PHARMA BOARDROOM

InFocus

5 Biotechs to Watch

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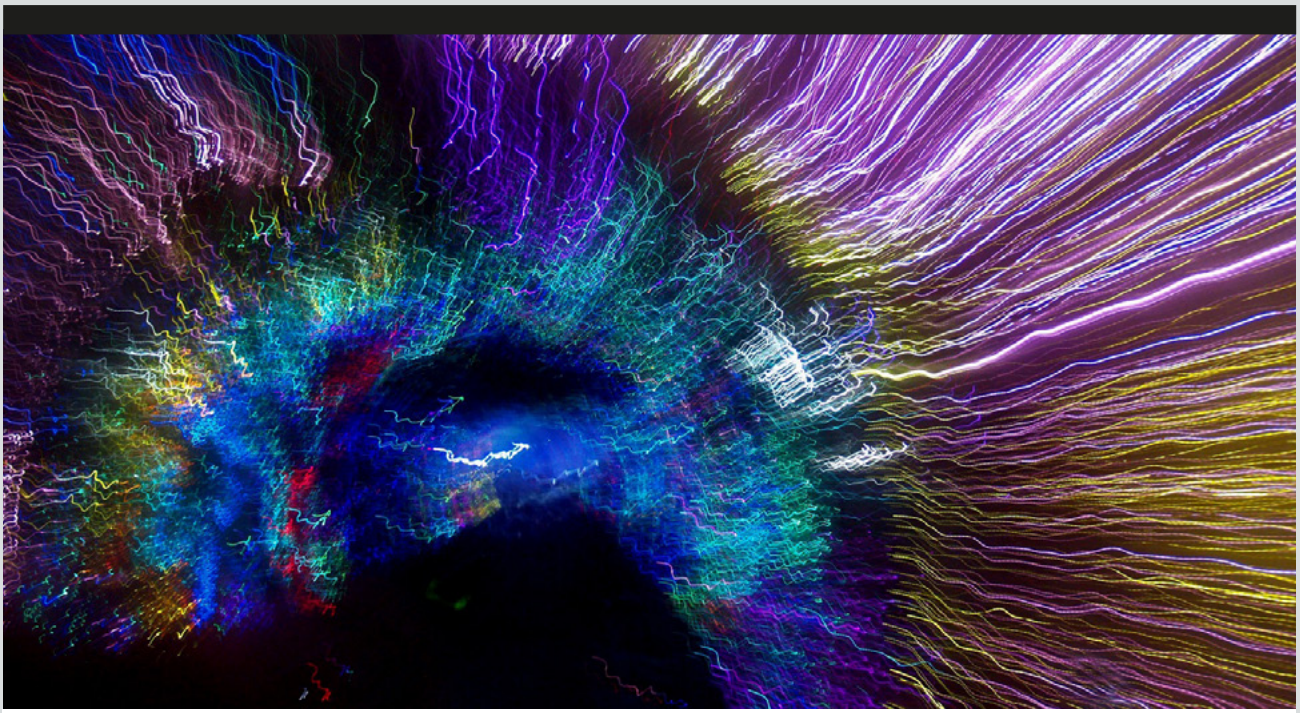

CHINA

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Preface

It is difficult to define the genesis of China's ascent in the global biopharma arena. Should we focus on the rash of healthcare reforms implemented across varying levels of government over the past few years, including the promulgation of a number of regulatory-related notices from the country's top leadership bodies, the 2016 launch of China's 'Healthy China 2030' strategic national plan, and China's entry into the International Council of Harmonization (ICH) as a full regulatory member in 2017? Or do we venture a decade earlier to the launch of significant healthcare system reforms beginning in 2009 under the oversight of then-Minister of Health Dr Chen Zhu?

Or perhaps we need to look further back to the 1979 opening-up of modern China under then-Premier Deng Xiaoping, which, among other things, led to unprecedented droves of Chinese students going abroad to further their education and careers in countries like the US and Canada? A couple of decades later, many of them returned to China, bringing a wealth of

industry experience that has proven crucial to kickstarting China's biopharma innovation journey. This period also saw the entry of foreign players and investment into the market. By 1997, 18 of the top 20 global pharma companies had established manufacturing plants in China (though there would be many exits and re-entries in the ensuing two decades), and approximately 40 percent of state-owned pharma enterprises in China had received some level foreign investment, creating a base for technology transfer and skills training.

Or perhaps we should trawl even deeper and look at the long and eminent history of traditional Chinese medicine, which can trace its roots as far back as the second century BC and, two millennia later, led to the discovery of the antimalarial compound artemisinin in 1972 by a Chinese team led by Dr Tu Youyou, who would go on to win China's first and only Nobel Prize in medicine, in 2015.

No matter when the odyssey is said to start, what is evident is that in 2020, the 'Chinese biotech revolution' is well underway, and with 1.4 billion people representing the second-largest healthcare market globally – and rapidly growing – there is no turning back. It is estimated that thousands of biotech companies have already been established in the past few years, with the majority clustered around the bustling cities of Shanghai, Beijing and Shenzhen. Flush with cash from both public and private sources, as well as aggressively supportive policies from the Chinese government, the homegrown biopharma sector has enjoyed an unprecedented level of growth in the past decade. With the majority of start-up entrepreneurs and founders boasting extraordinary scientific and industry credentials, a new breed of biotech companies with startlingly deep pockets, robust pipelines and portfolios, and a hungry global vision – has emerged in China.

This inaugural edition of the InFocus Five Biotechs To Watch in China has selected companies at different stages of the biotech journey in order to showcase the diverse and multifaceted nature of Chinese biopharma innovation. While these companies are no doubt bound by a number of similarities, it is the differences that make their individual stories so exciting.

A famous Chinese saying goes, once you have covered 90 percent of your trek, you are halfway there ("行百里者半九十"). We invite you to learn more about the compelling stories of the five companies profiled within this publication and join them on the long path towards biopharma innovation.

In recent years, with the unfolding of reforms within the pharmaceutical regulatory landscape and the establishment of a more open and inclusive capital markets structure, China has been working to improve its policy environment in order to encourage pharmaceutical innovation. Accordingly, the Chinese pharmaceutical industry has advanced in leaps and bounds. In 2008, the establishment of the National Science and Technology Major Project attracted a significant wave of overseas Chinese scientists and researchers to return to China to set up their own companies, advancing the cause of domestic pharmaceutical innovation.

In 2015, the Chinese regulatory regime began to undergo reforms in earnest, promulgating a series of policies intended to foster pharmaceutical innovation as well as strengthen intellectual property (IP) protection, accelerating the pace of new drug development and translational science. As the reforms have advanced, the regulatory hurdles impeding innovation have been steadily eliminated. As the globalization of drug R&D continues, China has also become a priority destination for global multi-regional clinical trials.

In 2017, the Chinese regulator, the National Medical Products Administration (NMPA), officially joined the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), highlighting the convergence of the Chinese regulatory system with international norms. As the second-largest economy in the world, China is a staunch supporter and defender of economic globalization. In the same vein, achieving mutual recognition of clinical trials data from China and global is the only way for Chinese pharmaceutical innovation to go global. On 30 March 2020, NMPA stipulated that it would now accept global clinical trial data in NDA filings for the China market.

Before 2015, there was a gap of between five to seven years between new drug approvals in the US versus in China. Following the aforementioned Chinese pharmaceutical reforms, this time lag has been reduced to one or two years, and in some cases, even a few months. As a result, the numbers of NDA approvals and launches have increased noticeably. It is clear that more and more global innovative drugs are now able to enter the Chinese market, offering more options to patients in China and allowing them to access and benefit from new therapies at the same time as patients globally.

In this process of internationalization, China's domestic innovation capabilities and achievements are gradually emerging. In December 2018, the biotech FibroGen's internally-developed first-in-class drug roxadustat became the first innovative drug to be launched first in China before other markets globally. In November 2019, the NMPA gave a conditional approval to sodium oligomannate, a therapy for Alzheimer's disease developed by the Shanghai Institute of Materia Medica (Chinese Academy of Sciences), which has the potential to fill the global gap in this

Dr Song Ruilin

chairman, PhIRDA

therapeutic area. Also in November 2019, BeiGene's internally-developed cancer drug, zanubrutinib, received accelerated approved by the US FDA, becoming the first Chinese-developed anticancer drug to be approved through one of their four expedited approaches for serious diseases.

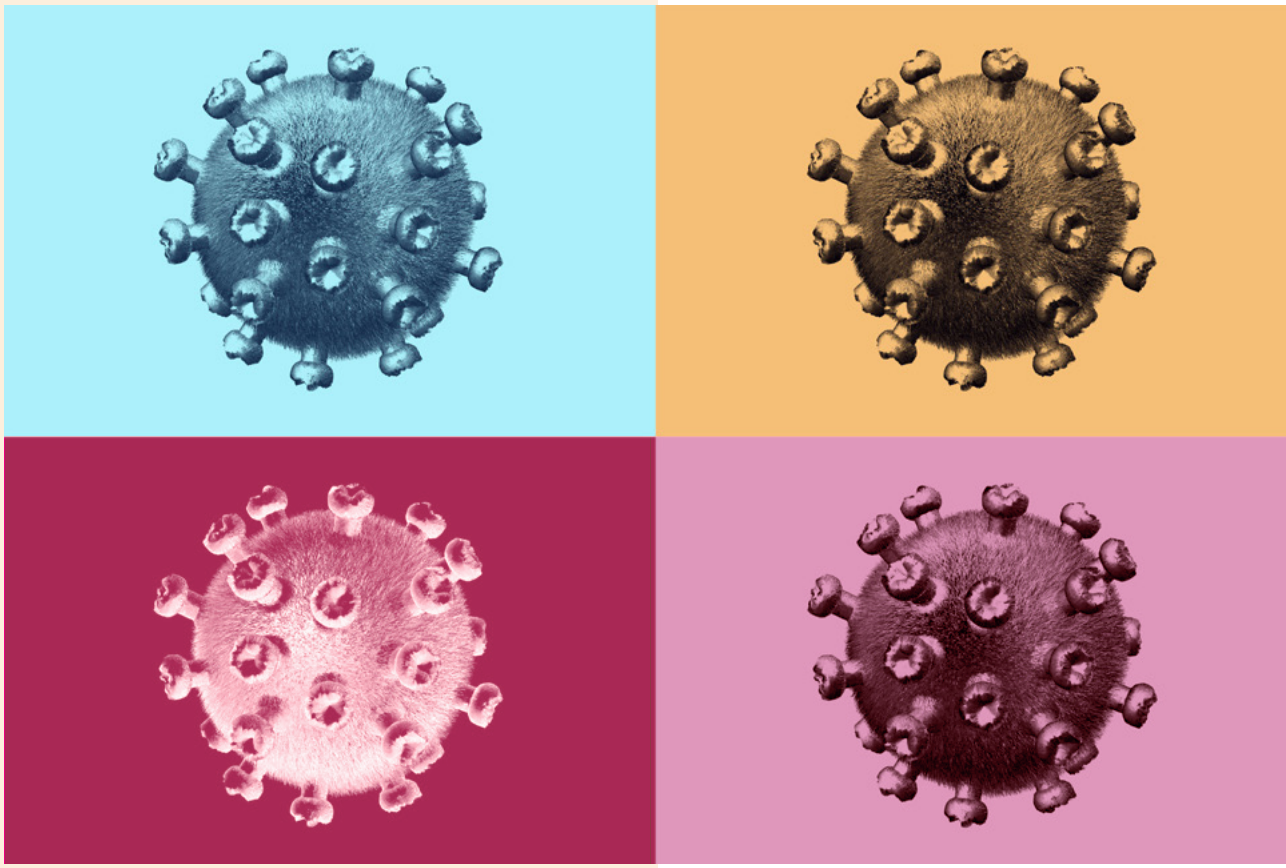
At the same time, many Chinese companies are expanding their global presence, including companies like Innovent Biologics, BeiGene, Jiangsu Hengrui, Hutchison MediPharma, Ascentage Pharma – to name just a few outstanding enterprises – who have begun working on global clinical trials. Through this progress, China is now becoming a contributor and provider of value to the global innovation ecosystem. In 2018, McKinsey added China to the list of second-tier innovator countries, alongside the innovative markets of Europe and Japan, reflecting the tremendous progress made in Chinese pharmaceutical innovation. China has now advanced from being a global innovation 'follower' to a 'parallel runner' – with the ultimate ambition of becoming a global innovation 'leader'.

A WATERSHED YEAR FOR CHINESE BIOTECHS

2020 will certainly go down in history as a watershed year for the global community, as a new strain of coronavirus – later named SARS-CoV-19 – originating from the city of Wuhan in China circulated around the world in just months, wreaking havoc on economies and disrupting the lives of effectively the entire global population of 7.8 billion.

Even as the pandemic has painfully exposed the inadequate levels of pandemic preparedness in many, if not most, countries, as well as underscored the profoundly deep integration of global networks and linkages across not only healthcare but virtually all other industries, over the past few months, the global healthcare industry has banded together with regulatory, academic and medical stakeholders to put up one of the most united fronts against disease – in history. Intense R&D efforts to identify, develop and deliver therapeutics and vaccines for COVID-19 – as the disease caused by Sars-CoV-19 is known – are now underway.

Quite naturally, China is now one of the frontrunners in what some industry observers have exuberantly termed the 'space race' of the 21st century. While Ground Zero for the pandemic, within a few weeks of the virus' public discovery, the country implemented severe measures, including a full-scale lockdown of the entire city of Wuhan with its 11 million citizens and significant travel restrictions. By April, just a few



months later, China seemed to be on the path towards some semblance of normalcy, even as other regions, particularly Western Europe, Latin America and the US, started seeing cases spike dangerously into the hundreds of thousands.

According to the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), at the beginning of May, there were already over 130 COVID-19 therapeutics under investigation and around 80 vaccines in development. Notably, half of the vaccines currently in clinical trials – ten in total (as of 5 June 2020) – were discovered by Chinese companies, partly driven by heavy Chinese investment. Other Chinese biopharma companies, even those primarily focused on other therapeutic areas like the following two biotech companies on our inaugural list, are also answering the call to arms, eager to serve in any capacity they can.

Dr Joan SHEN, CEO of I-Mab Biopharma, shared the sentiment common across many Chinese biotechs, "it is a very challenging situation the whole world has to face but if we work together, I believe we can turn challenges into opportunities." This is why, despite the company's portfolio focusing on oncology and autoimmune diseases, "when the pandemic unfolded, we decided to look at our assets to assess their potential relevance." Shen emphasized, we wanted to do something useful to contribute instead of simply waiting anxiously for the pandemic to end."

One of the potential complications of COVID-19 is what is known as a 'cytokine storm', a sort of hyperactive immune response that could become deadly for the patient. I-Mab Biopharma's TJM2 asset was discovered to potentially have an impact on this cytokine release syndrome (CRS). As I-Mab founder Dr Jingwu ZANG explained, "TJM2 is an antibody that inhibits GM-CSF, a cytokine that is known to contribute to tissue inflammation and degeneration in diseases such as rheumatoid arthritis (RA). Studies of COVID-19 patients have documented high levels of ... GM-CSF ... in the bloodstream of those who become severely ill. There is strong scientific evidence to suggest that inhibiting GM-CSF may have a beneficial impact on patients with CRS."

What TJM2's main indications will remain RA and other autoimmune conditions, Shen was proud that I-Mab was able to develop a new COVID-19 program so quickly, attributing this to their "cross-functional capabilities" and "drive". They have already received IND approval in the US and are finishing the first part of their study there.

Another immunology and immune-oncology company, Harbour BioMed, also believes they have much to contribute in this fight. The biotech announced in March 2020 a collaboration with the Mount Sinai Health System in the US to develop antibodies for SARS-CoV-19. Chairman and CEO Dr Jingsong WANG pointed out the rationale behind this: "despite having a laser-sharp focus on immunology-based therapeutic areas for our internal portfolio, our antibody-generation technology has broader applications across all therapeutic areas. With the immediate global needs in fighting COVID-19 pandemic, we will not shy away from the chance to be part of it," stressing, "this is another way for us to deliver value to patients."

The agreement is a multi-year, multifaceted one to develop novel, fully human antibodies for the treatment and prevention of various diseases including oncology and immunology, as well as the utilization of Harbour BioMed's proprietary H2L2 Harbour Mice® platform to generate monoclonal antibodies for both therapeutic and prophylactic purposes.

Dr Wang also reflected on the broader impact of the pandemic. Looking at things in a positive light, he mused, "this ordeal has emphasized the importance of delivering therapeutic solutions to patients during moments of crisis. We have seen the flexibility of regulatory systems globally to open the window for such innovations where necessary, for instance, in terms of the rapid approvals of COVID-19 diagnostic tests and clinical trials." For him, it goes without saying that "the value of biotech innovation is clear" but what is perhaps as important is "the ability and flexibility of healthcare systems to welcome and incorporate such innovations ... as quickly as possible."

While the race towards the COVID-19 finish line is far from over, and realistically, there will be multiple winners across different categories, it is patently clear that the pandemic has been a litmus test of sorts for the rapidly developing Chinese biopharma industry – and Chinese companies look set to pass with flying colours.

I-MAB BIOPHARMA

I-MAB BIOPHARMA

The only company on our list to be helmed by a non-founding CEO, I-Mab Biopharma has advanced since its establishment in 2017 at a pace that would seem to outpace the fast-moving China biotech industry. Founded through the merger of two Chinese biotechs, Third Venture Biotech and Tasgen, I-Mab Biopharma was given a strong boost from their complementary existing capabilities. As President Dr Zheru ZHANG revealed, "Third Venture Capital had its strengths more on the discovery and early clinical development side, while Tasgen was strong in CMC and non-clinical development so the combination of both companies formed a whole drug discovery and development value chain. I-Mab became an integrated biotech company with discovery, CMC, pre-clinical and clinical development capabilities, which is what has driven our fast growth over the past a couple of years."

In three short years, the company has established operations in Shanghai and Beijing, as well as Maryland, the US, in addition to achieving a successful IPO on NASDAQ in January 2020, raising USD 114.5 million. It is the first Chinese biotech to IPO on NASDAQ since 2017, bucking the steady trend of Chinese biotech IPOs on HKEX since revisions to its listing rules in April 2018. CFO Jielun ZHU, who joined the company in 2019 to prepare the company for its IPO, explained their strategic rationale thusly: "we have a number of very innovative and globally competitive assets in fairly early stages. In order for that potential to be assessed and valued correctly, we wanted to place them on a platform with the right levels of specialist knowledge and experience, and also a platform where our peer companies – with similar levels of early-stage cutting-edge innovations – have also IPOed. The NASDAQ has been working with biotech companies for over five decades."

Current CEO Dr Joan Huaqiong SHEN joined I-Mab in September 2017, initially assuming the position of president of R&D and director before being appointed CEO in October 2019. Her career journey has been remarkably diverse: a US board-certified physician, she advanced her pharmaceutical career at Eli Lilly and Pfizer before moving to China's largest pharmaco, Jiangsu Hengrui, to build their clinical team virtually from scratch, followed by two years with Janssen. This comprehensive view of both global and China pharma markets will no doubt serve her well in her leadership of I-Mab during the next stage of their development, which the company has fittingly termed 'I-Mab 2.0'.

I-Mab has defined two distinct portfolios: a lower-risk, fast-to-market China pipeline built around in-licensed assets with established Phase I/II clinical data demonstrating solid safety and efficacy profiles; and an in-house developed Global pipeline with innovative biologics, which they aim to validate clinically in the US initially before fast-tracking their clinical development in China. Within the latter portfolio, CEO Dr Shen is most excited about their proprietary CD-47 asset, TJC4. She enthused, "[this] is a great example of our in-house innovation. This is one of the hottest targets right now after PD-1/PD-L1 but the first wave of clinical-stage CD47 antibodies bound to red blood cells to cause significant adverse effects like severe anemia. Our CD-47 asset is unique because it has been designed to minimize this binding and therefore reduce the side effects. It is currently in Phase I in both the US and China, and we should have our Phase I single-agent safety profile from our US trial by mid- or third quarter of 2020."

Dr Joan Shen, appointed CEO of I-Mab Biopharma in October 2019, introduces her aspirations for the next stage of the NASDAQ-listed biotech's growth – I-Mab 2.0 – as well as the talent environment propelling this biotech to greater heights.

Dr Joan Shen
CEO, I-Mab Biopharma

Your appointment as CEO in October 2019 was followed shortly by I-Mab's NASDAQ IPO in January 2020. What can we expect from I-Mab 2.0?

JOAN SHEN (JS): Two months after I joined I-Mab, we made the strategic decision to build our US presence. That was an important step for us because we wanted to build a global portfolio, and we saw that we needed to have a US presence in order to operate successfully in China.

Secondly, we also wanted to keep the company dynamic, so we focused on building core competences in R&D and relying on external CRO capabilities to complement those. Even now, our R&D organization is still very lean with around 100 R&D employees across our locations in the US and China, managing 12 assets.

Subsequently, we raised two more funding rounds to advance our clinical portfolio. After that point, we believed we had built a healthy-enough pipeline with Phase I, II and III assets to file for our IPO in the US

For I-Mab 2.0, we are focused on building our commercial and manufacturing capabilities to become a vertically integrated biopharma company with global standards and a global reputation.

> "WE WANTED TO BUILD A GLOBAL PORTFOLIO, AND WE WAS THAT WE NEEDED TO HAVE A US PRESENCE IN ORDER TO OPERATE SUCCESSFULLY IN CHINA"

We also want to continue enhancing our level of innovation. Firstly, we want to build translational medicine centers in the US to leverage the top-notch innovation there. We also want to continue expanding our clinical capabilities. Finally, we will continue to invest in discovery science and innovation to complement our current focus on monoclonal antibodies and bispecific antibodies.

Another priority for I-Mab 2.0 is to form collaborations with reputable international partners. We are looking for companies with complementary pipelines as well as complementary teams and talents.

Why is it essential for a company like I-Mab to be present in both the US and China?

JS: One of the biggest aspects is clinical development. From my experience, the US has a mature system to reward and cultivate innovation while China is in a unique position when it comes to commercializing products and delivering them to the right patient populations. We can draw important learnings from both systems.

In our business, patients are the ultimate drivers of our purpose. The end game is delivering our products to patients, so we have to look at where the patients are. The focus should not simply be on doing innovation in silos, be it in your own lab or country. For I-Mab, when we develop new compounds, we first sketch out where the patient populations are, what the targets and therapeutic areas should be, and then we formulate our clinical development plans accordingly, always with an evolving view of what the countries are working towards in their own healthcare priorities. All countries need to work more collaboratively together and become more integrated in the way that their respective patient populations and patient needs are understood.

> “WORKING IN CHINA’S FAST-MOVING ENVIRONMENT, NOT ONLY DO WE NEED TO RESPOND TO WHAT IS HAPPENING NOW BUT ALSO PREDICT AND ANTICIPATE WHAT WILL HAPPEN A YEAR OR FIVE YEARS FROM NOW”

In the past 20 years, patient awareness and healthcare standards in China have improved significantly. The regulatory environment here has also changed significantly for the better. Working in China’s fast-moving environment, not only do we need to respond to what is happening now but also predict and anticipate what will happen a year or five years from now.

We also believe that China will move quickly out of the ‘me too’ and ‘me better’ modes of innovation. This means companies will need to collaborate with more academic institutions – in China and globally – to enhance their innovative capabilities. This is why it [is] essential for I-Mab to have discovery teams in both the US and China. We want to grasp all available opportunities for truly innovative R&D instead of following others.

Fundamentally, we need to keep an open mind about learning from existing models [but at the same time] avoid simply copying and pasting what has worked in other countries or what worked previously in China.

There is a huge competition for talent in the Chinese biopharma industry. How does I-Mab build an attractive working environment?

JS: At I-Mab, we like to stretch our talents. This helps motivate them to grow and stay interested in the projects. During our recruitment processes, we realized that talented people were leaving multinational pharma companies to join I-Mab because they wanted to experience the drug development process from beginning to end. In large pharma organizations, there tend to be fixed functional roles so people gain very deep knowledge but in a narrow area. Moving to a biotech like I-Mab gives these executives and researchers broader exposure to how innovation is realized.

For instance, we always encourage our employees to participate and expand their roles. We like to empower them. The scientist that discovered our CD-47 asset is very young but he is learning at an impressive pace. I bring him and other discovery team members to our meetings with key opinion leaders (KOLs) or investigators to expose them to these interactions, and their knowledge of the compounds and the science behind it also impresses the KOLs/investigators and builds our credibility.

In fact, we were recently approached by an international pharma about developing a secondment program for their talents to expose them to the end-to-end innovative R&D process at I-Mab. They thought it would be a unique opportunity for their talents to gain exposure to biotech operations without necessarily leaving their company. I think this is an important focus for companies in China: retaining talent. Today’s talent will not stay in the same position or department, much less the same company, for ten years, so we need to take innovative approaches to cultivating them.

ALPHAMAB ONCOLOGY

ALPHAMAB ONCOLOGY

Founded in 2009 by CEO Dr XU Ting, Alphamab started its journey as a protein engineering company with the ultimate dream of becoming, as many Chinese biotechs aspire, a global biotech company producing world-class innovations. Just over a decade later, Dr XU has taken Alphamab Oncology – the innovative portfolio of the original company – to a successful IPO on the Hong Kong Stock Exchange (HKEX) and their lead candidate, KN035, is poised to launch on the market in the near future.

Dr XU will be the first to admit that the journey has been a difficult but fulfilling one. Returning to China in 2008 after post-doctorates at Harvard University and Tufts University, and subsequently stints with US biotechs such as Archemix, Serono and Biogen, the first few years were a struggle for the nascent company. In order to survive, Dr XU had to out-license the first drug candidate he developed in order to finance company operations. However, in adversity the company found opportunity. The out-licensing of biosimilar drug candidates to other companies became a sustainable source of revenue for Alphamab, allowing it to develop a robust pipeline of innovative drugs while building proprietary technology platforms. It also meant that Alphamab did not have to face the vagaries of the capital markets until 2018, when they raised their Series A round. This was quickly followed by a Series B round in May 2019, which then paved the way neatly for their IPO in December 2019.

Today, Alphamab Oncology is a clinical-stage biopharma company with a robust pipeline in oncology and immunology. Their in-house proprietary platforms, including bispecifics, protein engineering and mixed-antibody platforms, allow them to develop multimodality-targeting therapies to address the complexity of cancer.

Their flagship product is KN035, a subcutaneous injectable PD-L1 antibody, which was codeveloped with another Chinese company, 3D Medicines. In China, a pivotal Phase II trial for high microsatellite instability (MSI-H)/mismatch repair deficiency (dMMR) advanced solid tumors has been concluded and a Phase III pivotal trial in biliary tract cancer is in progress.

In the US, they have collaborated with 3D Medicines and TRACON Pharmaceuticals to develop it for the orphan indication of soft tissue sarcoma. It has since received Orphan Drug Designation from the US FDA. Dr XU explained, "TRACON already has a sales team set up for this indication in the US. This is a good way to preserve our resources for our core priorities like more major indications." He sees great potential for their product in the US market, and the recent COVID-19 pandemic may even work to their compound's favor. Dr XU highlights, "due to the COVID-19 crisis, at least half of the US are discouraging patients from going to hospitals. As a result, more than half of the patients on, for instance, intravenous Herceptin, has now switched to subcutaneous infusions. I think once this switch has been made, patients will be reluctant to go back on IV drips because of the inconvenience. Our KN035 is still the only subcutaneous PD-1/PD-L1 in late-stage clinical development so we might have an interesting opportunity there in the US market."

Alphamab Oncology's founder, chairman and CEO Dr Xu Ting shares insights from their successful HKEX IPO in December 2019, his clinical and commercial development strategy, and the impact of COVID-19 on their operations.

Dr Xu Ting
founder, chairman and CEO, Alphamab Oncology

Dr Xu, since we last interviewed you in December 2018, you have taken Alphamab Oncology to an extremely successful IPO on the Hong Kong Stock Exchange (HKEX). Did the IPO meet your expectations?

XU TING (XT): We listed on the Hong Kong Stock Exchange (HKEX) on 12 December 2019, raising about USD 270 million, which ended up being on the high-end of our price range. We had mixed expectations: based on the previous IPOs of other Chinese biotechs, we thought our valuation could have been better but the few companies that did IPO right before us were not as well-received as before, so we decided to price the IPO with a reasonable valuation. The investment climate was rather tough during that period as well, so there was some pressure on the price.

However, we are happy with the outcome with significant support from long-only funds, including prominent names from the US and Europe, with the retail part seeing nearly 200-times oversubscription. Furthermore, on the first day of trading, our share price rose nearly 35 percent so that is a good sign. What is also positive is that it reversed the negative IPO performance trend. This helped paved the way for the IPOs that came after, for instance, with InnoCare and now Akeso Biopharma. I believe our IPO had a positive impact on the market, which is good for the whole China biotech sector.

Four months into running a publicly listed company, what has changed for you as CEO?

XT: The core business – our research-driven, data-driven approach to innovation – has not changed. We are committed to developing our portfolio and generate value for our stakeholders.

However, in terms of governance, as a publicly-listed company, there is a lot more work to do, certainly. We have had to add or improve functions like compliance, corporate social responsibility, financial reporting and budgeting, public and investor relations and so on. We are now in the process of implementing SAP systems to streamline the company's operations from research to commercialization. There is a lot more to think about beyond research. With R&D, you need to be creative and focused in your approach. With running a publicly-listed company, you need to be disciplined.

2019 was also a prolific year for Alphamab Oncology in terms of clinical development. Could you outline the most exciting milestones for your portfolio?

XT: 2019 was really critical for our pipeline development, particularly our three flagship candidates.

KN035, our subcutaneous injectable PD-L1 antibody codeveloped with 3D Medicines, has just finished the first pivotal Phase II trial for high microsatellite instability (MSI-H)/mismatch repair deficiency (dMMR) advanced solid tumors. Its Phase III pivotal trial in biliary tract cancer is also progressing.

KN026 is our anti-HER2 bispecific antibody. We formulated quite a few Phase II trials and we will start a pivotal Phase III in China soon. We will position KN026 quite aggressively against Roche's Herceptin® because the efficacy and safety are both great. In addition, we started using KN026 against patients with low and intermediate HER2 expression and we are getting some great preliminary data showing response. Roche's Herceptin® and Perjeta® combo only works on HER2+ patients so we think there is great potential for our compound to expand to other indications.

Our third pipeline molecule is KN046, a first-in-class PD-L1/CTLA4 bispecific antibody. It is more complicated in terms of its anti-cancer mechanism and we are still trying to understand it better. There has been a lot of effort on KN046. We initiated eight Phase II trials in 2019 and as of today, we have almost 400 patients enrolled across these studies. We want to understand better how the molecule works in which indications and with which combinations. Already we can see that KN046 has a lot of potential in many indications where PD-1/PD-L1 do not work well.

With so many trials across various indications for your pipeline, how will you start to prioritize resources as your candidates start to approach commercialization?

XT: Both KN026 and KN046 have the potential to work across multiple indications and multiple combos, so our strategy has been to demonstrate proof-of-concept (POC) in as many indications as possible. We will then take a couple of small indications to approve and bring to market as quickly as possible. We expect to file for BLA for KN046 as well as KN026 in the next one to two years. At the same time, we will start randomized Phase III trials for one or two major indications to position them to compete in more mainstream markets.

Our clinical development strategy is also well-established to leverage the advantage of different markets globally. For instance, our biliary tract cancer indication for KN035 is technically an orphan drug indication but we are looking at nearly 50,000 patients a year in China due to the incidence rate in the Chinese population. Within two years, we have already enrolled 400 patients in China. We can then use our China data to support our US filing because it would be extremely difficult to enroll that many patients in the US. When we are ready to file in the US, all we might need would be a small bridging trial. In this way, we can accelerate our clinical development in the US market.

> "I BELIEVE OUR IPO HAD A POSITIVE IMPACT ON THE MARKET, WHICH IS GOOD FOR THE WHOLE CHINA BIOTECH SECTOR."

We are also going to look at European countries, particularly in Eastern Europe, where some indications may have higher patient numbers or be less exposed to already approved drugs on the market, to see if we can generate clinical data from there as well.

Looking forward and considering the unfolding COVID-19 situation, what are your expectations for 2020?

XT: We have had to adjust our plans and expectations a little. We had previously considered investing more resources outside of China but with the current situation, we will continue to prioritize clinical development in China because many clinical centers in the country are already back on track while operations overseas are still experiencing disruption. At the same time, we have to explore how to improve the way we run clinical studies by implementing more remote monitoring to limit site visits, and how to maintain high quality at the same time.

Fortunately, we do not anticipate too much delay. We might see around two to three months delay for our first BLA filing but otherwise we are still on track with our clinical development plans.

HARBOUR BIOMED

HARBOUR BIOMED

The most international of the five companies on our inaugural list, Harbour BioMed chairman and CEO Dr Jingsong WANG has referred to his company as a "multinational", since Harbour BioMed boasts operations in Shanghai, China; Boston, the US; and Rotterdam, The Netherlands, despite having only been established in 2016 through the acquisition of Dutch company Harbour Antibodies and USD 50 million in funding. Prior to that, Dr Wang was Head of the China Research and Development Center and the Head of Translational Medicine in Asia-Pacific for Sanofi. Beyond industry, he had also served on the Research Grant Review Committee of the National Natural Science Foundation of China and as scientific grant reviewers for entities like the National Institute of Health Research and the National Health Service in the UK.

The company's innovation engine is founded on its two patented transgenic mouse platforms – known as Harbour Mice™ – which are used to generate fully human monoclonal antibodies with clinical and commercial potential. This technology was developed by Professor Frank Grosveld at Erasmus MC in the Netherlands, who now serves as the founding CSO of Harbour BioMed.

Through its proprietary technology platforms and a number of strategic acquisitions, Harbour BioMed has built a strong pipeline in immuno-oncology and inflammatory diseases. In 2019, the company successfully brought a de novo internally discovered program, HBM4003, into the clinic, which, in Dr Wang's words, "fully validat[ed] our capabilities to innovate on our own." HMB4003, a next-generation CTLA-4 antibody, has also received an IND from the US FDA. For their portfolio of in-licensed assets, their focus is on the China market. The frontrunner seems to be HBM9161, in-licensed from Korean biotech HanAll Biopharma. Harbour BioMed is set to run Phase II/III trials for Graves' ophthalmopathy and adult immune thrombocytopenia (ITP).

In addition to advancing its own pipeline portfolio, Harbour BioMed also collaborates with other institutions and companies. Leveraging on their experienced antibody discovery team, they started initially by licensing their Harbour Mice™ technology platforms but the model has since evolved to become more focused on co-discovery and co-development, or the 'Platform Plus' model. Dr Wang also indicated, "in 2020, we have also started to out-license our discovery programs to external partners", another exciting milestone for the young biotech.

In March 2020, Harbour BioMed completed a USD 75 million Series B+ round to support the company's advancement towards key clinical and development milestones. This came after the company's Series A+ round in January 2018 (financial details undisclosed) and USD 85 million Series B round in August 2018.

Dr Jingsong Wang
chairman & CEO, Harbour BioMed

Dr Jingsong Wang, Chairman & CEO of Harbour BioMed discusses the exciting clinical and commercial milestones of the prolific biotech in 2019, including their March USD 75 million Series B+ fundraising round and their preparations for several Phase II/III pivotal trials to come later this year.

Dr Wang, what have been the key milestones and achievements since our last interview with you in January 2019?

JINGSONG WANG (JW): Harbour BioMed has made significant progress across three different fronts: a robust portfolio; evolution of our platform technology; and an innovative business model. over the past 18 months.

From the time of Harbour BioMed's inception in 2016, we have always set out to be a patient-centric global biotech company with multiple forms of value generation for our shareholders. Over the last year alone, we created opportunities to make an impact for our patients, industry and our shareholders in various ways.

Starting with our portfolio, we made several significant advancements. First and foremost, we brought a de *novo* internal discovery program (HBM4003) all the way from discovery to pre-clinical to clinical trials. This is the first compound from our internal pipeline that we have advanced from pre-clinical to clinical, thereby fully validating our capabilities to innovate on our own. HBM4003 is a next-generation, fully-human anti-CTLA-4 antibody that has demonstrated superior clinical efficacy and a better safety profile compared to first-generation anti-CTLA-4 antibodies such as ipilimumab in preclinical settings. We started Phase I clinical trials in Australia at the end of 2019 and have also obtained US FDA IND, with additional INDs pending in other regions. We are very excited about this compound.

In addition to this, we also have a portfolio of our in-licensed programs for the China market where we have generated our own data and achieved multiple IND approvals for our HBM9161 compound, which is aimed at the treatment of multiple severe autoimmune diseases including myasthenia gravis, adult immune thrombocytopenia and Graves' ophthalmology. We plan to initiate Phase II/III pivotal trials in the first half of 2020. For our second compound, HBM9036, we have completed a Phase II study in China for dry eye disease. [We hope to] proceed with our Phase III registrational trial likely in the first half of 2020 as well.

In addition to these more advanced programs, we have built a strong pipeline with multiple discovery programs based on our Harbour Mice® antibody discovery platform.

Secondly, we are continuing to expand and enhance our capabilities to innovate by building discovery capabilities beyond our original Harbour transgenic mice technology. We have integrated another cutting-edge technology, a single-cell antibody screening and analysis technology, into our Harbour mice

platform, which further empowers us to compete at the global level.

> “OUR STRATEGY, BUSINESS MODEL AND APPROACH HAVE NOW BEEN VALIDATED AND I BELIEVE WE ARE IN THE POSITION TO ACHIEVE EVEN MORE IN THE COMING YEARS”

Finally, we have also transformed our business model from the previous legacy model of technology licensing to what we call the ‘Platform Plus’ model, which leverages the above mentioned discovery and platform technology capabilities to work with the best institutions and researchers around the world on co-discovery programs. We have done this with leading Chinese pharmacos like Chiatai Tianqing. Technology is of course still a component of these partnerships, but the collaboration model has switched to co-discovery and co-development thereby creating higher value and returns for all parties involved. We have also started in 2020 to out-license our discovery programs to external partners, demonstrating our capabilities to build innovative discovery programs valued by our partners.

In March, Harbour BioMed successfully completed a USD 75 million Series B+ fundraising round. How did you find the fundraising experience in light of the COVID-19 situation?

JW: It was indeed a unique situation, but to our benefit, much of the discussion and negotiations with investors had occurred before the COVID-19 pandemic outbreak. We built our portfolio with the goal of value generation and we have reached out to a broad network of partners around the world in order to capture the best of global science and innovation. As a result, we are confident that we offer a unique proposition, no matter where and how the funding comes. The milestones I outlined above over the past few years and particularly in 2019 gave our investors – existing and new – the confidence to (continue to) support us.

This is reflected in our geographic positioning, which aims to capture the best of innovations globally while mitigating the risks associated with biotech innovation. We have key locations in Rotterdam, Boston and Shanghai, with each site occupying a unique positioning and role. Our Rotterdam site is focusing on technology optimization and external partnerships. Our Boston site aims to fully leverages the innovation ecosystem in the region through collaboration with the best scientists and biotech centers, with the goal of capturing the sources of first-in-class innovation. Once these programs receive preliminary validation and we decide to invest further, we bring them to our China site, where we can advance programs on a larger scale at a faster pace in a bigger space.

Looking forward, what do you hope to accomplish in 2020?

JW: After over three years of operations, our strategy, business model and approach have now been validated and I believe we are in the position to achieve even more in the coming years.

In 2020, specifically, I hope to see significant advancement in our late-stage clinical programs. By next year, Harbour BioMed would have initiated at least eight clinical programs, of which three will be registration trials, which sets the stage for us to become a commercial-stage company soon. This is highly momentous for a biotech start-up and we are now lining up the resources to push and drive those programs.

In 2019, we signed a major partnership with a global top five pharma company for our HCAb antibody discovery technology platform, and we anticipate more of such partnerships with other global pharma giants, not just for our technology but on specific clinical programs.

ARCTIC VISION

ARCTIC VISION

The new kid on the block, Arctic Vision recently celebrated its first anniversary. Founded by a veteran industry team, the company touts itself as the first innovative ophthalmology-focused biotech in China, with the mission of bringing innovative therapies from abroad to patients in China. According to CEO and cofounder Dr Eddy WU, a company like Arctic Vision is overdue. In 2019, ophthalmology was the fastest-growing segment among all disease areas in China. For instance, macular degeneration affects 34 million people across the country, while around 28 million have moderate to severe forms of dry eye.

Having trained as a molecular pharmacologist before starting his career with Novartis, during which he spent five years at Novartis, leading multiple clinical development programs across various therapeutic areas and subsequently also heading up Health Economics and Outcomes Research (HEOR) for the Asian, Middle Eastern and African markets, Dr Wu then moved to Allergan and Terns China, a NASH-focused biotech, before starting Arctic Vision in May 2019. Joining him on the journey are his compatriots, Dr Qing LIU (VP of Clinical & Regulatory Affairs) and Dr York Chen (VP of Operations & Commercial Planning), who both also have extensive ophthalmology industry experience, with stints at Allergan and Alcon.

The company's evocative name, 'Arctic Vision', is intended to reflect the company's ambitions to improve the lives of patients with ophthalmological conditions. As Dr Wu shared, "globally, the animals that live in the Arctic face the most challenges with sight. Reindeer, polar beers, Arctic fox and so on must survive and thrive in an environment that is in continuous darkness half the year and in perpetual daylight the other half of the year." As a result, these animals have developed evolutionary advantages to help them see better. Dr Wu enthused, "Arctic reindeer 'change' their eye color from gold in the summer to blue in the winter. The blue helps to increase the sensitivity of the eye to the limited winter light." He pointed out poignantly, "it is common knowledge that the Arctic is a very harsh environment but probably most people do not consider the impact on sight. For humans, I think there is a tendency to overlook the difficulties and struggles of people living with sight issues as well." For this reason, the company is dedicated to addressing the entire pan-ocular space.

Arctic Vision has already closed a deal with US biopharma Clearside Biomedical for XIPERE™, or ARVN001, which has a novel drug delivery approach. Dr Wu introduced, "[it] is designed to enable the rapid and adequate dispersion of medicine to the back of the eye, offering the potential for the medicine to act longer and minimize harm to the surrounding healthy parts of the eye." They are currently preparing for clinical trials. The first indication for this product in China will be macular edema associated with uveitis, and the company is also exploring a second indication of diabetic macular edema (DME).

Not content to rest on the laurels of their first commercial partnership, Arctic Vision is in talks with a number of other firms, and Dr Wu has hinted that by the end of 2020, if not earlier, they could have a portfolio of between three to six relatively late-stage, validated assets – certainly a feat for such a young company.

Dr Eddy Wu, founder and CEO of Arctic Vision, the only innovative ophthalmology-focused biotech company in China, shares how his global career in ophthalmology motivated him to establish the company in 2019 and the exciting potential of their first asset.

Dr Eddy Wu
founder and CEO, Arctic Vision

Eddy, after an extensive international career across Big Pharma companies like Novartis and Allergan, as well as a stint with Chinese biotech Terns Pharma, what motivated you to establish Arctic Vision in May 2019?

EDDY WU (EW): The first is my personal mission. I started my career at Novartis and since then, I have mainly focused on ophthalmology. During my time at Novartis, I oversaw the Lucentis® program, overseeing the launch of the product in Asia-Pacific, Middle East and Africa. In 2012, I organized an advisory board meeting with eleven of the top ophthalmology KOLs in the world, where I shared an epidemiological report on the positive impact Lucentis® has had. Since its launch, there had been a dramatic decrease in the incidence of blindness globally.

On its own, the graph was just a flattening curve and statistics but for us sitting in that room, it was a very impactful representation of the way the lives of patients globally have been improved. Beyond the numbers, we are talking about grandparents being able to see and play with their grandkids for a longer period, of people being able to enjoy the beautiful sights of the world for longer. This achievement had only been made possible through the close collaboration of industry and physicians. That really cemented my commitment to continue working in industry and specifically, ophthalmology, which I found a meaningful area.

From an environmental perspective, when I joined Allergan China in 2015, I observed that most of the other therapeutic areas in China – oncology, NASH, for instance – already had good existing linkages with the innovative technologies and therapies being developed by leading companies in the US and Europe. However, in terms of ophthalmology, the available technology and therapies in China were significantly lagging behind those in developed markets. Patients were not benefiting from the most advanced treatment options globally.

I wanted to create a company in China and Asia to bring in the latest innovations and therapies to fulfil the significant unmet medical needs in ophthalmology, for the ultimate benefit of patients and society.

What are the most important unmet medical needs in ophthalmology in the China market?

EW: The unmet medical needs are pan-ocular – across the entire field of ophthalmology. For instance, in the retina area, physicians in China currently rely heavily on anti-VEGF drugs, which is the gold standard internationally, but in the US, companies are already developing newer therapies like longer-lasting anti-VEGF. Another example is dry eye. The only treatment available in China is artificial tears, compared to other available procedures in other markets. Gene therapy is also an area that has

huge potential in ophthalmology but there are not many gene therapy companies in China, and even fewer – maybe none – focus on ophthalmology specifically.

From an R&D perspective, what is critical in ophthalmology is the development of a novel drug delivery mechanism. In other therapeutic areas, there are different ways to deliver the drug: intravenous infusions, oral, etc. but for eye diseases, the retinal-brain barrier complicates drug delivery. If patients must take a high dose of a drug, they risk experiencing significant systemic side effects. Overcoming this issue is a huge topic in ophthalmology generally but there has unfortunately been very little focus on this in China thus far.

Could you tell us more about your partnership with Clearside Biomedical?

EW: The first product in our portfolio is XIPERE™ or ARVN001, in-licensed from US biopharma company Clearside Biomedical. It is a proprietary suspension of the corticosteroid triamcinolone acetonide formulated for suprachoroidal administration via Clearside's proprietary SCS Microinjector™. [This] novel drug delivery approach is designed to enable the rapid and adequate dispersion of medicine to the back of the eye, offering the potential for the medicine to act longer and minimize harm to the surrounding healthy parts of the eye.

The first indication in China will be macular edema associated with uveitis. We are currently preparing for IND in China, and we expect to receive feedback soon. We are also exploring a second indication: diabetic macular edema (DME), which Clearside has already taken to Phase II studies in the US.

Clearside brought XIPERE™ to the NDA preparation stage in the US They have out-licensed the US, Canada, U.K, and European rights to Bausch + Lomb while we have the rights to this product for Greater China (mainland China, Hong Kong, Macau and Taiwan) and South Korea. We have been very fortunate to be able to close this first licensing deal in our first year. There was a very competitive bidding process as many other pharma companies were interested in this asset. Ultimately, I believe that Clearside chose Arctic Vision because of the profile of our management team and our long-term focus and strategy.

> "WHILE ARCTIC VISION ITSELF MAY BE A YOUNG COMPANY, OUR TEAM COMPRISES INDUSTRY VETERANS WITH SOLID TRACK RECORDS AND STRONG CAPABILITIES"

Starting from myself, I have extensive industry experience in ophthalmology globally and in China, which is rather rare for Chinese executives, as well as start-up experience in a well-regarded Chinese biotech like Terns Pharma. Beyond myself, my core team is also extremely experienced [and we] all worked together in Allergan so we have a strong and good working relationship, which gives a new company like Arctic Vision a lot of core stability. Ultimately, what was clear to Clearside was that while Arctic Vision itself may be a young company, our team comprises industry veterans with solid track records and strong capabilities equal to any other Big Pharma affiliate in the China market.

With your first asset secured, what can we expect from Arctic Vision in terms of pipeline development in the upcoming year or so?

EW: I am excited to announce that we have several other promising deals on the table. By the end of 2020 or even as early as Q3, we could have a portfolio of between three to six assets in total. This would be very impressive for a company of just two years. All these assets would be relatively late-stage, validated assets, with at least human proof-of-concept data available, so that we can accelerate our development in China.

We want to bring in cutting-edge innovations from other regions to the China market to quickly fill the gap in China. Focusing on a relatively lower-risk portfolio would also allow us to establish a solid foundation for Arctic Vision.

As an integrated company, our focus ultimately is not on any specific area of the eye – we are dedicated to addressing the entire pan-ocular space. The major driving forces for us are to address unmet medical needs and to bring in cutting-edge innovations to the China and Asia markets. These are the two selection parameters for our portfolio.

After building this foundational portfolio, in the longer run, we will of course start to develop our own R&D capabilities as well, particularly in the discovery and pre-clinical stages.

Dr Qing Liu

VP, Clinical & Regulatory Affairs, Arctic Vision

During my earliest medical training, I was amazed at the fact that even though the eye is such a delicate organ and of very small size, it had an extremely complex structure and function. After so many years in this field, as both clinician and industry professional, I am still deeply passionate [about ophthalmology]. Throughout my industry career, I have been fortunate to have led the clinical development and medical work for different types of top ophthalmic products, from pharmaceuticals to OTC products, as well as medical devices (both Surgical and Vision Care), in China and other countries in Asia-Pacific, which is not very common in the China market. In addition, I had the opportunity to work with top-level KOLs in not only China but also in Asia and even globally. ophthalmology is an area full of cutting-edge innovation and biotech companies will become increasingly important players and innovation drivers.

Our product ARVN001, combining the new formulation of a classic steroid and the novel SCS injection platform for an improved safety profile, is a perfect example of such innovation. Some [KOLs in China] have already seen this technology in publications, and they are very excited that we are bringing this innovative product to China.

[Looking] at the technologies and sub-disease areas we [are] interested in, gene therapy [is] the unmissable space but there are still many risks involved so we want to be bold and careful in our exploration here. We also have a strong desire to develop new drug delivery mechanisms, which is very important for eye diseases. We will undertake proper science- and data-driven evaluations of any technology we are interested in.

Dr Yi (York) Chen

VP, Operations & Commercial Planning, Arctic Vision

Over the next two to five years, the focus will be on building our commercial team as our first and then potential product(s) prepare to launch in the market. My previous commercial experience at Alcon and Allergan has given me a deep understanding of the unique distribution channels in the ophthalmology industry and the differentiated pricing strategies. With my experience in launching commercial projects, I am very excited and confident about our first asset, XIPERE™ to treat uveitic macular edema (UME), as well as our upcoming new assets.

Since inception, we have realized that we need to stand out from the crowd. In the last decade, [many] Big Pharma have [acquired] pure-play ophthalmology companies. The perception is that Big Pharma is usually more interested in 'blockbuster' products. Their distribution channels are very broad and as an emerging biotech, we should not compete directly in the same way. Arctic Vision's differentiation comes from three aspects. The China ophthalmology market is still a relatively blank slate with huge potential for innovative therapies. We are confident that we are capable of identifying and introducing global cutting-edge technologies to China. In terms of portfolio, [our] premier and innovative portfolio would allow us to focus on reaching hospitals in top-tier cities, instead of competing directly with Big Pharma across broad distribution channels. Although we are a China-based biotech, our science will align with global developments. Our strong international KOL network will help us familiarize ourselves with novel products.

ZAI LAB

ZAI LAB

Probably one of the most recognizable 'Chinese biotech' globally, Zai Lab may only be seven years old but the company has progressed rapidly in becoming a NASDAQ-listed company with not just one but two commercial assets through a stunningly effective strategy of forming productive collaborations with the most innovative biopharma companies globally and in-licensing clinically validated assets for the Greater China market. This was in large part made possible through the management team's extensive global industry experience, particularly founder, Chairman and CEO Dr Samantha Du.

Dr Du spent seven years with Pfizer in the US before cofounding and helming another iconic Chinese biopharma company, ChiMed, as CSO and subsequently CEO, for a decade in total. She then joined Sequoia Capital for a couple of years before venturing out to set up Zai Lab. The company also saw a leadership revamp between 2017 and 2018, which was when most of the members of its current executive team joined the company.

As listed in their 2019 SEC filing, "Zai Lab was built on the vision that, despite having a significant addressable market and sizable growth potential, China has historically lacked access to many innovative therapies available in other parts of the world and its drug development infrastructure has been underutilized. There remains the need to bring new and transformative therapies to China." Driven by these goals, Zai Lab has formed partnerships with a number of leading US biotechs including Incyte, MacroGenics, Paratek Pharmaceuticals and Entasis Therapeutics, with their portfolio focusing on oncology and infectious diseases.

By the time Zai Lab IPOed on NASDAQ in September 2017, it already had four clinical-stage assets in its portfolio and its first product, ZEJULA®, was launched just a year later for the treatment of ovarian cancer, first in the Hong Kong market and subsequently Macau and mainland China. ZEJULA® is in-licensed from Tesaro (now part of GSK). Their second commercial product, OPTUNE®, in-licensed from Novocure, was again first launched in Hong Kong in December 2018 for glioblastoma, and has since been approved by the China NMPA as well, becoming the first innovative treatment for glioblastoma to be approved in mainland China in over 15 years. Zai Lab has since built up a commercial team of around 300 employees.

ZEJULA® (NIRAPARIB, ZL-2306) IS A HIGHLY POTENT AND SELECTIVE ORAL, ONCE-DAILY SMALL MOLECULE POLY (ADP-RIBOSE) PARP 1/2INHIBITOR.

OPTUNE®, A PORTABLE DEVICE THAT DELIVERS TUMOR TREATING FIELDS (TTFIELDS), IS A NOVEL CANCER THERAPY THAT USES ELECTRIC FIELDS TUNED TO SPECIFIC FREQUENCIES TO DISRUPT CELL DIVISION LEADING TO INHIBITION OF TUMOR GROWTH AND DEATH OF TUMOR CELLS.

As Dr Du explained in her 2019 interview with us, "we made the decision to launch our products in Hong Kong with a pure-play commercial platform, and this is the strategy we will take with our future launches in the mainland Chinese market." Despite their still-diminutive size compared to most of the other cancer players in the market, she was confident that Zai Lab had the right strategy to penetrate the market, highlighting, "in China, the top 100 hospitals account for approximately 80 percent of innovative oncology products so our sales and marketing efforts can be very focused and science-based. The commercial platform we are developing is driven by medical information and education. It is very important for doctors to be educated by qualified medical representatives rather than simply relying on a commercial distribution network and including it on hospital procurement lists. Chinese patients rely on their doctors and respect their opinions and knowledge, so it is very important the biopharma companies like us provide correct and informative medical education on our products."

> "THERE REMAINS THE NEDD TO BRING NEW AND TRANSFORMATIVE THERAPIES TO CHINA"

She also pointed out, "incidentally, this would help Big Pharma multinationals as well because they have historically not focused on penetrating lower-tier cities and community hospital centers. If local companies like us with the reach invest in such efforts, it raises the medical awareness in the entire ecosystem."

According to company-provided data, ZEJULA® overtook its main competitor, AstraZeneca's LYNPARZA® to capture 71 percent of the market (by value) in 2019. Total revenue for both products in 2019 reached USD 13 million. With two China NMPA approvals and a number of successful launches across the Greater China markets under their belt, Zai Lab has certainly positioned themselves as the "gateway to China for innovative assets" and continue to sign high-profile in-licensing deals, the latest being with Regeneron for their CD20xCD3 bispecific under clinical development for a range of blood cancers.

Complementing their commercial capabilities, Zai Lab has also built a commercial small-molecule oral solid dosage manufacturing

Dr Samantha Du
chairman & CEO, Zai Lab

facility and a biologics pilot manufacturing facility in Suzhou.

Where Zai Lab has been overtaken by many of her contemporaries is in terms of their in-house discovery pipeline, though the company is working hard to remedy this, having established discovery operations in 2016 and 2018 in Shanghai and San Francisco respectively. To boost their efforts, they are also working with leading academic institutions in China like the Shanghai Institute of Materia Medica and Tsinghua University. However, 2020 might be the year for them as they have stated that they expect to file at least one IND this year for their internally-discovered assets.

This remains an important priority for the company, given Dr Du's fervent belief in the necessity of China developing its own homegrown innovations. She has exhorted, "as a country rises to the position of second-largest global pharma market, I believe it becomes responsible to not only benefit from other countries' innovations but also to bring innovations to the world! When Japan became the second-largest pharma market in the world, we started to see the Japanese pharma multinationals emerge. China needs those kinds of companies too and today we are fully capable of moving in this direction." After all, she added, "we have the talent, the financial engine and the patient population to run accelerated clinical programs."

Her final message to the global industry community? "As a leader, we always need room to learn, adapt and grow. We have somehow become a reference for the Chinese biotech industry. Last year, there was a lot of talk about the 'Zai Model', 'Zai Better, 'Zai 2.0' and so on. But Zai Lab itself is already a Zai 5.0! We are always innovating." Having proven its late-stage development and commercialization capabilities, we look forward to seeing how Zai Lab continues on its transformative journey further upstream into the deeper waters of discovery R&D.

Creating a Corporate Culture

One of the toughest challenges for any biotech founder and CEO to manage is the transition from the start-up phase to the growth phase, particularly as the company grows through multiple financing rounds and new hires. Dr Du had the following advisory comments: "I believe successful biotech companies must create this sense of ownership amongst all its employees. In our last Annual Meeting, Zai Lab employees came up with a slogan: 'all in, all win'. This is what drives us forward. When I started the company, the motto was 'one company, one dream'. That came from me. But today it is about 'all in, all win'."

Probably in a manner reminiscent of much larger pharma companies, Dr Du also added, "we built this business to last so it is very important for us to have a strong, ethical corporate culture. To prioritize this, we have an active Culture Committee in the company. People need to feel comfortable working in Zai Lab." As a result, she exults, "our staff turnover rate is phenomenally low and well below industry average! This is very rare within the biotech scene."

More pragmatically, she underlined, "part of this is due to a deliberate decision by me to ensure that we maintain a strong sense of ownership through stock options across all levels of employees. Today, employees still maintain a large ownership position in the company. This is rare in a biotech company, particularly in China."

TWO YEARS ON

It has been just over two years since the Hong Kong Stock Exchange (HKEX) revised its listing rules to allow pre-revenue biotechs to IPO as long as they met certain criteria. In May 2020, during the first in a series of webinars organized by the HKEX to celebrate the second anniversary of this Biotech Chapter, Head of Listing Bonnie Chan highlighted that 18 companies had since IPOed under this Chapter, raising a total of HKD 44 billion (USD 5.67 billion), emphasizing that many of them were not simply mainland Chinese or even regional players but companies harbouring global aspirations. All this activity pushed HKEX to become the world's second-largest biotech fundraising hub – after the NASDAQ – in 2019.

The HKEX has also taken the second anniversary of the Chapter as an opportune moment to reflect and improve its operations. As Michael Chan, SVP of Global Issuer Services, contextualized, "the introduction of our biotech chapter [did] not represent the completion of a mission, but rather the start of a long and

exciting journey. We are seeking to continuously enhance and upgrade the listing regime to keep pace with the rapid development of the biotech and life sciences industry, which is becoming ever more complex and diverse."

Even since before the launch of the Biotech Chapter, HKEX has made active forays into the global investor community to canvas insights, support and investment, and two years on, Chan stressed, "we have received great support and very positive feedback on our biotech chapter from both Chinese and international investors, issuers, market participants, and experts. The biotech chapter is a great and timely addition to the vibrant and rapid development of biotechnology in China and Asia. [Notably], at the IPO stage, issuers have access to both Chinese and international investors. During the IPO process, these biotech companies were not only able to secure access to funding, but also to put in place important partnerships and alliances to further their business strategies."

That being said, HKEX is also open to constructive criticism. Chan revealed, "moving forward, the feedback is that the market would like to – and indeed expects to – see more diversity in terms of different subsectors, including medical devices, diagnostics, biologics, genomics, artificial intelligence, and other therapeutic areas. Greater diversity in terms of geography is also expected. Companies that list on the Hong Kong market expect to see themselves listed alongside other reputable international peers," adding, "[we] expect the entire ecosystem to accelerate in terms of maturity." Indeed, of the 18 companies that have IPOed so far, all except one are headquartered on mainland China with the outlier being based in Hong Kong, and all except one are biopharma companies.

2020 has also seen a number of headwinds buffet HKEX, from the outbreak of the global COVID-19 pandemic, chilly US-China relations, and the escalation of tensions in Hong Kong. In addition, in May 2020, HKEX CEO Charles Li, who has steered the HKEX adeptly to its current height of success, announced that he would not seek reappointment once his current contract term ends in October 2021, putting the wheels in motion for a succession plan to be developed.

At the same time, HKEX might benefit inadvertently from recent moves by NASDAQ to discourage IPOs from Chinese companies as a result of a number of concerns, ranging from political pressure, controversies like the extensive fraud subsequently discovered in Chinese company Luckin Coffee (which IPOed in the US in 2019), as well as the low liquidity of the shares of such companies post-IPO. Li stated in the recent Piper Sandler industry conference that he expects 2020 to be "a big year for IPOs, including both huge IPOs from China but also very substantial returnees … from the US [as] the atmosphere in the US is becoming less friendly." Here he was referring to the Chinese legislature's passage of controversial national security legislation for Hong Kong on 28 May 2020, which was quickly met with an announcement by US President Donald Trump that he would eliminate Hong Kong's privileged trade status.

Nevertheless, in terms of regional competition, Chan struck a rather sanguine note about staying ahead of the game as other Asian biotech hubs like Taiwan, Singapore and South Korea also look to boost their stock exchanges. "Rather than competition, we see a positive feedback cycle from other stock exchanges, including those of Shanghai, Shenzhen, and other Asian markets. We are all working towards the same goal: to develop Asia's capital markets as a whole and facilitate the flow of capital between East and West and West and East. There are numerous synergies between the exchanges to be leveraged on."

Chan's final message to biotech companies was unequivocal: "if you are interested in diversifying your investors and tapping the Asian market, especially the Chinese market, you should consider listing in Hong Kong."

THE CES HK BIOTECHNOLOGY INDEX

In November 2018, China Exchanges Services Company limited (CESC), a joint venture of the three stock exchanges in Shanghai, Shenzhen and Hong Kong, launched the CES HK Biotechnology Index (CES HK Biotech) as a benchmark to measure the performance of Hong Kong-listed biotech stocks. This index includes not only pre-revenues biotech companies listed on the Biotech Chapter but also other healthcare-related companies listed on the HKEX Main Board.

In terms of performance, as of March 2020:

- the three-years annualised return of CES HK Biotech reached 31.43 percent.
- The constituent total market capitalisation was HKD 410.6 billion (USD 53.0 billion)."

Code	Name	Weight (%)
1801	INNOVENT BIOLOGICS, INC.	19.60
2269	WUXI BIOLOGICS (CAYMAN) INC.	15.80
1177	SINO BIOPHARM	14.57
2359	WUXI APPTEC CO., LTD	11.47
1548	GENSCRIPT BIOTECH CORPORATION	9.49
1530	3SBIO INC.	8.13
6185	CANSINO BIOLOGICS INC.	8.00
1873	VIVA BIOTECH HOLDINGS	3.72
1877	SHANGHAI JUNSHI BIOSCIENCES CO., LTD.	3.40
2616	CSTONE PHARMACEUTICALS	2.44

Source: CESC (data as of 4 June 2020)

Chan elaborated, "the formation of CES HK Biotech was driven by increasing demand in the capital markets for benchmarks that track and reflect the development of the whole biotech sector. Biotech stocks are prone to volatility as most of companies' products are still at the R&D stage and to a large extent stock prices are subject to the results of clinical trials. Therefore, there was a real need for an industry benchmark to help investors diversify the risk of investing in biotech stocks."

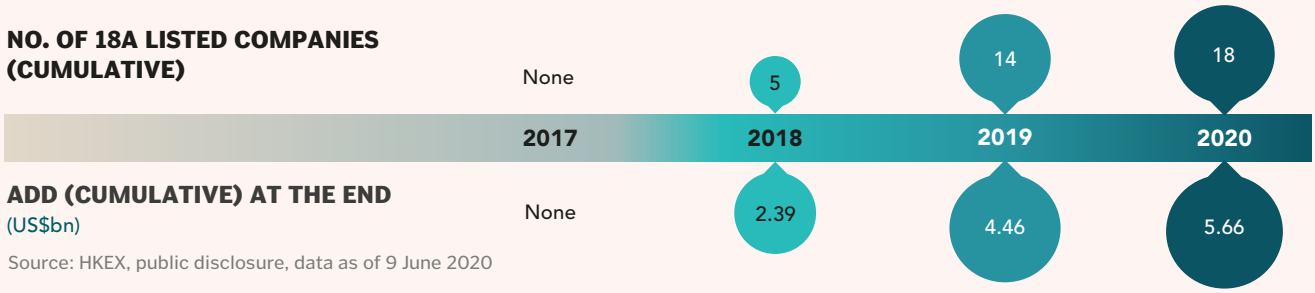
Michael Chan
SVP Global Issuer Services, HKEX

Advantages of a HKEX listing

Accessibility: "access to global capital and global investors, as well as the world's largest customer base, given our close proximity to Mainland China as well as other large Asian markets[, and to] the world's top business institutions and corporates."

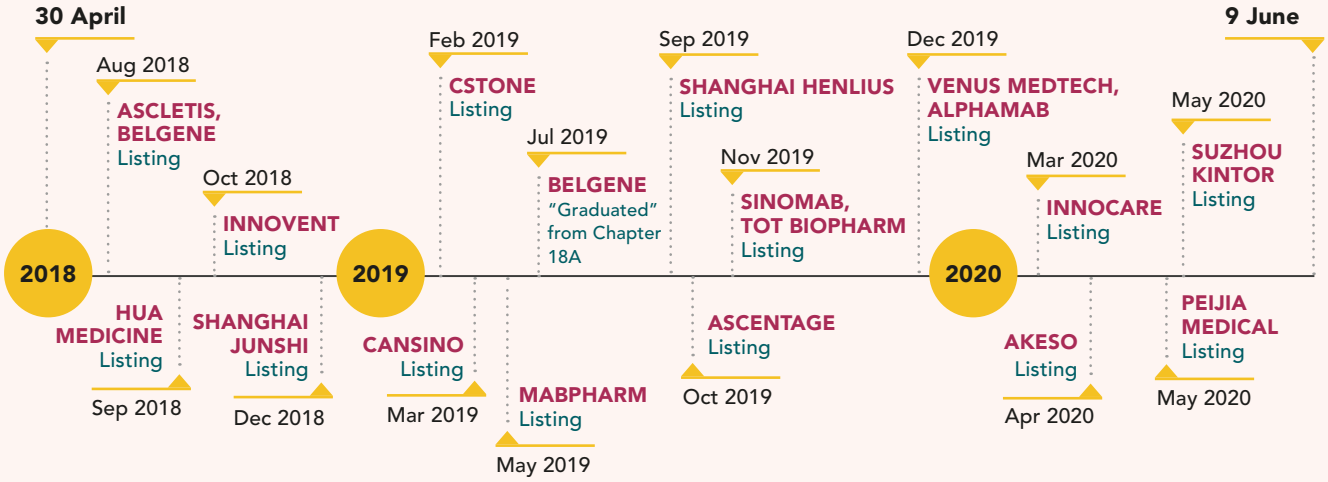
Sustainability: "Hong Kong has been the world's number one IPO market seven times in the last eleven years, including both 2018 and 2019. We have a very strong record of IPO fundraising capability [and] a very robust secondary market"

Credibility: "We have a legal regime, listing platform, financial centre, banking and audit infrastructure, and business centre that conform to the highest international standards on quality and transparency."



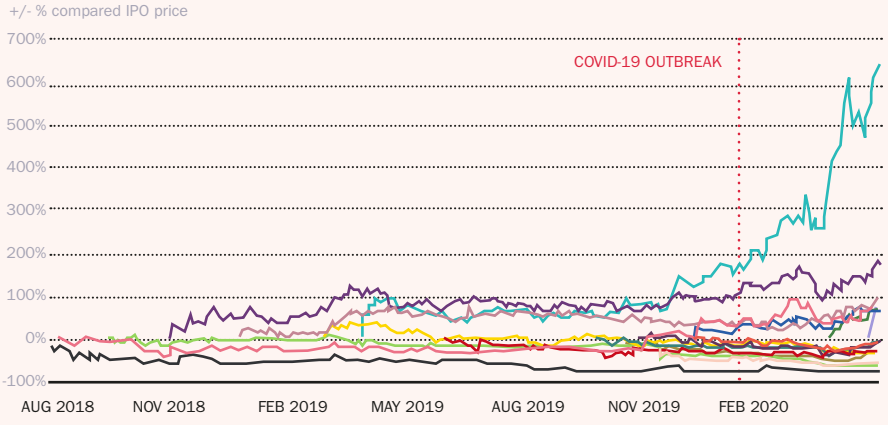
Source: HKEX, public disclosure, data as of 9 June 2020

HKEX CHAPTER 18A IPOS



Source: HKEX, public disclosure, data as of 9 June 2020

HKEX BIOTECHS STOCK PERFORMANCE



	SINCE IPO	FROM 20/01/20
Cansino	+648%	+159%
Innovent	+175%	+17%
Junshi	+93%	+45%
Alphamab	+67%	+16%
Venus Medtech	+62%	+18%
Akeso	+62%	+62%*
InnoCare	+60%	+60%*
Ascentage	-4%	+5%
Henlius	-8%	+9%
Beigene	-10%	-9%
Mabpharm	-31%	+3%
CStone	-33%	-26%
TOT Biopharm	-36%	-9%
SinoMab	-58%	-26%
Hua Medicine	-64%	-38%
Ascletis	-80%	-9%

Source: Bloomberg, Refinitiv, data as of 30 April 2020

*InnoCare and Akeso listed on 23 March 2020 and 24 April 2020 respectively.

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