable opportunities. He pronounces decidedly, "with the COVID-19 pandemic, we must take advantage of the situation and capitalize on available opportunities. It has provided opportunities for small companies to work together and perhaps grow together." For instance, he considers, "there may also be opportunities for M&A activity between Taiwanese companies and international companies. In fact, one of my companies, Personal Genomics, has received interest from both American and European companies." Ultimately, "such collaboration and consolidation could result in Taiwanese companies becoming stronger and more competitive."

Johnsee Lee and Eric Yang of Taiwanese precision medicine diagnostics firm Quark Biosciences outline their technology's unique characteristics and strengths in the areas of oncology and reproductive medicine.

Johnsee Lee
CEO, Quark Biosciences

Can you introduce the idea behind Quark Bio's products?

JOHNSEE LEE (JL): In precision medicine, a researcher is not looking for a single biomarker or gene, but for many. They use next-generation sequencing (NGS), which provides a broader spectrum of genes so that they can get the result in one test. However, sequencing today is still not very clinically friendly. It takes at least a few days – on average two weeks – to get results. Secondly, it is very complicated and requires very sophisticated bioinformatic analysis.

An alternative is amplification: to amplify from one to tens of thousands within a short period of time so that even very low concentrations of signals can be detected with high specificity and sensitivity. Traditionally, if a researcher or doctor wanted to run many different markers using conventional amplification, they would have to do a lot of manual manipulation, which takes a long time and is more susceptible to human error.

NextAmp™ Analysis System is our platform for simultaneous amplification of many biomarkers in a chip within two hours. NextAmp™ allows users to be precise and fast while also testing many markers at once. Additionally, we have also pre-loaded the probes and primers for each marker on the chip with our high-speed arraying technology so that the user does not have to do any pipetting.

What kind of products do you provide in oncology?

JL: One of our key products is a Tumour Micro-Environment (TME) test for cancer immunotherapy. This test uses around 100 markers so that physicians are able to evaluate the micro-environment around a tumour and its immunopheno score based on the gene expression. With this technology, doctors are able to decide whether a particular patient is suitable for immunotherapy. It is extremely important to develop TME, perhaps in combination with other markers, to increase the accuracy of selecting appropriate patients.

Another of our key products is MoDEL, a liquid biopsy for non-small-cell lung cancer. Blood plasma is used in the detection of variation in certain genes to judge whether [the cancer] is recurrent after treatment and also the detection of drug resistance.

Quark is also present in reproductive health. What is your footprint in this area?

ERIC YANG (EY): WHO has stated that infertility will be the third most significant disease of this century. Globally, IVF has a success rate hovering around 25-30 percent. One major factor is the window of implantation (WOI). We have developed a best-in-class assay that can predict the window, providing the exact time that is best for personalized embryo transfer to increase implantation success. We have already launched MIRA in China and Taiwan. We will launch MIRA in the US in late 2020 and in Europe in 2021.

Eric Yang
VP, Quark Biosciences

What are your key priorities for the future?

EY: First, it is important to ensure that we develop a variety of tests on the system. We want NextAmp™ to become a common platform for performing multiple diagnostic assays in the field of oncology and reproductive genetics.

Second, we want to become the leading platform for gene expression biomarkers.

Third, in the immediate future, we need to establish business operations in neighbouring regions such as China, Japan, and Southeast Asia. We have found a number of very capable partners in China to distribute our products. We continue to seek world-class partners in Japan and Southeast Asia. We have a golden chance in the era of precision medicine to take the NextAmp™ Analysis System to the global stage.

Uncertainty Today, Answers Tomorrow

Enable real time precision medicine through NextAmp™ Analysis System

QUARKBIO

Dr Albert Yu, chairman of the Hong Kong Biotechnology Organization (HKBIO) gives his expert insights into the crucial importance of diagnostics in countering the COVID-19 pandemic and other public health crises.

Albert Yu
chairman, HKBIO

> “WHEN IT COMES TO A PANDEMIC LIKE COVID-19, DIAGNOSTICS IS THE FIRST PRIORITY”

Albert, COVID-19 is not the first epidemic Hong Kong has had to deal with. What is your perspective on the current situation?

ALBERT YU (AY): What is clear is that technology can help us resolve the situation but what surprises me is that we do not seem to have enough of the right technology!

When it comes to a pandemic like COVID-19, diagnostics is the first priority. You first have to find out where the disease is before you can respond to it. Vaccines and therapeutics will take a long time to materialize. For vaccines, the development period is a minimum of one year.

Nevertheless, COVID-19 diagnostics are still messy right now. Antibody testing is being mistakenly used as a method of early detection when it can only tell you if the person has had COVID-19 at some point, not whether he or she currently has the virus or when he or she had it. The molecular diagnostics sector is rather advanced but many countries are facing problems with low accuracy and specificity of these tests. While this technology has been around for many years, it seems that globally, there is not a lot of know-how when it comes to deploying it in crisis situations. This is worrying because COVID-19 is a natural disaster but the world is potentially under threat from other infectious diseases stemming from biological warfare or biological errors. We need to be better prepared.

Hong Kong is managing it relatively well at the moment but at the beginning, it was difficult. We knew we had to diagnose around 8,000 people a day but our hospital capacity could only handle 1,000. Where would the remaining 7,000 people go? Other countries are still facing such capacity issues in terms of infrastructure, hospital resources and healthcare professionals.

I believe countries should be outlining a clearer strategy to deploy the maximum level of available resources. The first line of defence is, of course, hospitals and medical centres but once they are at maximum capacity, the biotech sector should be mobilized. We have the necessary laboratory equipment and diagnostic capabilities. Once the biotech sector is at full capacity, then the final line of defence should be the academic sector. Academic and research institutions also have the necessary state-of-the-art laboratory and scientific equipment to run diagnostic tests.

How do you think this will impact the global healthcare industry?

AY: This is a global problem and it requires a global solution. As the World Health Organization (WHO) has emphasized repeatedly, countries have to work together. Cooperation, not competition, is key.

For the industry, I do view the situation as a positive opportunity for us to advance and contribute. The crisis has illustrated the importance of the biotech and healthcare industry, as well as the need to foster, support and utilize each country’s biotech sector.

Diagnostics actually have much lower barriers to entry compared to drug development. The amount of time and resources needed to develop and commercialize products is comparatively lower so the sector is easier to develop.

Dr Desmond Hau, CEO of Pangenia Inc, sits down with PharmaBoardroom to shed light on the company's progress and their Southeast Asian strategy.

Desmond, how has the company developed since you became CEO in 2017?

DESMOND HAU (DH): In terms of product profile, we have improved significantly when compared with three years ago. Currently, we offer a DNA testing service which is subdivided into seven major categories, including reproductive medicine, prenatal and neonatal health, women and men health, hereditary and recessive disease, oncology, personal lifestyle and research services tests.

For our DNA testing services, we are now divided into three brands. One of these is Pangenia Lifesciences. This focuses on the medical diagnostics area. We are using innovative technology such as MDx (molecular diagnostics) and sequencing methods in order to provide a DNA testing service.

Furthermore, we are also no longer focused solely on Hong Kong and have since established a footprint in Southeast Asian markets through our affiliated company DiagCor Life Science. DiagCor offers clinical diagnostic services in Global Markets and is also the inventor and manufacturer of a number of in vitro diagnostic (IVD) reagent kits and devices. We export using our authorised distributors that have a pre-established relationship with DiagCor and are working closely to commercialise our products with doctors and patients alike.

We hope to further expand our footprint to Southeast Asia through our brand 22 Plus. These are personal lifestyle-based tests available to the general public and are geared towards personal risk assessment testing for our customers, all while utilising DNA testing technology. The types of tests we offer include the potential talent discovery test, athletic aptitude DNA testing, responsiveness to dietary nutrients test, and a physical and mental health test. 22 Plus is geared to corporate customers and companies who can utilise these services for risk assessment purposes. We are advancing this testing platform using online orders, thus increasing our digital marketing footprint.

My personal mission is to position Pangenia to be one of the largest molecular diagnostics companies based in Hong Kong, facing the Southeast Asian markets.

Desmond Hau
CEO, Pangenia

What has been your strategy to penetrate your target markets in Southeast Asia?

DH: In terms of product positioning, we started providing our personal lifestyle testing service, although it is far more price-sensitive. We are accepting a reduced margin on simple testing in order to develop and establish our brand name overseas. Our personal lifestyle tests fare better on these markets because of the competitive pricing compared with our clinical diagnostics tests. By increasing our brand awareness, we hope to subsequently promote the uptake of our clinical testing, which is a higher margin service for Pangenia. Thus, lifestyle testing acts as an entry door into the market.

Sales have been most successful in highly populated countries, namely the Philippines, Indonesia, Malaysia, Thailand and Vietnam.

We can also benefit from being a Hong Kong-based company. It is well recognised that Hong Kong possesses strong technology and high-quality medical services. Consequently, Hong Kong-based products and services are well established in South East Asia and are highly esteemed.

> "MY PERSONAL MISSION IS TO POSITION PANGENIA TO BE ONE OF THE LARGEST MOLECULAR DIAGNOSTICS COMPANIES BASED IN HONG KONG, FACING THE SOUTHEAST ASIAN MARKETS"

Kelvin Chiu and Isabelle Dutry of Sanwa BioTech in Hong Kong highlight the critical importance of personalised fast-track diagnostics in countering the COVID-19 pandemic, exciting milestones for the company, and what the future holds for Sanwa.

Kelvin Chiu
CEO, Sanwa Biotech

Kelvin, since we last interviewed you in 2018, many things have changed for both Sanwa BioTech as well as the world. Firstly, what are your reflections on the COVID-19 situation?

KELVIN CHIU (KC): It has been four months since social distancing and quarantine measures were initially announced [in Hong Kong], and these have only grown stricter as the COVID-19 situation deteriorated. Many countries globally have undertaken such preventative healthcare measures, resulting in the shutdown of non-essential aspects of their economies but I think we have to accept that this is not a sustainable long-term solution to COVID-19. The evidence seems to be growing that the virus is something that is likely to recur in future seasons and may last for decades. This means that we need to start thinking about how to return to work and live our lives under this 'new normal' condition.

This situation has also emphasized the critical importance of personalised fast track diagnostics. The world is focusing on the development of vaccines and therapeutics against COVID-19 but the reality is that this takes years to develop. In the meantime, effective diagnostics should be efficiently integrated into our healthcare systems so that infectious diseases can be traced, tracked and prevented from spreading. In the short-term, this is the only way of managing the situation.

Hong Kong is an international travel hub. Currently, travelling into Hong Kong for non-residents is banned. Hong Kong residents returning to Hong Kong [are] taken to the nearby exhibition centre to be tested for COVID-19. Due to the technology used [now], they have to wait a day or two for the test results. If more POCT diagnostics for COVID-19 were available, the waiting process could be shortened to just a few hours. For instance, we have developed a personalised respiratory diagnostic solution that can produce results from nose swabs within 15 minutes. This would improve the entire testing process immensely.

> "THE WORLD IS FOCUSING ON THE DEVELOPMENT OF VACCINES AND THERAPEUTICS AGAINST COVID-19 BUT THE REALITY IS THAT THIS TAKES YEARS TO DEVELOP"

How is Sanwa Biotech responding to the COVID-19 situation?

KC: We are working relentlessly to obtain regulatory approval for our COVID-19 antigen testing in Hong Kong.

Coronavirus testing is not as straightforward as one seems. There are three major types: antigen(protein) testing, which shows whether the patient is currently carrying a viral protein component (e.g. Nuclear Protein); antibody testing, which shows whether the patient is carrying an immunoglobin (e.g. IgG, IgM); and last but not least, PCR (DNA) testing to show whether the patient is carrying a genetic trace/fragment of the virus. There is some debate about the different types of tests that different companies have developed, in particular, relating to their accuracy, sensitivity, time and condition of proper usage.

At Sanwa Biotech, we provide diagnostic solutions based on our microfluidic disposable Lab-On-Chip (LOC) platform. The platform has three components: our Array-based LED-induced fluorescence ImmunoAssay

platform (ALiA) device; a single-use biochip; and the biomarker array for the diseases you want to test for. This test platform is based on a well-established antigen-antibody interaction, a protein-based immuno-assay with a 'key to keyhole' mechanism, which is well-proven and easily adapted to the diagnosis of different diseases.

Our system is able to diagnose a range of respiratory diseases, including COVID-19 antigen, within 15 minutes, and with an accuracy of between 90 to 100 percent. The system is also easy-to-use, fully automated and portable, which relieves the requirement of trained medical technicians and brings convenience to medical professionals already overworked and overstretched during this period. We are starting to run clinical studies and we hope to be able to launch this in the upcoming months.

This would be a great opportunity to demonstrate our knowledge and expertise in this field. Once our test is approved, we will be able to support the Hong Kong community as well as some of our Asian neighbours. However, due to our limited production capacity, we would take a bit longer to expand to other international markets.

What else is new for Sanwa Biotech since our last interview in 2018?

KC: We were recently granted new manufacturing facility space, which should be ready by 2022. This would help us expand our manufacturing capacity and start supplying our diagnostic solutions to Asia and other international markets. We have so far obtained HKD 25 million (USD 3.2 million) to fund this expansion.

We also need to grow our headcount. We currently have around 42 employees and we expect to reach around 80 soon. [This] is rather challenging because we need people with a certain level of medical/scientific expertise and experience, and Hong Kong's talent pool in diagnostics and healthcare solutions is still small compared to other markets. This is why we are also looking overseas, particularly in EU countries like France.

Our French affiliate in the Normandy region is also a new milestone. We decided to establish the affiliate in France to gain access to the incredible talent pool in the country as well as the great healthcare infrastructure. Our presence in France will certainly support our mission to develop and commercialize high-quality products.

Isabelle Dutry
CSO, Sanwa Biotech

ISABELLE DUTRY (ID): I had the pleasure to join Sanwa Biotech a year after its establishment and I am very excited to see the progress the company has made as well as the immense potential of our technology. As a French national and CSO of the company, our affiliate in France helps us strengthen our international network. France has a strong tradition in public health and particular expertise in infectious diseases, notably through the research institute, Institut Pasteur, where I spent a number of years, which now has a global network of 33 institutes globally, and this connection between Europe and Asia will generate new ideas for Sanwa Biotech's development.

What continues to motivate you?

KC: Sanwa Biotech's mission is to transform the diagnostic landscape to promote the better and more efficient performance of personalised Point-Of-Care diagnostic tests (POCT), and accordingly, preventative healthcare, which will ultimately contribute to patients receiving the right treatments more quickly, more effective healthcare systems and healthier societies.

We also need to remember that the biotech and healthcare technology industries are global industries. Science and innovation require international cooperation and collaboration. No city or country can do it alone.

Sanwa BioTech

Accurate Assay Anywhere

ALiA® includes an IVD device and a disposable biochip. The biochip is based on a user-friendly microfluidic Lab-On-Chip to auto-process fluorescent immunoassay on a protein microarray. It enables healthcare providers to process a rapid test in a convenient manner without lab support and provides front lines a powerful diagnostic tools for medical decision in 15 minutes.

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Dean Tsao
chairman and CEO, PlexBio

> "by putting high complexity molecular information at the focus of disease management, PlexBio will help transform the delivery of care for patients"

PlexBio was founded in 2010 by Dr Dean Tsao, who brought back over 30 years of extensive experience in the US IVD industry to Taiwan. With his background as a laboratory and clinical scientist, the serial entrepreneur has leveraged his expertise and creativity into an enviable career of establishing and growing profitable businesses. PlexBio is his fourth IVD enterprise and the previous three have all undergone successful acquisitions.

Since its inception, PlexBio has been designing, developing and manufacturing its proprietary cutting-edge multiplexing platform and assays to enable a broad range of genetic research and more specifically, cancer diagnostics. PlexBio's proprietary πCode™ MicroDisc technology uses a precision image micro disk for the detection of specific molecular targets, giving it the charming moniker of 'pi-Code'.

While next-generation sequencing (NGS) is seen as the quintessential workhorse of genome medicine today, Dr Tsao enthuses, "PlexBio's approach is a real alternative to NGS. [We] hope to disrupt and displace the use of NGS where ease-of-use, time and cost are at issue. PlexBio believes that performing high multiplex assays does not need to be complex or costly." Accordng to him, virtually any probe used in clinical diagnostics can be conjugated to pi-Code MicroDiscs, including DNA, RNA, antigens, antibodies, proteins, and chemical compounds. To bring pi-Code MicroDisc technology to every laboratory, PlexBio offers a series of convenient, pre- activated pi-Code MicroDisc products as a simple solution for the conjugation of virtually any desired capture reagent.

Having worked in the industry for over three decades, Dr Tsao is able to comment on the current opportunities and challenges within the diagnostics landscape. He reveals, "it is well-documented that, in general, clinical laboratory test results are indispensable for routine patient management. Imagine attempting to treat a diabetic patient without knowing their blood glucose levels or trying to stabilize a dehydrated patient without knowing of their electrolyte levels!" Similarly, in cancer management, direct understanding of the patient's genetic status is key. In addition, physicians are increasingly understanding the role that tumor heterogeneity can play in the progress of cancer in different patients.

As Dr Tsao elaborates, "we have applied this multiplex detection technology to a variety of molecular targets, including infectious diseases, food safety, and general life-science research tools. But our core business strategy rests in developing a comprehensive menu of tests for use in cancer diagnosis and management."

The current IVD product menu from PlexBio focuses on molecular tests that use tissue biopsy samples for diagnosis and management of cancer treatment. But the company is also working diligently to perfect additional oncology products for liquid biopsy samples. Traditional tissue biopsies require solid matter to be removed from the patient, either from the tumor or through the bone marrow, while liquid biopsies (with the exception of cerebrospinal fluid, which must be extracted through a spinal tap, a relatively painful procedure), are usually obtained through non-invasive and less expensive means. Most importantly, liquid biopsy sampling can be done throughout the course of treatment for monitoring the patient for re-occurrence of the cancer or resistance to the therapeutic agent being used.

To his mind, while it is positive that precision medicine has begun to flourish in recent years, attracting more attention to the diagnostics sector, which is often overlooked in relation to the pharmaceuticals sector, the main challenge is reimbursement. Dr Tsao laments, "these procedures are not yet reimbursed by national health and insurance systems – they must be paid for out of pocket by patients." For instance, in Taiwan, only tissue biopsies, not liquid biopsies, are covered by insurance systems. This is because NGS remains the primary platform for conducting liquid biopsies. The average cancer patient might require between four to six yearly tests for regular monitoring, and with the current costs associated with NGS, it is simply not feasible for healthcare systems to cover all these tests.

This is also an arena in which PlexBio hopes to contribute. Their πCode™ Micro-Disc technology is able to perform liquid biopsies at a lower cost, facilitating its reimbursement by the under-resourced Taiwanese healthcare system. Ultimately, Dr Tsao emphasizes, "appropriate IVD testing enables the correct early-stage interventions and treatment and will ultimately reduce late-stage healthcare expenditures for all stakeholders."

True to his tireless entrepreneurial spirit, Dr Tsao already has a vision for PlexBio's next five years, proclaiming, "looking to the future, PlexBio will continue to focus on the expansion of company's brand image, leading the market with high-complexity multiplex technology, and the promotion of clinical and scientific research to firmly establish PlexBio reputation as a high-quality supplier of key IVD and life-science products. By putting high complexity molecular information at the focus of disease management, PlexBio will help transform the delivery of care for patients."

With such a profound legacy of entrepreneurship and innovation, Dr Tsao also shares some wise words on managing a productive marriage between business and science. He opines, "I do not look at them as separate entities needing to be joined. Rather, I view PlexBio as simply being in the business of science. From the business perspective, we have focused on unmet needs in the market and we used our science and technology to develop innovative solutions to meet those needs. It is a simple formula applicable to almost any field. We see our IntelliPlex™ system as being the right product at the right time for the market. But as our team and I have worked on this day in and day out, it also helps that there is a deep passion for the science and problem-solving."

HONG KONG

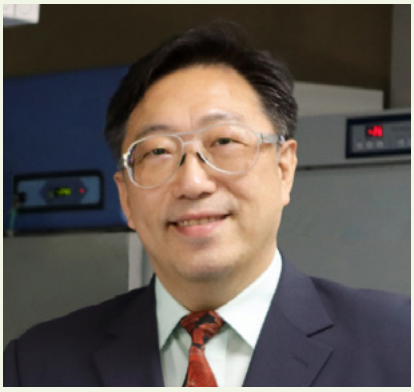
Hong Kong, with its distinguished history as the financial and commercial hub of Asia, is perhaps slightly late to the game when it comes to precision medicine, with the Hong Kong administration only laying out its blueprint for what it termed genomic medicine in May this year. The blueprint included the launch of the Hong Kong Genome Project, which aims to start recruiting people in mid-2021 with the goal of sequencing 20,000 genomes. Other recommendations included the establishment of a biobank network for genomic research as well as the promotion of the proper use of genetic and genomic tests, particularly relevant in Hong Kong as direct-to-consumer genetic tests have become a consumer trend.

Despite the still-nascent biomedical industry in the city-state, Hong Kong does have a number of attractive competitive advantages when it comes to precision medicine. The heavily subsidized healthcare system was ranked by Bloomberg as the most efficient in the world in 2018 and Hong Kong citizens have one of the longest average life expectancies globally. An electronic health record (EHR) sharing system was introduced in 2016 to improve the continuity of patient care, promote more public-private collaboration, and enhance the quality and efficiency of healthcare services. Hong Kong's universities are also well-recognized, with five ranking in the top 100 globally, creating a strong talent pool of academics, researchers and scientists. In 2018, the Hong Kong Stock Exchange – the fourth largest in the world by market capitalization – amended its listing rules to allow pre-revenue biotech companies to list, paving the way for innovative biotechs in the region to access public markets. In addition, with its international legal and IP conventions, Hong Kong has always been seen as a bridge between East and West, facilitating cross-border transactions and collaborations between China and Western markets. For instance, global AI medicine innovator Insilico Medicine relocated from Johns Hopkins University in Baltimore, USA to base themselves in Hong Kong. As CEO Alex Zhavoronkov explained succinctly, "Hong Kong provides close proximity to mainland China, while possessing a stable legal framework that respects property rights and patent law."

Industry stakeholders remain cautiously optimistic about Hong Kong's potential as a biomedical and precision medicine hub. The Chinese University of Hong Kong (CUHK) Professor Dennis Lo, who developed the pioneering non-invasive prenatal testing (NIPT) technology and co-founded a number of diagnostic companies including liquid biopsy cancer diagnostic start-up Cirina, stressed, "we need to be humble. In many aspects, Hong Kong is a relatively latecomer to the biotechnology space." What he does hope for is "more success stories". As he highlighted, "Our strength is our people. We need more people who are academics, scientists, engineers and entrepreneurs to start our own companies and make a name for ourselves. I hope that people will look at [Cirina] as a success story and with time that we are able to create a technology that has a global impact."

Indeed, the niche of Hong Kong companies thus far seems to be in diagnostics, owing to the relatively lower barriers to entry as well as Hong Kong's proximity to Shenzhen, the electronics manufacturing mecca of mainland China. Hong Kong companies have proven adept at quickly developing and commercializing various diagnostic tools and technology platforms, and subsequently constructing profitable commercial models, including with global pharma companies. Moving forward, it is still unclear how Hong Kong companies and the overall Hong Kong ecosystem would continue to advance in the field of precision medicine but what is undeniable is that momentum is building.

Alex Wong, CEO of Xcelom sat down with PharmaBoardroom to discuss the company's non-invasive prenatal testing (NIPT) technology and his growth strategy for the future.



Alex Wong
CEO, Xcelom

Can you tell us about the strengths of Xcelom's NIPT technology?

ALEX WONG (AW): Generally speaking, all NIPT technology uses the same background theory and follows a similar formula: using foetal DNA found in maternal blood to detect a corresponding foetal genetic anomaly. The major differences between the various NIPT service providers lie in how they conduct their quality control and their basic format of testing. Some use in-house platforms such as DNA chips or PCR-based methods, which, aside from having a lower sensitivity, can only offer a very limited scope of data.

Our NIPT was invented by a research team from the Chinese University of Hong Kong (CUHK) and we are currently the exclusive licensee of this NIPT patented service from CUHK. We are responsible for the Hong Kong, Macau and all overseas markets, while the mainland China market is handled by our mother company.

Our technology is based on DNA sequencing, which, in comparison, is more sensitive and reliable. Also, Xcelom's NIPT follows much more stringent protocols. This, together with the use of our unique combined algorithm (one that looks at an extra set of parameters instead of just the standard ones), makes our test extra accurate and reliable.

Above all, Xcelom pushed the envelope with the introduction of performing NIPT at as early as 10 weeks of gestation. At such an early gestation, there is only around 0.8 to one percent foetal genetic material. Previously this low percentage could sometimes lead to uncertainty in the reading. However, Xcelom was able to successfully overcome this difficulty by increasing both the detectability and sensitivity of its NIPT.

Lastly and most distinctively, our reports are endorsed and supported by one of Hong Kong's most recognised academic/medical teams. I think it would be safe for me to claim that our reports are better and more comprehensive than others. Our pursuit and pioneering of cutting-edge improvements, along with our partnerships with various medical expert KOLs in Hong Kong, are what made us the NIPT market leader we are today.

Diagnostics have lower barriers to entry compared to pharmaceuticals. How do you assess the competitive landscape in the region?

AW: Although the market appears crowded at first glance, that is not actually the case. The market is currently flooded with academic research companies that are trying to turn their ideas into commercial products rather than already having marketable solutions. Regrettably, only very few of these tests survive to be commercially viable.

Another reason the market looks more congested than it actually is is the big gap between supply and medical needs. Many new tests are developed for genes that are of great research value but might not be in high demand by medical practitioners nor actually meet the true need of medical professionals and their clients.

In terms of product type, I do not see any other genetic test on the market that is comparable to NIPT in terms of its demand and reliability. Xcelom has strengths that no other NIPT service providers on the market can compete with.

What is your vision for Xcelom?

AW: Our company vision is to become a leading genomic service provider in the world. In 2019, we relocated to a much bigger office, expanding from 5,000 to 20,000 square feet. We expect to acquire another floor of office space as well as another 6,000 square feet laboratory.

Although we are currently financially self-sustainable, given our future plans, new revenue streams will be necessary. Thus, we are looking forward to [becoming] a listed company in the near future.

Alex Zhavoronkov, CEO of Insilico Medicine, lifts the lid on the role of AI in target discovery, identification, and validation. He also offers his opinion on the future of innovative drug development in China, and the challenges of establishing a biotech company in Hong Kong.

Alex Zhavoronkov
CEO, Insilico Medicine

What inspired you to establish Insilico Medicine?

ALEX ZHAVORONKOV (AZ): Insilico began as a multi-omics target discovery company. In 2014, deep learning started outperforming humans in areas such as voice, image, and text recognition. Prior to this, we had already seen the writing on the wall and by 2013 we started using deep neural networks to identify novel targets in the vast amount of omics data, primarily focusing on protein expression and gene expression data. This is achieved by training deep neural networks to predict a disease state, and then de-convoluting this data to make it explainable. Subsequently, the protein targets responsible for a particular disease formation are identified. Insilico undertakes this process for a number of diseases and for research into ageing.

Our platform is designed to work at every stage of the pharmaceutical R&D process, which takes around ten years from beginning to end. We can join at any time within that process because our algorithm not only detects novel targets but can also make certain predictions about phase I-II or II-III transitions. Our algorithms are also used in precision medicine. Thus, it covers a broad spectrum of the development cycle.

In our field, we are the most published company, completing around two papers a month. This vastly outpaces our competition, who publishes at an average rate of only two papers per year. I have personally published 180 papers. The number of research citations of Insilico is also growing.

Where are Insilico's main areas of expertise?

AZ: Our main expertise is in target discovery. We have assisted in identifying novel targets for multiple companies. Our in-house pipeline also stems from target discovery expertise. I believe Insilico is most famous for generative chemistry; we are renowned as a chemistry specialist that can design small molecules for chosen targets.

We have also started designing and selling software. We have a software system called Pandomics, which aggregates the data from clinical trials and research. This system enables the user to study any disease and compare samples from different parts of the body of those with the disease to those to samples. Furthermore, the software can also be used for identifying targets. The software uses AI to identify and rank novel targets, based on the criteria and parameters selected by the user.

While we were very excited about our technology and its capabilities, justifying its merits to the rest of the world required a method of validation. By 2015, it became clear that findings in target discovery lack credibility without validation through real chemistry. Consequently, most of Insilico's validation is now realised through phase II clinical trials.

Our research within AI does not stop. We have new systems that can generate biological data indistinguishable from real biological data and can now imagine high-quality human data. Our AI tools can imagine a human with particular features and use parameters to increase precision. I believe creating this artificial data can be a method of getting around data privacy laws

What is your perspective on this?

AZ: I am a believer that history is an indication of the future. Consider 5G technology, where China is the inventor. Huawei outperformed its competitors globally and had been developing this technology since the late 90s. Although they had brought less innovative products to market during that time, their innovation platform continued to accelerate. Huawei not only succeeded in bringing it to the market earlier but also outperformed its competitors.

I think we will see the same situation in the pharma industry. The market started with genetics and then moved to in-licensing. Regrettably, the current business model is employing a former Big Pharma executive, in-license a product, take it to late-stage trials, and then list through an IPO (initial public offering).

However, the Chinese government is shrewd; they are trying to incentivise innovative development and the pursuit of higher-risk targets. The Chinese government is already doing a great job but it would be great to see further incentives for local pharma companies to utilise AI and to search for novel targets. Target discovery, identification and validation are the highest-risk areas of the pharmaceutical industry. At the same time, the development of a novel medicine is the ultimate reward.

Switzerland is one of the best examples of how to build a pharma industry. Roche and Novartis are headquartered in Basel. Thus, one city controls 20 percent of the world's pharma industry. To achieve that, you need to build a culture of excellence in the field of drug discovery. This demands an acceptance that failure will often occur and a willingness to assume the risks of new technologies. Consequently, local Chinese companies need to begin taking greater risks and show a willingness to pursue novel targets without fear of failure. This is happening slowly but will rapidly accelerate as they grow in experience. Most of our revenue in China still comes from large multinationals. Nonetheless, there is a visible trend of the most innovative companies beginning to partner with Insilico.

Pharma is traditionally reticent to adopt sweeping change. What is your strategy to establish collaborations in the industry?

AZ: Given our reputation thro-ugh our published papers, we benefit significantly from word of mouth and work with those who already know the AI landscape. We begin by looking for the most innovative people within the industry. Unfortunately, the industry is composed of many people who are risk-averse and will spend lots of time on pilots and evaluations. Nevertheless, our search usually starts from a problem that needs to be solved. We can reach out to those looking for a solution and willing to be innovative enough to test a new technology and seek out a short cut through the use of AI.

> "UNFORTUNATELY, THE INDUSTRY IS COMPOSED OF MANY PEOPLE WHO ARE RISK-AVERSE"

Where do you see Insilico in 5 years?

AZ: For Insilico, five years is a long time. My goal is to get some of our preclinical assets into human clinical trials. We already have a pipeline of small molecules that have been discovered and everything is new.

My main vision for the company is to create a yin and yang between our software and pipeline. We develop software for internal and external use. Other companies can acquire our tools and replicate our model. It can cover 5000 possible targets and 5000 possible diseases. We are very selective about how to provide this software. It is being launched in the summer with orders already in place.

We are also developing our own pipeline. If an AI company cannot show that its pipeline is composed of great molecules that can make it to clinical trials, the company will lose its relevance. At Insilico, we need to be willing to take risks and make big bets on our own software to find great products.

TAIWAN

In 2016, Taiwan unveiled a Biomedical Industry Innovation Program, which was entrusted to then-Minister without Portfolio Tsung-Tsong Wu, who became Minister of Science and Technology in May 2020. In a 2019 interview with us, Minister Wu captured Taiwan's potential in precision medicine succinctly: "Taiwan is already in a commanding position to link the hardware of resources and infrastructures with the software of information and policies to meet the future needs of society. We may look like a minnow on the world stage but we are highly adaptable and possess unique abilities to rapidly adopt new technologies."

Indeed, the seventh-largest economy in Asia is one of the region's most developed and efficiently managed markets, boasting a veritable embarrassment of strengths when it comes to the development of precision medicine. With around 24 million citizens possessing relatively homogeneous genetic background, a decades-old tradition of excellence in semiconductor and later industrial manufacturing sectors, an extremely well-educated workforce, and an advanced healthcare system with universal healthcare coverage and impressively comprehensive electronic medical records (EMRs), Taiwan is poised to become a model of excellence in the development and deployment of precision medicine – or as Minister of Health and Welfare Shih-Chung Chen has termed, "intelligent healthcare".

Not content to rest on their laurels, however, Taiwanese authorities have advanced a number of initiatives to plug the gaps identified and bolster Taiwan's credentials in precision medicine. For instance, in 2019, the Taiwan Precision Medicine Initiative (TPMI) was established through the joint efforts of Academia Sinica and 13 partner hospitals across the nation, identifying the need to achieve the "the foundation work of [the] collection of genetic profiles and clinical data from Taiwan population must be done." TPMI hopes to collect the data of a million Taiwanese citizens by 2022. In October of the same year, the Taiwan Precision Medicine National Biobank Consortium was also launched, with the mission of harmonizing all the existing 31 biobanks in the country to form a comprehensive database network, which collectively have accumulated nearly 4.5 million samples and recruited nearly half a million participants. The Ministry of Health and Welfare has also stated the intention to eventually integrate other healthcare resources including the national Cancer Registry System, the National Health Insurance System and the rare disease database. A month later, the National Health Research Institutes (NHRI) launched the G2020 Population Genomics Pilot, partnering with global gene sequencing leader Illumina to sequence 10,000 genomes by the end of 2020, with the intention of constructing an operational architecture for population genomics, so that genome and exome sequencing can be embedded within the existing healthcare system by 2025. The hope is that this can eventually act as a foundation for other stakeholders to plug into, be it for academic, scientific or industrial research.

For many Taiwanese biomedical innovators, the sweet spot has been squarely in the development of more efficient and effective novel technologies for the advancement of precision medicine, primarily in molecular testing and diagnostics. The relatively small size of the domestic market has compelled the majority of successful companies to venture abroad, typically to mainland Chinese or American markets, with varying degrees of success. As a result, industry experts are increasingly advocating for some level of productive consolidation within the domestic industry in order to compete more strategically against its peers based in far larger regional markets.

Rongjin Lin
chairman, Center Ventures

Taiwan was one of the first Asian stock exchanges to facilitate the listing of high-tech companies including those in the biotech industry. This, in conjunction with the established semi-conductor and other high-technology manufacturing industry, helped boost the local biotech and life sciences ecosystem – and chairman of Center Ventures and Center Laboratories Rongjin Lin is one of the most active proponents. He shares, "when considering how to build Center's investment portfolio, I consider what Taiwan's needs are. I identified a gap in drug development, so I invested in PharmaEngine. This was the same when it came to medical devices when I invested in Medeon. The strategy of Center is to create synergies and build an ecosystem within Taiwan."

While championing the local industry, he also remains realistic about Taiwan's position in the global industry. He laments, "I do not believe that Taiwan can truly be in competition with China or Hong Kong. Taiwan faces an impossible challenge in its small market size. Many pharma MNCs are not interested in co-developing or licensing a product until the late stages of development. However, global Phase III trials are tremendously expensive and Taiwan's stock market is too small to support these activities. Having access to outside resources and support is crucial even for larger Taiwanese companies."

Nevertheless, Taiwan retains highly attractive strengths. Lin advocates, "the quality of academia and the integrity of data are excellent. There is a high level of transparency and trustworthiness, with plenty of support to help nurture the beginning phases of a biotech company. However, to truly reach full potential and operate on a worldwide scale, acquiring global funding is crucial to support growth."

With the establishing of the HKEX Biotech Board and the Shanghai STAR Market, Taiwan has also lost one of its key financial advantages. Lin laments, "Center Ventures helped launch Lumosa Therapeutics Co., Ltd. with the merger of three companies, which gave Lumosa three assets in the early, middle and late clinical development stages. With the Taiwanese government's IPO regulation amendment, the company was able to go public in 2016 without any revenues and still raise funds. However, Shanghai and Hong Kong have followed in our footsteps and Taiwan's competitive advantage in this area no longer exists."

Ever shrewd, Lin has fingers in many pies. He points out, "when it came to finding an investment, the best opportunity was to go to China due to Taiwan's small market size. in 2010, we invested in TOT Biopharm, a Chinese biotech specializing in oncology." In 2019, TOT Biopharma IPOed in Hong Kong, raising around USD 75.2 million.

> "the quality of academia and the integrity of data [in Taiwan] are excellent"

He believes there are many opportunities for closer cooperation between Taiwan and mainland China, outlining, "I believe that we should try to win together in the world and be able to share our resources for early phase trials. Taiwan needs China's patient population and as long as we are both able to follow global guidelines of the International Council for Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), this could be mutually beneficial. For example, to collect just 100 patients for a stroke trial in Taiwan would take several years – our patient pool is too small."

TAIWAN'S LEADING GENOMICS CHAMPION

Taiwan's ACT Genomics may have been founded just six years ago in 2014 but the company has certainly kept busy. Through its cutting-edge NGS platform, medical reporting and other integrated services, the company has expanded rapidly across the region and today boasts laboratories and operations serving patients across Taiwan, Hong Kong, Singapore and Japan, as one of the leading cancer precision treatment solution provider in Asia.

As their mission states, their ultimate objective is to "rewrite the existing model of cancer diagnostic, cancer treatment and cancer monitoring" – in other words, "Make Cancer Manageable". ACT Genomics have developed a two-pronged portfolio offering catering to both healthcare professionals and patients, as well as industry players. In a 2017 interview with us, CSO Dr. Shu Jen Chen emphasized, "our main purpose is to provide clinical service to cancer patients." COO Joe Hsueh complemented, "we offer complete solutions and there is nobody who can compare to the quality of the service we provide at the moment."

Their flagship panel, ACTOnco® +, is a comprehensive genomic profiling service covering tumor mutational burden (TMB), microsatellite instability (MSI) status and immune-related genes to provide a more accurate prediction of responses to immune checkpoint inhibitors. They also offer a range of other panels testing for other concerns including ACTBRCA® targeted at ovarian cancer, breast cancer and other solid tumors; ACTMonitor®+ for cancer monitoring; and ACTRisk™ for hereditary risk evaluation, among others. According to the company, their ACTOnco® + allows 83.9 percent of patients to find corresponding treatment solutions. CEO Dr. Hua Chien Chen highlights, "we see a lot of patients, especially in Southeast Asia and China. We invest a lot into education and [our relationships with] local oncologists, not only in Taiwan but also in Singapore, Hong Kong and Japan. Our objective is to continue educating the community. We have received very good feedback from oncologists so far."

On the industry side, ACT Genomcis is also helping pharma companies close the distance between early target discovery and commercial launch by identifying biomarkers of treatment efficacy, focusing on both immunotherapy and targeted therapy.

The company raised USD 8 million in their first private financing round in 2015 and have continued to see modest success on the capital markets, including another round in 2018.

The company's thirst for growth has not abated over the years. In June 2020, ACT Genomics became the first to receive approval for Laboratory Developed Tests and Services (LDTS) in Taiwan. The company also established a joint clinical research collaboration with key Taiwanese institutes like Kaohsiung Medical University (KMU) and the National Health Research Institutes (NHRI), utilizing NGS technology to investigate biomarkers associated with melanoma. As CSO Dr. Chen expresses, "we will be one of the most dominant genomic service companies in Taiwan and [in the] wider [region]!" For her, the company's name symbolizes 'turning information into action – diagnosis, prevention, treatment selection and monitoring' – their company's mission.

Cell & Gene Therapies

One of the most revolutionary advances in medicine, cell and gene therapies typically target the underlying cause of disease rather than simply attempting to ameliorate symptoms, and for that reason, have proven to be particularly adept at treating genetic and chronic diseases. Cell and gene therapies are also fundamentally different from small and large molecule therapeutics because they are – thus far – far more individualized, implicating complex clinical, manufacturing, commercial and sustainability considerations. To cite just an example, the total therapy preparation ('vein to vein') time for the CAR-T products approved thus far in the US is between 30-50 days, and they incur price tags of nearly half a million USD. In 2019, the US FDA approved Novartis' Zolgensma with a staggering price tag of USD 2.1 million per patient.

Nevertheless, Asia has become a hotspot for cell and gene therapy. Over the last few years, the Asia-Pacific region (excluding Japan) was involved in around 40 percent of global gene therapy trials. In 2014, Japan introduced two laws, offering fast-tracked and conditional approvals to allow regenerative medicines to reach the market quicker. South Korea, in particular, can be seen as a leader in regenerative medicine, possessing the largest approved cell therapy product portfolio in the world with a total of 18 products approved on the market in 2019. In 2018, Taiwan become the ninth regulatory agency in the world to approve cell therapy treatments. Spurred on by the increasingly favourable regulatory environment, many biotech companies have developed their own novel therapies for various diseases and are now looking to launch them on regional and global markets.

Dr Jan-Mou Lee, founder of FullHope Biomedical, explains their company's revolutionary platform that is leading Taiwan's cell therapy sector.

How is the cell therapy space in Taiwan at the moment?

JAN-MOU LEE (JL): Six years ago, when we began, the cell therapy space was very barren and not many stakeholders had experience in immunotherapies. However, working with the Centre for Drug Evaluation (CDE), we were able to determine how to properly design a formal cell therapy clinical trial in Taiwan. Furthermore, the government has passed new regulations to allow the use of six cell therapies in Taiwan. Under the new "Regulations Governing the Application of Specific Medical Examination Technique and Me-dical Device", stem cell therapies are able to be applied to patients one phase I trials are complete. In fact, I was one of the consultants to help develop this amendment.

Many doctors in Taiwan were in opposition to the cell therapy reform. They had not seen the clinical data and to them, cell therapy is very unsafe but they do not consider the efficacy of the treatments. That is why FHB is participating in the partner studies to inform health professionals and we carry out the screenings so we can find the correct target populations to use correct treatment methods.

FHB is collaborating with several major medical centres such as National Taiwan University Hospital and Taipei Veterans General Hospital to conduct cell therapy clinical trials. Our development strategy is to take advantage of our innovative research power and translate our lab findings to the clinic while collaborating intensely with leading KOLS in the fields of oncology and autoimmune disease.

Thus far in Taiwan, FHB has completed six pilot studies, in which 60 percent of patients responded to the treatment. We are working to convince doctors that cell therapies are viable methods of treatment for patients and we currently have two cell therapy protocols under review by the government.

Tell us more about FullHope Biomedical's comprehensive immune function detection and analysis platform.

JL: Our platform is focused on conducting precision diagnosis before preparing personalized immune cell therapies. This immunoprofiling platform uses a patient's blood sample against over 600 monoclonal antibodies. Through this, we can successfully identify over 1,700 cell therapy options. This platform has been Taiwan Accreditation Foundation (TAF) certified in terms of the quality insurance of our immune cell products.

> "WHEN WE BEGAN, THE CELL THERAPY SPACE WAS VERY BARREN AND NOT MANY STAKEHOLDERS HAD EXPERIENCE IN IMMUNOTHERAPIES"

We have also created a database from the blood samples of subjects of different gender and age groups which we are comparing with different disease models such as cancer and autoimmune disease. In the immunoprofiling, we can design patient-specific regiments that best fit their disease condition, such as combination treatments using both targeted medicine, chemo, or PD-1 plus cell therapy.

In addition to immunoprofiling, we also conduct clinical trial services. For example, we established a predictive biomarker in a 12-week trial for PD-1 inhibitor drug. We profiled the patients before, during, and after the treatment regimen to conduct a retrospective analysis on the PR (partial response) and DP (disease progression) groups of patients. This way, we were able to determine the patient immune difference and identify biomarkers which can predict patient response to the treatment.

Founder, CEO and CTO Dr Chae-Ok Yun introduces GeneMedicine, a pioneer of the oncolytic virus approach in gene therapy. Dr Yun outlines the significance of a recent capital injection, ongoing clinical trials, and the complementarity of oncolytic virus with other gene therapies such as CAR-T.

Chae-Ok Yun
founder, CEO and CTO, GeneMedicine

GeneMedicine is a pioneer of the oncolytic virus (OV) approach in gene therapy. What are the benefits and opportunities inherent in this technology?

CHAE-OK YUN (CY): Despite the recent success of targeted cancer therapeutics and immunotherapeutics, tumour recurrence and metastasis are eventually observed even in patients who initially responded well to these treatments. Additionally, only a small subset of patients responds well to immunotherapy. These apparent limitations in advanced cancer therapeutics necessitate the development of novel therapeutics that can address these unmet needs of cancer patients.

To this end, the OV, which replicates and selectively destroys cancer cells, can be a promising alternative. Importantly, OV-mediated destruction of cancer cells induces a systemic antitumor immune response which is capable of destroying metastasized cancer cells at distal sites, making oncolytic viruses promising next-generation cancer therapeutics. Additionally, OVs in combination with conventional cancer therapeutics (chemo- or radiotherapy) as well as cancer immunotherapeutics can elicit a synergistic antitumor effect.

OV is not necessarily a competitor of standard therapies that are already present in the market, such as CAR-T or checkpoint inhibitors. OV works synergistically with those technologies and, if used together, can significantly enhance therapeutic efficacy. We have a lot of proprietary data, as well as data from other companies, demonstrating the strong synergistic potential of OV in combination with other immunotherapeutics. For example, phase II clinical trials of the immune checkpoint inhibitor, Keytruda, in combination with commercialized oncolytic herpes simplex virus was shown to significantly improved patient outcomes.

What makes GeneMedicine a leader in OV technologies?

CY: GeneMedicine has a great deal of experience in the development of systemically deliverable OV. Late-stage cancer patients who need a new treatment option must be injected systemically to get rid of all the metastatic tumour cells.

In addition to these technologies, we have also developed several potent combinations of therapeutic genes that can concurrently be delivered via a single OV, thus maximizing OV's therapeutic index.

We have several pioneering technologies which allow our OVs to exert potent anticancer effects in a highly cancer-specific manner with minimal off-target toxicity in normal tissues.

What is the key to building a successful R&D team in cell and gene therapy?

CY: To build a successful R&D team, there needs to be a solid technology base. Good technology cannot be mimicked in a short period of time. In the past, some pharma companies have identified OV as a technology that can easily and quickly be appropriated using public files. However, there is a lot of know-how in the lab and it cannot easily be mimicked. There needs to be a very good understanding to the functionality of OVs and the unmet needs of cancer patients.

We have spent over 20 years developing our technologies. This is one of the main reasons why so many VCs have been drawn to the company.

How do you see GeneMedicine scaling up?

CY: When discussing potential collaborations or licensing-out deals, I always ask potential partners to keep us involved. Without sufficient experience in OV,

the development process can be challenging. While we are happy to transfer out our technology, we need to be involved for a certain period of time to help them understand OV and provide our expertise to them, ultimately aiming to aid our collaborators to successfully develop our OV at their facilities.

GeneMedicine does not have an in-depth experience handling later stages of clinical trials or the financial capacity to launch them as a small company. We want to collaborate with big commercial companies after Phase I or II clinical trials. Upon completion of our initial clinical trials, we will be working on licensing out our technology or acquiring investment from pharmaceutical firms or international investment banks.

What are your hopes for the future?

CY: We have a very strong knowledge base and over 20 years of experience in the development of OV technologies. We are able to make OV extremely potent and safe. Additionally, our proprietary technologies regarding systemically administrable OV platform could be of great importance in addressing some of the inherent limitations of locoregional delivery, which remains preferred delivery route of OVs in clinical trial to date.

> “WHILE WE ARE HAPPY TO TRANSFER OUT OUR TECHNOLOGY, WE NEED TO BE INVOLVED FOR A CERTAIN PERIOD OF TIME TO HELP THEM UNDERSTAND OV AND PROVIDE OUR EXPERTISE TO THEM”

For the development of really successful OV therapy, we need a strong collaboration with a good pharmaceutical company. We are looking for the right opportunity!

Kyung Suk Kim, CEO of Corestem, introduces their stem cell therapy for Amyotrophic Lateral Sclerosis (ALS) in Korea, and outlines their international ambitions.

Kyung Suk Kim
CEO, Corestem

Dr Kim, can you introduce Corestem's main activities?

KYUNG SUK KIM (KSK): NEURONATA-R® is our pioneering treatment for Amyotrophic Lateral Sclerosis (ALS). ALS is a disease where motor nerve cells deteriorate and eventually die. This gradually results in paralysis of skeletal muscles, progressing across the entire body. In the latter stages of the disease, a patient cannot swallow or breathe properly. The prevalence rate is 4-6 in 100,000 per year, which has increased with an ageing population.

NEURONATA-R® is an autologous bone marrow mesenchymal stem cell therapy that acts as a neuroprotective effect and relieves progression of the disease through prevention of motor nerve cells and survival extension of motor neurons, releasing the nerve's inflammatory and immune regulation function.

In 2014, NEURONATA-R® was the first commercially licensed stem cell therapy for ALS, receiving conditional approval. We finally received Orphan Drug Designation from the US FDA in 2018 and from the European Medicines Agency (EMA) in 2019.

Since its conditional approval in 2014, NEURONATA-R® has treated more than 300 patients and has demonstrated its safety and efficacy from the Phase II results. In particular, the number of foreign ALS patients travelling to Korea to receive treatment is on the rise since the world's first ALS treatment approval. The Phase II report has also attracted attention from the academic side.

NEURONATA-R® has a shelf life of just 48 hours, making it difficult to distribute to patients outside of Korea. How do you plan to realise your international ambitions?

KSK: We plan to first enter countries that are highly active in their policy considerations of innovative treatments for patients with rare diseases, such as the US. However, it is true that considering the size of the company, it is hard to penetrate these markets alone. Thus, we have been looking for partners to license-out our technology after receiving IND approval. Fortunately, some of the major players within the top 50 pharma companies have already declared an interest in collaborating. They are awaiting the outcome of our current clinical trials before finalising any agreement.

In the future, we also have ambitions to form partnerships in Europe. We are open to collaborations with different partners in different regions, rather than a comprehensive global deal.

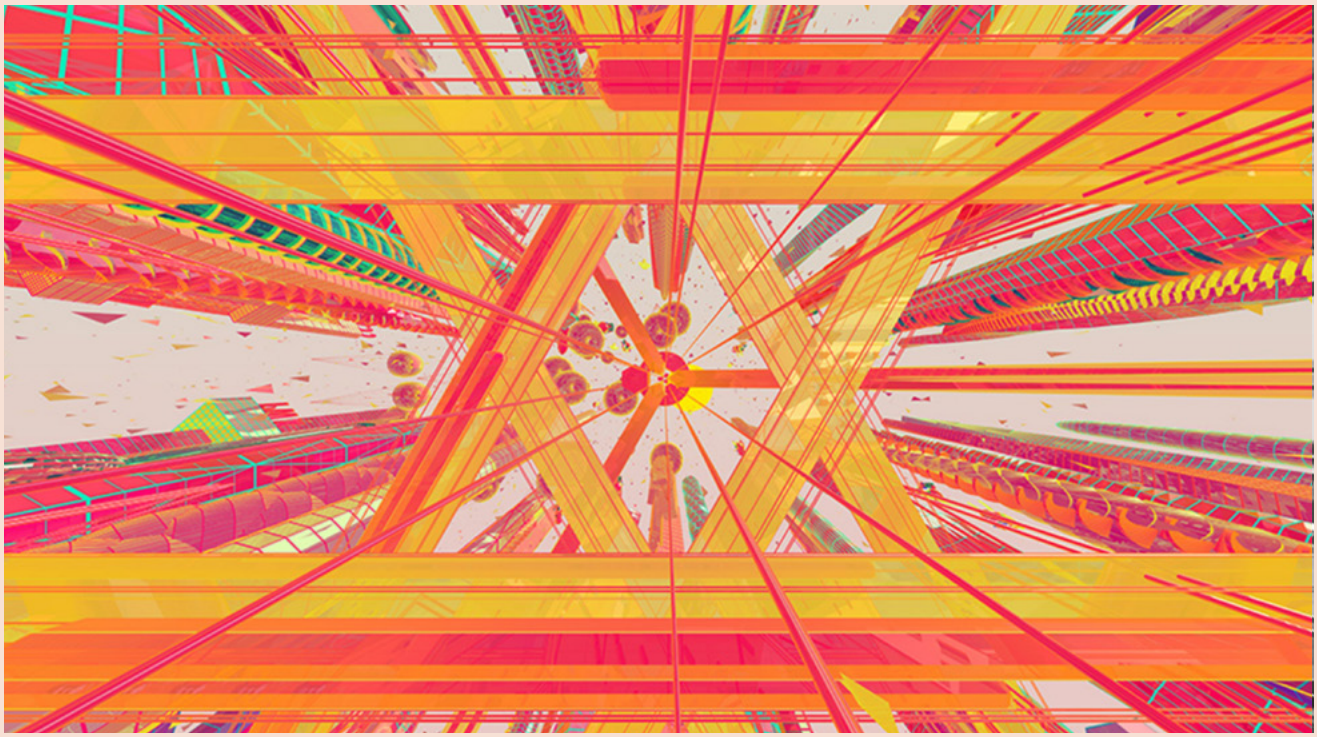
Since the treatment only lasts up to 48 hours after manufacturing, shipping or flying the product from Korea is unrealistic. Consequently, manufacturing NEURONATA-R® in accordance with current Good Manufacturing Practice (cGMP) is the most critical point in discussions with potential partners.

How do you see the future of the Korean industry?

KSK: Over the course of the next year, we are expecting [Phase III] IND approval from the US FDA [for NEURONATA-R®] and a tech transfer agreement with a partner.

Corestem is already listed on KOSDAQ. Although stem cell and gene therapies are a relatively uncertain market for investors, interest has grown significantly in Korea, offering a favourable environment to attract further investment and to boost the value of the company.

As the pioneer of Korean stem cell companies, I firmly believe that other companies will follow our strategy as a route to achieving success in launching stem cell products from Korea and [other] markets. [This] interest will ultimately provide treatment for all patients regardless of country, race and income.



Jongmoon Kim
CEO, ToolGen

> “Our slogan [is] ‘innovate genome’ – to innovate within the gene therapy project”

ToolGen CEO Jongmoon Kim has witnessed his country’s stunning industrial transformation since the end of the Korean war into one of four Asian economic tigers – and today, he hopes to be at the vanguard of South Korea’s innovative biotech story. He highlights, “Korea has grown from a poor nation into a highly developed one. Nonetheless, we have never led in a platform technology. We are always following.” With a rather unorthodox background in IT, having previously worked with IBM Korea and pioneering Korean IT companies like TriGem Computer and ThruNet, the first Korean company to be listed on NASDAQ, these days Kim is bringing that extensive commercial and internationalization experience to ToolGen, a Korean genome editing company.

While CRISPR is probably one of the most exciting new technologies to have emerged in the past decade, and many companies are exploring this transformative platform technology, ToolGen prides themselves on being the only company in the world to develop three generations of landmark genome editing tools, with the first emerging in 2006 called Zinc Finger Nuclease (ZFN) technology, the second developed in 2011 called the TALEN (TAL effector nuclease), and finally the

most recent third-generation technology known as CRISPR/Cas9 in 2012.

Kim shares, "our technology is able to edit specific gene sequences. Our genome editing technology uses a targeted cleavage in the genome for efficient genome editing. CRISPR simplifies some of the complex tasks required of researchers, which is why our technology is being utilised around the world to develop new solutions to gene-based challenges."

While CRISPR and other gene-editing technology today is all the age, Kim is quietly confident, revealing, "what differentiates us from our competitors is that we own the ground IP, so can license it out to various players in the industry under special agreements. We can create our own projects and form collaborations across industries like biotech and agriculture. In 2017, for example, Monsanto in-licensed our IP for some seed developments." Furthermore, he adds, "CRISPR's innovation stems from its accuracy, cost-effectiveness, and simplicity to use. Conversely, the alternative technologies are more difficult to use, expensive, and lack accuracy.

He enthuses, "we have since developed two new advancements in our technologies: our Cas9 technology is significantly smaller than the previous versions, and thus the vessel can be more easily transferred into the cell. Our other development, called sniper cas9, has a much higher level of accuracy in its delivery." These strengthen their core IP and technology platforms.

Korean biopharma enterprises have shown a propensity for fruitful international collaborations and partnerships, and ToolGen is no exception. As Kim puts it, "we are a small and medium-sized biotech enterprise, so collaboration is non-negotiable. We aim to develop partnerships with the strong players across sectors, like Monsanto in agriculture, Thermo Fischer in life sciences, or the New York Stem Cell Foundation in stem cell therapies, with whom we recently signed a collaboration agreement along with nSAGE, a stem cell technology firm in Korea. Our main clients work in pharmaceutical companies, and other related sectors."

Excitingly, CRISPR's reach is not limited to healthcare. The US FDA ruled in March 2018 that it will not regulate CRISPR-edited crops as GM products, the agricultural industry has potential to become a client too. Moreover, CRISPR not only has the potential to reduce development costs but also cut development timelines from 13 to five years. The company has even achieved success in using their CRISPR technology in livestock too. Through the removal of certain gene expression, ToolGen developed the world's first muscle-strengthening pig, increasing the leanness and quality of the meat as well as the productivity and profitability of the farming.

Amidst all these efforts, ToolGen has also built their own proprietary portfolio for severe and life-threatening conditions such as Huntington's disease, age-related macular degeneration and diabetic retinopathy, hemophilia, and Charcot-Marie-Tooth disease. They have also developing a number of CAR-T therapies.

Having joined the company five years ago, Kim has grand plans for the company. He reveals, "the company is structured with the ambition of internationalization in mind and a view to taking the company global. To do this, we are developing both our scientific expertise – 56 percent of our employees are involved in R&D and 25 percent of our employees hold PhDs – and our administration services, to be prepared for the complexities of international business", adding, "our successes will be ensured in two ways: by thinking differently and implementing differently. All leading companies need a vision. Our slogan [is] 'innovate genome' – to innovate within the gene therapy project. Our ambition is to develop products which promote a healthy and wealthy life."

SOUTH KOREA

The industrial development of South Korea over the past six decades transformed the agrarian-economy of the 1960s into the world's 12th largest economy in terms of GDP in 2019. Korean industrial and electronic giants like Samsung, LG and Hyundai are household names globally, testament to the excellence of the Korean ICT and industrial infrastructures. During this period, the country has also undertaken monumental efforts to develop its healthcare ecosystem to foster the health and wellbeing of its citizens, with universal healthcare coverage achieved as early as 1989. Today, the compulsory National Health Insurance Scheme (NHIS) covers 97 percent of the population, and the country's overall healthcare system is regularly ranked amongst the best in the world.

In the past decade or so, the biopharma industry has also emerged as a leading sector in the country, bolstered by government support, a well-educated and industrious population, supportive financial markets, and more recently, the entry of Korean industrial conglomerates (chaebols). Already, South Korea is seen as one of the top clinical trials hubs globally and the ecosystem of innovative biotechs is thriving and energetic.

Blessed with these advantages, South Korea is well-positioned to excel in the field of precision medicine, where technology and medicine converge. As early as 2006, the Korean Genome Project (KGP) was initiated and homegrown genetics champion Macrogen's sequencing of a whole Korean genome was in fact the first sequencing of a North Asian genome. In 2017, the government unveiled its strategy to embrace the fourth industrial revolution under the direction of the Presidential committee on the fourth industrial revolution (PCFIR), which placed an explicit focus on precision medicine. In the same year, the Ministry of Health and Welfare also launched a precision medicine promotion body, led by the Korea University Medical Applied R&D Global Initiative Center (KU-MAGIC), with around USD 36 million dedicated to cancer therapeutics, the Precision Medicine-Based Cancer Diagnosis (K-Master) Project, and another USD 17.7 million to the development of a cloud-based hospital information system, the Precision Medicine Hospital Information System (P-HIS) Project.

Electronic medical records (EMR), an essential component of a healthcare system equipped for precision medicine, are already adopted in the vast majority of hospitals and clinics. In 2018, the Ministry of Science and ICT launched the Korea Advanced Research Network (KOREN), a blockchain-based medical data network to collect health data on a decentralized system in order to facilitate its transfer and sharing between hospitals. More recently, in January 2020, the Korean National Assembly introduced major amendments to its previously rigid privacy laws, allowing the use of pseudonymized health data for various purposes, including scientific research. What is even more impressive is that the South Korean medical system already provides next-generation sequencing (NGS) panel screening for all citizens – a first in the world – so genomic and clinical data from patients are being collected systematically.

Encouragingly, public sentiment is also very positive. In 2018, the Ministry of Interior and Safety conducted a national survey to examine their attitudes towards a Korea Centers for Disease Control & Prevention (KCDC) project to collect various clinical information to support the advancement of precision medicine. An overwhelming 94.5 percent of respondents supported the project with 83.5 percent intending to participate.

It is little wonder that Korean precision medicine companies are some of the most prolific and international players in the region, typically having already succeeded in launching novel products and technologies on the domestic market, and are now making forays abroad, forming ambitious ventures with foreign companies and positioning themselves for global growth. The next challenge would seem to be scaling up for operational success in overseas markets.

Jeong-Sun Seo
chairman, Macrogen; & president, KoreaBIO

Dr Jeong-Sun Seo, Chairman of Macrogen & President of KoreaBIO, illuminates the importance of precision medicine and the current hurdles impeding its widespread adoption.

What is the significance of precision medicine for Korea?

JEONG-SUN SEO (JS): Both Korea and the rest of the developed world face the challenge of an ageing population. The US government spent almost 18.9 percent of their budget on healthcare alone in 2019. Looking to the future, it is unsustainable to continue increasing healthcare expenditure. As a result, both in Korea and abroad, we must control healthcare costs.

Through precision medicine, we can receive lots of data, be it genomic data or EMR (electronic medical records). In the past, patients' EMR could not be used outside of the hospital. At the start of 2020, the key data privacy statutes, including the Personal Information Protection Act was relaxed to allow pseudonymized information to be used (without need of the individuals' consent) for scientific research, public record-keeping or business purposes, such as commercial market research.

> "MACROGEN WANTS TO FOCUS ON ASIAN PRECISION MEDICINE"

Korean companies, such as Macrogen, possess very good technology to analyse genomes. Combining genomic data with EMR data, healthcare and life information, as well as the already strong IT technology in Korea, offers precision medicine a good chance of success.

What do you view as some of the main challenges in advancing precision medicine and genomic sequencing?

JS: Although the cost of collecting genomic data has fallen over time, it is still around USD 600 per individual. Collecting a sufficient sample of data, say of 100,000 people, would require up to USD 80 million – a significant investment beyond the reach of most private institutions.

The Korean government has a goal of collecting the genomic data of one million patients. To share this data requires a large data ser-ver. Other companies with smaller ser-vers lack the capacity to analyse large genome sequencing. To facilitate collaboration, we should use a cloud server.

88 percent of patients enrolled into clinical trials in the USA are Caucasians. While this trend is now slowly changing, with greater diversity of patients, there remains some way to go. If we consider the number of Asians, it is 4.5 billion. Many of the Asian countries are not wealthy. Nonetheless, developing countries need healthcare and better treatments.

Macrogen wants to focus on Asian precision medicine. Last year, Macrogen published almost 1700 sets of Asian genome data through the GenomeAsia 100K Initiative, an international consortium. This is a large sample and was well received by researchers. We hope to acquire the genome data of 100,000 Asians in the near future. In 2016, we published a Nature paper displaying the characteristics of Asian genomic data, which has helped to build our reputation in this area of study.

Some believe that the responsibility to develop these tools should be with the public sector. The reality is that procedures within the public sector are often excessively bureaucratic, making progress too slow. Furthermore, the government lacks the expertise required. In my view, the private sector should be given the task, under strict guidelines and support from the government. This strikes a balance between speed, innovation, and benefit for the society as a whole.

A GLOBAL APPROACH TO KOREAN REGENERATIVE MEDICINE

Under the stewardship of regenerative medicine industry veteran BG Rhee, Korean firm SCM Lifescience has engaged in several global M&A deals in the past year with the end goal of finding a combination of assets that will bring value to both investors and patients. With a US manufacturing facility now in place, as well as R&D operations in Italy, SCM has raised USD 25 million by listing on the Korean Stock Exchange (KOSDAQ) on June 17th, 2020 and propelling the company to the next level

FROM US MANUFACTURING...

In February 2019, SCM – in partnership with fellow Korean firm Genexine – acquired the US immuno-oncology company Argos Therapeutics for around USD 11.1 million. Argos, listed on the Nasdaq until early 2018, was a Durham, North Carolina-based biotech that developed personalised anti-cancer treatments with mRNA loaded dendritic cells. Argos had conducted Phase III clinical trials on 462 renal cancer patients in the US, Europe and Israel through more than 120 clinical sites but was not able to prove the statistical effectiveness of its treatments.

The acquired company – renamed Co-Immune – now operates as an independent entity in the US and gives SCM the ability to manufacture high-purity stem cell treatments in the US using its original isolation of stem cell technology as well adding Argos's original technology immuno-oncology using dendritic cells to its pipeline. Speaking at the time, SCM Lifescience CEO BG Rhee said that this would allow the company to make greater inroads into global markets.

SCM is not alone in being drawn to advanced manufacturing in the US. With the global regenerative medicine market expected to grow at a 23.7 percent CAGR and reach USD 50 billion in value by 2021, global firms are increasingly looking towards the infrastructure, talent and capabilities of the US market to meet their advanced biomanufacturing needs.

...TO ITALIAN R&D...

In the wake of the Argos acquisition and the rebranding to CoImmune in the US, a SCM project that had been on the back burner for some time reappeared: the acquisition of Formula Pharmaceuticals, a firm focused on the development of a best-in-class CAR-therapy platform to overcome key shortcomings of existing CAR-T approaches. Formula Pharmaceuticals'

CAR-CIK (Cytokine Induced Killer) technology leverages allogeneic cells from cord blood and proprietary non-viral transfection through the SB100X gene transfer system.

The merger between CoImmune and Formula went through in January 2020 and the merged company has continued to focus on running a Phase IIb trial for lead asset, CMN-001, in advanced metastatic renal cell carcinoma (mRCC). The US FDA approved CoImmune's investigational new drug application (IND) CMN-001 in February 2020 and cleared it to move forward with the Phase IIb trial.

> "CURRENTLY THERE ARE 6-7 STEM CELL PRODUCTS ON THE GLOBAL MARKET. FOUR OF THEM ARE KOREAN PRODUCTS."

The close of the Formula deal was accompanied by a USD 6 million investment in the combined entity to fund the CAR-CIK program, which is currently in Phase I of the clinical trial process. Through sponsored research contracts with the M. Tettamanti Research Center, University of Milano-Bicocca and MBBM Foundation, San Gerardo Hospital, CoImmune will conduct non-clinical research and other necessary work for the development of CAR-CIK in Monza, Italy.

...TO THE KOREAN MARKET...

SCM will be looking to market its treatments firstly in Korea. Against the backdrop of a government push for Korea to be recognised as a global leader in the field of regenerative medicine, in August 2019 a framework was set out for conditional approvals of next-generation treatments for rare diseases and cancer that had only passed through Phase II of the clinical trial process.

Speaking to PharmaBoardroom in late 2018, Rhee commented on SCM's role in putting this framework in place. "We are currently in discussions with the Korean government with the aim of amending the laws relating to advanced biopharmaceuticals and regenerative medicines," he noted. "In Japan, which is now very aggressive in the field of stem cells and regenerative medicine, their laws were amended in November 2014, so that after phase I trials there is conditional approval, and the next seven years are spent collecting the data from the patients for phase II and III trials. In the worst case, there is no efficacy, but the product is safe then the product will be left on the Japanese market."

Rhee continued, "In Korea, conditional approval may be granted only after phase II trials. Currently there are 6-7 stem cell products on the global market. Four of them are Korean products. This is thanks to the special committee which helped small companies such as Pharmicell and Medipost to receive conditional approval."

...AND BEYOND?

Although SCM does not have plans to merge the USA manufacturing and Italian R&D operations, the company has raised around USD 25 million through a listing on the Korean Stock Exchange (KOSDAQ) on June 17th, 2020

Funding for regenerative therapies, though still difficult to source, is more readily available than ever before. As Rhee admitted to PharmaBoardroom, "[regenerative medicine] is a new area for investment, which has a high return, and some risk involved. However, nowadays, it is more secure – even without 100 percent efficacy in an indication, it is still possible to find good and promising data." The question remains how much funding SCM can secure and whether its next-generation therapies can eventually reach patients worldwide.

Cancer Precision Medicine

Cancer is the second leading cause of death globally, accounting for a quarter of all deaths in 2019. Driven by the fundamental genetic component in cancer and the high level of disease heterogeneity, the majority of precision medicine efforts in therapeutics have centered on cancer. Broadly speaking, over 100 different types of cancers in different organs and tissues have been categorized but in recent years, some cancer types have undergone increasingly finer classification as our understanding of the diseases has advanced. These efforts have given rise to a number of new therapeutic approaches including targeted therapy, as well as cell and gene therapy.

Breast cancer is perhaps one of the hallmark examples: today, after cancerous cells have been identified from the patient's biopsy, one of the tests performed is a HER2/neu test to evaluate the levels of the human epidermal growth factor receptor 2 (HER2) gene. This is important as a number of cancer therapies specifically targeting HER2-positive breast cancer have been developed. Even before any cancerous cells have been found, women can also undergo a BRCA gene test to assess their potential risk of developing breast and ovarian cancer.

Cancer precision medicine is a critical topic in Asia not only because the region possesses a significant incidence of cancer globally but also because there are sharp differences in the prevalence of certain types of cancer, notably gastrointestinal cancers. Over two-thirds of the world's liver, esophageal and gallbladder cancer cases occur in 15 Asian countries, with the vast majority of that coming from China. In recent years, a number of companies have answered this call to arm and similarly to global trends, a significant part of precision medicine efforts in the region focus on cancer.

At the same time, the heterogeneity of the region also makes it difficult for precision medicine approaches to be adopted widely across healthcare systems. Many of the less-developed countries lack the healthcare infrastructure required for the molecular testing and dedicated cancer care facilities, as well as the public health expenditures to afford the effective but costly new therapies, be they immuno-oncology therapies or targeted therapies or cell and gene therapies, which usually surpass six figures USD. Comparatively, the annual health expenditure in Southeast Asian countries is USD 550 per capita. Companies in Asia have to confront not only the complexity of disease but also the challenges of access and affordability.

Yeul-Hong Kim, Director of K-MASTER, details the project's success in creating a shared database of genomic data for Korean oncology professionals. Kim also explains the importance of collaboration with Big Pharma in their oncology projects, and the potential to become a pan-Asian venture in the future.

Yeul-Hong Kim
director,
K-MASTER

How do K-MASTER's operations fit within the ambitions of the Korean government regarding precision medicine?

YEUL-HONG KIM (YK): The Korean government set a goal of collecting 10,000 cancer patients' genomic profiling data and clinical observations to form the initial database. The second goal was to widen the general coverage for precision medicine in Korea, expanding the participation in the project to every area of the country. We currently have 54 large university hospitals participating in the project and the clinical trials are run by the Korean Cancer Study group. All oncologists in the major hospitals are therefore participating in the project, which makes it truly nationwide.

Initially, the government wanted to focus on the most prevalent cancer types within the Korean population. However, the new targeting genes are observed in every form of cancer, so we can find mutations across types. Thus, we collect data on all cancers and from as many tissues as possible to maximise our data collection.

The Korea precision medicine initiative includes two projects sponsored by the Korean government. One project, P-HIS, is focused on cloud-based data collection systems, which can be shared across all of the hospitals in Korea. In that way, we can share patient data together and initiate one database.

The second project, K-MASTER project, is focused on cancer diagnosis and treatment. This project involved the next generation targeted sequencing and genomic profiling of tumour and circulating tumour DNA from cancer patients. We also connect this genomic data with clinical data by merging the databases, which can then be utilised for new drug development and for prognoses. It is very important that we have collaboration with pharmaceutical companies so that we can act as a bridge between patients and the developers of future treatments. Pharmaceutical companies also want to utilise this data in drug development.

Finally, we are establishing a big cancer genomic database with clinical information. We are not only establishing a large database but are investigating how we can utilise this data for new drug development while keeping within the restrictions of data privacy.

Compared to Japan, Europe and the USA, what is your assessment of the level of Korean science?

YK: Especially in the field of medical oncology, Korean scientists are very advanced and well-educated. There are around 350 medical oncologists in Korea with a well-organised training programme. Moreover, most oncologists have at least 1-2 years' experience of working in the USA or Europe, exposing them to very advanced clinical trials systems. They are well aware of precision medicine and accustomed to applying it to patients.

Notwithstanding that, the rapid pace of development in oncology research leaves many struggling to stay at the forefront of the field. Furthermore, there

is still so much that we do not understand regarding the role of germline or somatic genomics in cancer.

To keep our oncologists up to speed, we have developed a portal site and decision-assisting program for better utilization of our genomic data. Through this platform, doctors and researchers can look up the landscape of certain mutations and find out what type of clinical trials are ongoing around the world. This programme supplies the necessary tools to aid the decision-making process of doctors.

What is the level of interest amongst global multinational companies towards the K-MASTER project?

YK: Innovative Korean pharma companies are still in their infancy, and thus have smaller pipelines and limited capabilities for drug development. Hence, we need to connect larger, experienced pharmaceutical companies around the globe and seek their assistance through partnerships.

> “WE NEED TO PLAY OUR PART IN ENSURING THAT WE CAN CREATE A SYSTEM TO OVERCOME SOCIO-ECONOMIC CONDITIONS TO OFFER THE BEST ACCESS TO PATIENTS ACROSS THE CONTINENT, NOT ONLY IN THE DEVELOPED ASIAN NATIONS”

In general, the global pharmaceutical companies are very responsive to our projects. However, each company has an interest in a specific stage of development, which varies widely across the industry. Often, we find that we are in a slightly earlier or later stage than the general development roadmap of the specific new drug and thus there may only be limited interest, particularly in the early investigative phases. Regrettably, their development policies sometimes change, abandoning the partnership to pursue other developments. This leads to some pipeline candidates being discontinued. These are amongst the main challenges that we at K-MASTER face.

Nonetheless, our ambition is to run as many clinical trials as possible to maximise Korea’s chances of developing oncology treatments. We ask the pharmaceutical companies to supply the drugs for clinical trials and cover specific expenses such as customs and shipping. The remainder of the financing for conducting trial is covered by our fund.

Are you looking to expand your projects to include other Asian Nations?

YK: While the current plan is only for Korea, my ambition is to share this data and open up our portal system. At this time, we have uploaded the data of 6,500 of our 10,000 patients into our portal, which scientists in Korea can access online. Sharing this data and collecting more data from other Asian countries will be paramount in the long term for our project.

I am the president of the Asian Oncology Society, in which most Asian countries are represented. This also includes a clinical trial committee and a committee for standardised treatment guidelines. Across Asian countries, the main stumbling blocks are the unequal levels of scientific know-how and the variable quality of medical systems, ranging from world-leading to highly underdeveloped in some of the poorer nations. In developed nations, like Japan and Korea, most cancer drugs on the market have been approved. However, in underdeveloped nations, there are very few cancer drugs currently available. This makes it difficult to expand our current approach to developing Asian countries. We need to play our part in ensuring that we can create a system to overcome socio-economic conditions to offer the best access to patients across the continent, not only in the developed Asian nations.

Gencurix was the first Asian company to develop a prognostic diagnostic test for breast cancer. Its CEO, Dr Sangrae Cho, discusses the importance of creating a test tailored to Asian patients, explores the company's expansion plans into China, Japan, and Southeast Asia, and the synergies in their partnerships with big pharma.

What have been the major achievements in Gencurix's history?

SANGRAE CHO (SC): Our biggest achievement is developing Asia's first prognostic diagnostic test for breast cancer. While there were already several prognostic diagnostic tests available internationally, none were developed in Asia. We are the first to develop a test designed specifically for Asian patients. One of the main problems was that other tests were over-classifying the majority of patients into high-risk groups, in which patients are advised to undergo chemotherapy. Thus, patients were over-treated, with toxic results. Our prognostic diagnostic test accurately identifies low-risk patients that do not require chemotherapy.

The main differences between Asian and Caucasian breast cancer patients are that in Asia, 50 percent are under the age of 50. Finding the unique algorithm specifically engineered for pre-menopausal Asian patients was an important step for us and was crucial in confirming the accuracy of our test.

A key pillar to our success has been utilising open source big data to discover unique unpatented biomarkers which are accurate predictors and highly detectable. We also look at developing early diagnostics through specific biomarkers.

You are also developing the GenesWell ddEGFR Mutation Test for lung cancer. What is the current status of this project?

SC: We have already received approval from the Korea FDA. It is the first product in the world to receive regulatory approval based on a digital PCR system. The hospitals that possess digital PCR have already adopted our GenesWell ddEGFR Mutation Test. The current product can detect 43 mutations, with a second-generation product based on plasma to detect over 100 mutations currently in the pipeline.

Sangrae Cho
CEO, Gencurix

In addition to the EGFR lung cancer test, we are also investigating the viability of a comprehensive diagnostic solution package for patients with a screening test for colorectal cancer and with further companion diagnostics available for breast cancer testing.

How important is collaboration with pharmaceutical companies?

SC: Cancer treatments now consist of first, second, and third-line therapies [as] over time patients begin to develop a tolerance to the drug.

We have three current collaborations with Big Pharma. The first is with Pfizer for our GenesWell BCT Test. Pfizer has a drug, palbociclib, which is designed for patients suffering a relapse of breast cancer. Our joint project studies how well palbociclib can prevent the recurrence of breast cancer in patients categorised as high-risk by our test. This collaboration has proven to be highly synergistic. This demonstrates how we are able to expand our offering into companion diagnostics services, helping Pfizer's treatment to target the high-risk patients.

For our EGFR test, we have been in collaboration with AstraZeneca for their treatment Tagrisso. This is administered to patients with the T790M mutation, which our tests can detect. We have conducted many clinical evaluations, and given our digital PCR system, we have very high sensitivity in detecting this mutation.

We are also working with another company to develop a new drug [targeting] lung cancer patients with the C797S mutation.

Microbiome

Over the past few years, the microbiome has emerged one of the hottest research topics at the forefront of cutting-edge science. Referring to the collective genomes of our microbiota – the community of diverse micro-organisms that live in and on us – technological developments in genome sequencing have opened the doors to closer study of our most intimate neighbours, the vast majority of which live within our gut. Large-scale metagenomic projects like the Human Microbiome Project have found 3.3 million unique protein-encoding genes within our microbiome compared to the paltry 23,000 found within our own genome. A growing body of research is uncovering links between our microbiome and a host of diseases including but not limited to cardiovascular disease, obesity, infectious diseases, gastrointestinal conditions and even cancer, though the development of therapeutics has been hampered by the lack of clarity surrounding the exact nature of the relationships between dysbiosis (microbiota changes associated with disease states) and the diseases themselves.

While microbiome research is accelerating globally as well as in Asia, it remains a fairly niche field. Regionally, a number of initiatives have been established to drive momentum, including the Japan Microbiome Consortium comprising 17 leading pharma companies; the Asian Microbiome Project based out of Singapore; and the Taiwan Microbiota Consortium. A handful of enterprising companies are also developing new therapies and advancing this field, with eventual hopes of colonizing the global market. Notably, Korean genomic medicine leader Macrogen acquired the top microbiome company in the US, uBiome, in 2019.

Genome & Company, with a market cap of USD 280 million, is the highest valued microbiome company worldwide. Dr Jisoo Pae, its co-founder and CEO, sat down with PharmaBoardroom to shed light on the company's origins, its collaboration with Big Pharma, and the ease of gaining capital investment for a Korean biotech.

Jisoo Pae
co-founder and CEO, Genome & Company

As the CEO and co-founder of Genome & Company, what led you to establish a biotech firm specialised in microbiome technology?

JISSO PAE (JP): I began my career as a psychiatrist, but later took an MBA programme at Duke University, and subsequently worked for Bain & Co as a management consultant and subsequently at MSD.

I founded Genome & Company with my friend from medical school, Dr Hansoo Park, who is the co-founder and current CTO. Having studied as a post-doctoral student at Harvard Medical School, Dr Park continued his research at Jackson Laboratory and became an expert in microbiomes. He approached me five years ago with the idea of setting up the company. Upon explaining the science behind it and its advancements in the US, we agreed to set up Genome & Company.

Five years ago, when I was introduced to microbiome technology, it was almost unknown in Korea. I predicted that interest would expand rapidly in the future, following a similar trajectory to the stem cell or antibody medicine markets. The healthcare industry is a large industry. Many new trends emerge and establish themselves. I was convinced this would be one of the critical emerging trends. Knowing that Genome & Company could benefit from taking the first-mover position in the market, it seemed like the right moment to make the move and kick-start our operations.

Can you introduce the main activities and areas of interest for Genome & Company?

JP: We are focusing on the microbiome and how to develop this into medicines. Our current most advanced programme is a microbiome immuno-oncology treatment. We have just received clearance from the US FDA for our Investigational New Drug Application (IND) and we are now entering phase I/Ib clinical study. Following this, we will finally have patient data to analyse. We are looking at a timeline of around eight years before approval. However, we will be able to commence discussions on licensing out sooner, depending of course on the findings of this initial data.

We also have a dermatologic and infertility programme, which utilises microbiome technology. Moreover, we are developing novel targets within immuno-oncology.

Microbiome treatment, originating from the human body, has several advantages compared to other treatments. The most significant is that it produces little to no side effects, which has very good implications in the development of our anti-cancer drugs. Whereas most anti-cancer drugs have punishing side effects, ours have very little, making it an obvious choice for patients. This also facilitates its use in combination therapies such as with anti-PD-(L)1 antibody treatments. This is just one example of the possibilities at our disposal: the potential for microbiome technology is unbounded.

What is Genome & Company's strategic business model?

JP: Licensing-out is our major ambition and we are actively engaged with multinational pharma in preparation for this. Our ambition is to continue to develop

innovative drugs and out-license, repeating this process for every development within our pipeline.

> WE WANT INDUSTRY PROFESSIONALS TO REALLY PAY ATTENTION TO WHAT WE DO AND WHERE WE ARE HEADED IN THE UPCOMING YEARS

We are currently undertaking a Clinical Trial Collaboration and Supply Agreement with Merck and Pfizer, combining our product with their anti-PD-L1 drug, Bavencio®. The success of companies developing anti-PD-(L)1 candidates is very beneficial to our business. The more successful and competitive the market in the PD-(L)1 sphere, the greater Genome & Company's possibilities for collaboration.

For the East Asian region, we are in also in a partnership with LG Chem for a licensing agreement. The negotiations prior to signing these partnerships has required Genome & Company to make significant efforts to give scientific proof that microbiome can be a viable drug candidate. The stumbling block was the ability to provide the necessary data. Convincing these companies to undertake partnerships with us was challenging not because of the lack of necessary data but because the microbiome-based drug candidate was a newly introduced modality. We had to convince them through a full set of research evidence and references at the pre-clinical level to give them the confidence that microbiome medicine could be applied in human trials. Nevertheless, having overcome this hurdle, it became easier to negotiate.

You mentioned that you filed an IND in the USA. What was the rationale behind targeting the US market before the Korean market?

JP: Naturally, the US market is the largest and fuels our global ambitions. Moreover, one of the intricacies with microbiome treatments is that they can react differently across races. We have sought out, from the outset, to verify that our programme works in Caucasian patients without modifications. That is why we entered the US first. Moreover, the US is an ideal location for this clinical purpose with ethnic diversity.

We are also beginning clinical studies in Korea, which will commence next year. This will target a cancer common in Asians but found infrequently in Caucasians. Hence, our studies target Caucasians in the US study, and Asians in the Korean study.

Advancements in microbiome technology are hampered by the insufficient manufacturing capabilities of this new industry. Tell us about your ambitions to expand your manufacturing footprint to fill that gap?

JP: Indeed, the number of microbiome ventures is increasing, and it is becoming popular amongst venture capitalists. Worldwide, there are around 500 microbiome companies. However, this uptake in microbiome venture companies is rapidly outpacing the growth in manufacturers. In fact, Contract Manufacturing Organisations (CMOs) remain hesitant to involve themselves in the market. As a result, demand is far outstripping supply and I see this gap widening even further in the next ten years.

Consequently, we have plans to expand our operations into contract manufacturing to consolidate and safeguard our future capacity. Genome & Company will provide contract manufacturing, not only for our in-house products, but as a partner for other upcoming industry players. Our profits will be reinvested to fund both development and clinical activities.

What is your final message to our international audience?

JP: We want industry professionals to really pay attention to what we do and where we are headed in the upcoming years.

Yan Tan, CEO of Xbiome, the first AI-based microbiome drug development company in China, outlines the rationale behind the firm's founding, what makes its technology platform unique, and the challenges of attaining funding for cutting-edge innovation.

Yan Tan
CEO, Xbiome

As the first AI-based microbiome drug development company in China, could you share what makes your drug development platform unique?

YAN TAN (YT): When we established Xbiome, I approached some of my former colleagues at the Broad Institute as well as companies in the US to learn from their approaches but we soon discovered that this area is really extremely new, particularly when it comes to using the microbiome to develop therapeutics. We could not even find a CRO in China to meet our needs. As a result, for the past two years, we have been focused on developing our own in-house capabilities.

To explain briefly, a number of different approaches and methodology have been developed to study the relationship between human gut microbiota and other parts of the body. There are a number of different challenges when it comes to studying gut microbiota. Traditionally, researchers used to study each microbial species as an isolated unit. However, most microbial species cannot be successfully isolated. A new field of research called metagenomics seeks to study a collection – known as a consortium – of different microbial species taken from samples directly extracted from natural environments. Due to the presence of many different strains of microbes, a lot of work is required to assemble, handle and clean this 'mixed' data so that it becomes usable. We, therefore, had to build our own AI-based metagenomics platform, develop our own databases and build our own modelling capabilities – all within the China context.

We also had to build our own 'culturomics' platform, which is complementary to our AI platform. We describe it as our link between the digital and the physical fields of our work. Metagenomics analysis allows us to infer what strains or combinations of microbial species could have therapeutic effects on specific diseases but that knowledge only becomes useful for drug development if we can isolate and culture these strains for production. We are working with Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences to leverage their laboratory facilities.

> "WE ARE ALSO COLLABORATING WITH OTHER ACADEMIC AND RESEARCH INSTITUTES IN CHINA TO ADVANCE THE BASIC SCIENCE OF GUT MICROBIOME RESEARCH"

We also had to develop our own in vitro assays to screen for potentially useful microbial consorta as well as build our own in vivo animal models.

Based on all these platforms and in-house capabilities, we have developed a couple of fecal microbiota transplantation (FMT) capsule products for the treatment of autism and graft versus host disease (GvHD). These are currently in investigator-initiated trials (IIT) in humans in China and we expect to use that data to file for US IND

later this year, with Phase IB trials expected to start next year.

The field of microbiome studies is still very new globally. What are some of the challenges when it comes to working with such cutting-edge science?

YT: Generally speaking, the mission for this new area is to establish causality and gather evidence for the mechanism of action for the efficacy of such treatments. In my view, there are two major challenges here. Firstly, compared to the development of small and large molecule drugs, not enough assays have been developed to assess the functionality of potential treatments. Functional assay screening for drug target identification is very mature in small and large molecule drug development, and most of the popular drug targets have been studied fairly extensively.

Secondly, most of the assays that we do have are based on microbial consortia, which produce a huge amount of complex data, so a lot of different computational approaches and methods have to be used to analyze the data. This makes it harder for us to identify the mechanism of action. We have to leverage sophisticated data analysis tools to strengthen the evidence demonstrating the therapeutic effects of certain microbial consortia.

In AI and machine learning, there is a concept called 'the curse of dimensionality'. It refers to data sets with too many features or variables. Specifically in our case, we are dealing with data sets with very high dimensions but a relatively small sample size, since it is difficult to procure clinical samples. We, therefore, need to apply modern AI approaches like network analysis and knowledge graph inference methods to reduce the dimensionality of our data in order to facilitate predictive modelling. What is positive is that AI technology is developing continuously. New algorithms or methods developed by Big Tech companies or academic researchers and programmers will also benefit the advancement of AI medicine.

At the same time, we continue to try to collect as much data as possible. We decided to start with human-first clinical trials to gather as much human data as possible, e.g. cohort data with healthy subjects, data of patients receiving FMT capsules as treatment, etc. At the beginning, we decided to acquire as many clinical samples as possible of different types – blood, stool, tissue, etc. – so that we could identify which therapeutic indications showed the most promise for FMT capsules.

We are also collaborating with other academic and research institutes in China to advance the basic science of gut microbiome research. In autism, for example, a lot of research has been done recently in terms of developing useful mice models for Tier-3 autism (the most severe level) for in vivo studies as well as developing functional in vitro assays for microbial screening. This is very important work because autism is quite a heterogeneous neurodevelopmental disorder that is still not well-understood. The diagnostic criteria for autism are behavioral so we need to have accurate mice models and the correct assays to establish mechanism of action and clinical efficacy.

A final message for our international audience?

YT: Xbiome's vision is to leverage emerging AI technologies to advance scientific frontiers in exciting areas such as microbiome to treat diseases globally. We are an international company and our team has a very international background. We want to open our platforms to potential collaborators all around the world, and we are very open to different collaboration opportunities including clinical and commercial co-development as well as the in-licensing of later-stage assets from global companies for the China market.

REGIONAL COOPERATION

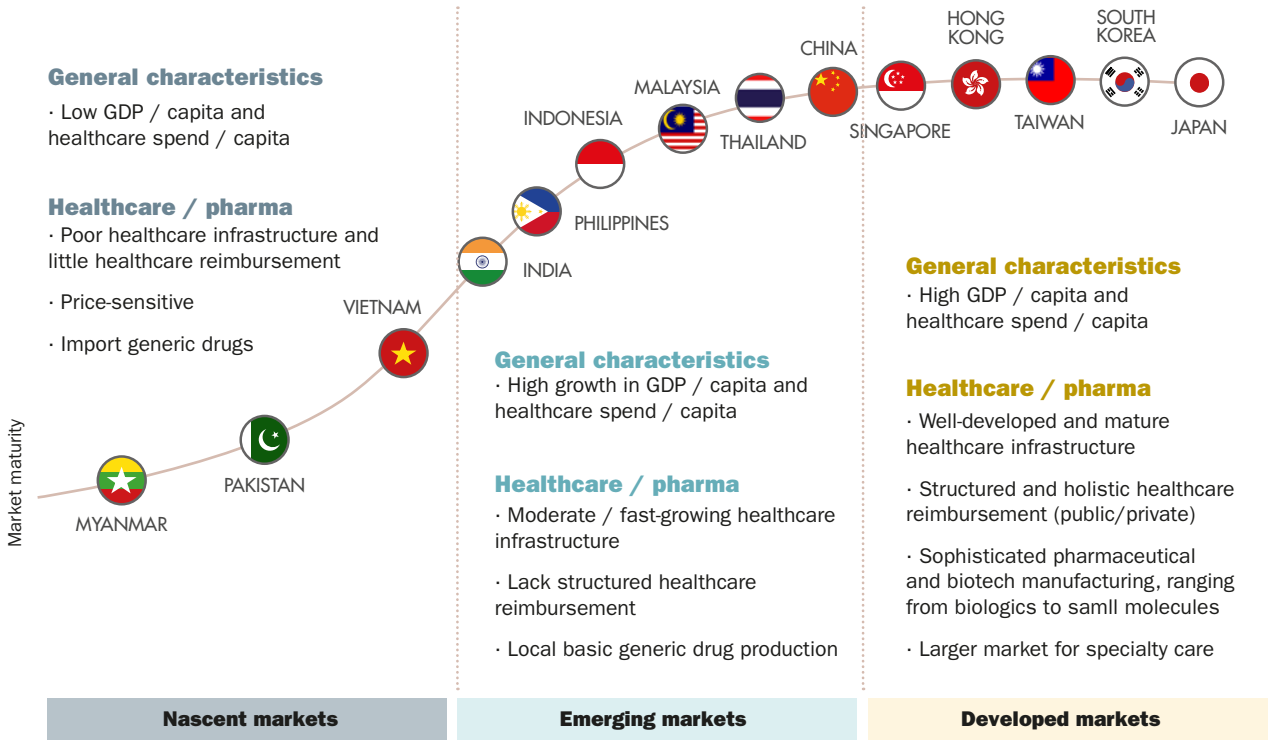
With Asia covering 60 percent of the world's population but accounting for just around 30 percent of global pharma spending, it goes without saying that healthcare needs in the region must be addressed effectively, quickly and comprehensively. Who better to accomplish that than the Asian companies on the ground, closest to the patients and the markets? However, while many Asian companies have proven adept at developing novel therapeutics and technologies, they often falter on the road to market.

As this report has highlighted, there are exciting hotspots of innovation across different aspects of precision medicine in the region, with countries leveraging their respective areas of strength to emerge as technology leaders in certain areas. Given the multidisciplinary nature of precision medicine, the distinct and often complementary strengths of different Asian countries across technology platforms in molecular diagnostics as well as therapeutic modalities, coupled with the large patient populations, seem to be the perfect recipe for Asia to leapfrog and lead the world in the advance of precision medicine.

However, despite their geographic proximity, the different Asian markets are not as well-integrated as one might expect, leaving many of the potential synergies uncaptured. One major cause of that is the high market heterogeneity within the region. Markets like Singapore, Hong Kong, Taiwan, South Korea and Japan behave much like developed markets with fairly high healthcare spending, developed healthcare infrastructure with well-articulated reimbursement systems, as well as their own biopharma industrial sectors. Most other Asian markets, however, fall on a spectrum between less developed and even less developed. With the exception of China and India, the second- and the eleventh-largest markets globally, the less developed markets are often deprioritized and even overlooked by the industry due to the challenges and costs of operating there.

Another roadblock to closer regional cooperation is the relatively low degree of regulatory harmonization amongst the different countries. International initiatives like the ICH and PIC/S have increased this somehow, as have region-specific actions like the Association of Southeast Asian Nations (ASEAN) Medical Device Directive (AMDD) approved by all member countries in August 2014. Asian regulators have also taken steps to increase exchanges and linkages between each other. For instance, Japan's Pharmaceuticals and Medical Devices Agency (PMDA), one of the most respected regulators in the world, offers HR development programs through its Asia Training Center (ATC) for Pharmaceuticals and Medical Devices Regulatory Affairs, established in 2016.

MARKET FEATURES OF SELECTED ASIAN MARKETS



Source: L.E.K. analysis based on IQVIA and IMF

Nevertheless, with the obvious exceptions of China, Japan and India, most of the markets in the region are far too small to successfully commercialize homegrown product and service offerings, no matter how novel or transformative – a structural weakness that many industry stakeholders have observed. This means that regional cooperation is not an option – it is the only way forward.

Another comparative area of weakness is the still-developing capital markets in the region when it comes to biopharma or biomedical investments. Though the landscape has evolved rapidly over the past few years, growing in size and sophistication, the general consensus amongst industry players seems to agree that investor appetites in Asia (excluding China) are still fairly cautious, especially when it comes to the sector's longer investment horizons. When investment dollars do flow, Chinese companies receive the lion's share. As Hong Kong-based cancer diagnostic player Sanomics CEO Stanley Sy muses, "how can a company like Sanomics survive between two giants: China and the USA?"

How should homegrown champions in other countries deal with the hefty gravitational pull of the China market? For Sanomics, the trick is understanding the realities of regional markets. He shares, "patients in South East Asia are often overlooked. For companies in the US, it is difficult for them to penetrate these markets, mainly because the regulatory environment is very bureaucratic. In China, the idea of genetic testing is not well-received there, and as a result, there are fewer genetic companies in the market. This means that the Chinese market is sufficient for the limited number of companies in operation, reducing their incentive to expand into Southeast Asia." As a result, Sanomics has been able to penetrate over 20 countries with a sales and marketing team of only seven people.

Other companies have also realized that the region offers tremendous opportunities to those bold enough to take the first step. For instance, Korean diagnostic company Gencurix has already outlined a pan-Asian strategy. CEO Sangrae Cho shares, "we already have plans to enter the market in China. Even without receiving regulatory approval, there are still channels to enter the Chinese market. We are going to establish a partnership with a company in China to set up a lab [to] provide our BCT tests to Chinese patients. In Japan, we have conducted feasibility studies with some of the main hospitals. These studies have shown promising results. For the rest of Asia, we will provide a centralised service. The customers will send the samples directly to our lab in Korea, where they will be analysed. This will remove the need for further regulatory approval. Dependent on market growth in the future, it may be beneficial to set up another local lab based in Singapore to handle demand from the Southeast Asian market."

> "patients in South East Asia are often overlooked"
>
> **Stanley Sy** SANOMICS

The diversity of languages and cultures within Asia may not facilitate communication and cooperation between companies and institutions but as long as all stakeholders speak the language of patient-centricity, the region can advance in its development and deployment of precision medicine to deliver more precise, effective and efficient therapeutics to its patients.

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