

China's biotech revolution

Shifting **Asia**



Contents

03	Foreword
04	Executive summary
05	Why is China's medical biotech sector booming?
11	How does China source the talent and technology to grow biotech?
14	Oncology: A driving force for innovation in Chinese biotech
23	China's great genomics advantage
28	How to invest in China's medical biotech revolution

Shifting Asia

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Editorial

Dear reader,

Welcome to the next edition of our *Shifting Asia* series. In each publication, we dissect the impact that key structural developments across the Asia region have on markets and industries over a 5–10-year time horizon. Unfolding technology is an important driver of disruptive trends in Asia, which we addressed in our last three editions on artificial intelligence and fintech. The focus of the current edition also relates to technology, but technology in the field of medicine: specifically, biotechnology (biotech).

Rapidly ageing societies are translating into higher national healthcare bills across Asia. Medical cost inflation is also compounded by rising incidences of non-communicable diseases, resulting in part from the swift urbanization rates in the region. Providing a quality and competitive healthcare system with an appropriate level of public subsidy is likely more important today than at any time in recent history. Can technology help achieve this goal in Asia? Is China succeeding where others have not?

In this report, we identify trends and opportunities in the rapidly growing biotech ecosystem in China. We draw on the insights and shared visions of leading pioneers in China's biotech sector through a series of interviews. A recurring message is the strong support of the Chinese government to grow biotech as part of a broader strategy to raise the quality of domestic healthcare treatment and lower medical costs over the longer term. Not only are biomedicines regarded as the

most efficient way of treating China's high incidences of cancer and other chronic age-related diseases, but they pave the way for preventative and precision therapies. In the long run, these initiatives could have a profound impact on reducing the national healthcare burden.

The rapid rise of China's nascent biomedicine capability offers a case study in how regulatory reform, tax breaks and policy support can transform an industry and rally the capital necessary to grow it. China's unique competitive edge, including rapid digitalization in diagnostics and genomics, big data and AI development, as well as its ability to draw on a deep pool of overseas Chinese scientists, also provides a foundation for the development of homegrown technology.

Investing in biotech carries the unique risk of high failure rates. The creation of novel biologic drugs in China will require a gestation period, in our view. Still, China has demonstrated capabilities even in the early stages of niche biotherapies. A new generation of Chinese biotech companies has also emerged that is taking its research outside of China for validation, and could one day even challenge established Western companies in some markets.

We hope that you too are excited by the growth implications of China's biotech revolution, as well as the investment channels we identify to tap into this growth.



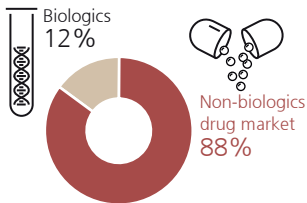
A stylized, handwritten signature in black ink, appearing to read 'Min Lan Tan'.

Min Lan Tan
Head of APAC Investment Office

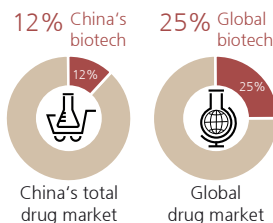
Executive summary

“Everyone is entitled to the highest standard of health, equally available and accessible.”

— Chinese government white paper on public health, September 2017



China has the world's second-largest drug sector yet biologic drugs, or biologics, only make up 12% of the market.



China's biotech market accounts for 12% of China's total drug market, compared to a 25% total market share for the global biotech sector.



Carl Berrisford
Analyst

- China's healthcare sector is at a critical juncture: 200 million Chinese people will reach the age of 60 by 2020, and medical cost inflation is soaring due to the expensive costs of treating non-communicable diseases (NCD). One in four new global cancer cases are now in China, and over 100 million Chinese people have diabetes – the largest diabetic community in the world. China now has the world's second-largest drug sector (including traditional Chinese medicine), yet biologic drugs, or biologics, only make up 12% of the market, and China has a high reliance on expensive imported biomedicine to meet the growing demand for NCD treatment.
- Biologics have become one of the fastest-growing segments, as well as one of the most profitable areas, within the global pharmaceutical industry, with eight out of ten top-selling drugs being biologics. A major reason for such voracious demand is due to their efficacy in treating age-related diseases. China's government believes that developing homegrown biotech capabilities can reduce the country's dependence on imports, make treatment costs more affordable and reduce the domestic healthcare burden over the long term. China's private enterprise and investment communities view biotech as an opportunity to participate in one of the highest growth and most lucrative parts of the global healthcare industry, in a mostly captive market where demand growth is virtually guaranteed.
- China has been fully cognizant that a culture of innovation is required to develop a thriving biotech industry. To this end, it has embarked on a multi-pronged strategy to bring in technology from the outside and foster the right environment for innovation. This has included luring a large pool of overseas Chinese life scientists with attractive incentives and packages; supporting multinational corporations (MNC) and foreign drug companies to conduct clinical trials and manufacture biologics in China; and facilitating Chinese mergers and acquisitions of biotech companies in the US and Europe.
- Following deep regulatory reform and a surge in venture capital and equity financing from 2015–2017, China's biotech sector has made considerable progress within just a few years. By 2017, 800 innovative molecules were under development in China, ranging from preclinical to phase III stages in the pipeline, of which 10% were at clinical stage III. And despite its nascent stage, clinical trials for 25% of Chinese molecules are already being conducted outside of China – currently 41 innovative biologics are being developed globally.
- China's biotech market accounts for 12% of China's total drug market, compared to a 25% total market share for the global biotech sector. Yet the incidence of NCDs like cancer and diabetes in China is well above the global average. Frost & Sullivan forecasts China's biotech market to grow at a five-year growth rate of 16.4% by 2021, making it the world's fastest. Grand View Research forecasts the global genomics market to grow 10% each year, with an estimated value of USD 22bn by 2020. China, which now has the second-largest genomics market worldwide, is set to outpace global biotech growth to become the largest globally. In the longer term, China has the potential to go global by either out-licensing molecules to overseas markets or by developing assets in the US, EU and elsewhere. China is currently pursuing trials for one-quarter of its innovative assets overseas.
- The total value of Chinese biotech initial public offerings (IPO) at home and abroad reached USD 2.8bn in 2017, a record high. Investors can gain exposure to early-stage innovation in the sector via private equity, new IPOs, recently listed Chinese biotech companies in both onshore and offshore bourses, and legacy Chinese pharmaceutical companies moving into biologics.

Why is China's medical biotech sector booming?

"China wasn't even on the radar 10 years ago. Now it is impossible to ignore."

— Judith Li, Partner at Lilly Asia Ventures



Biomedicine:

Medicine based on the principles of the natural sciences and especially biology and biochemistry. An application of biomedicine is biologic drugs (see Biologics on page 20).

Non-communicable diseases (NCD):

Medical conditions or diseases that are not caused by infectious agents, i.e. they're not infectious or transmissible. These include cardiovascular diseases like heart attacks and strokes, cancers, chronic respiratory diseases like asthma, and diabetes.

"Healthy China 2030 Plan" introduced in 2016 by the Chinese government is modeled on the UN Sustainable Development Goal 3 to reduce premature mortality.

As with many other strategic industries that the Chinese government has targeted for development in recent years, the domestic medical biotech sector has enjoyed dynamic growth in a short period of time due to a combination of policy support, industry deregulation and deep pockets. In 2011, China named biomedicine one of its seven strategic priorities and in its 13th Five-Year Plan (2015–2020), the government mandated that biotechnology should exceed 4% of GDP by 2020 in market size. By the end of the decade, China is

slated to have 10–20 science parks with an output of CNY 10bn (USD 1.5bn). In 2015, China launched its "Made in China 2025" strategic plan citing that high-tech fields, including the pharmaceutical industry, should increase the domestic content of core materials to 40% by 2020 and 70% by 2025.

Following this ambitious policy announcement, a wave of regulatory reform (known as the "CFDA big bang") ensued from 2015 to 2017, planting the seeds of the biotech sector that is emerging today.

Investigational new drugs (IND): Clinical trials of non-generic drugs considered to be IND can be fast tracked through China's approval process.

Contract manufacturing organizations (CMO): Companies that are hired by pharmaceutical firms to develop and/or manufacture drugs on a contractual basis.

Contract Research Organization (CRO): A CRO provides support to the pharmaceutical, biotechnology and medical device industries in the form of research services that are outsourced on a contract basis.

National Reimbursement Drug List (NRDL): A list of drugs the Chinese government will reimburse as part of its national insurance scheme.

Biosimilar: A biologic medical product that is an almost identical copy of an original product that is manufactured by a different company.

The Chinese government regards the rapid development of biotechnology as critical to tackle the looming challenges facing China's healthcare system. These include caring for a rapidly ageing population, the rising burden of public and private healthcare spending, and high morbidity from non-communicable diseases. The latter challenge has become so severe that in 2016, the government announced a "Healthy China 2030 Plan" modeled on the health targets of UN Sustainable Development Goal 3, which aims to reduce premature mortality from NCDs by one-third through prevention and treatment. China's high incidence of cancer (refer to oncology statistics on page 15) and diabetes also makes it highly dependent on expensive imported patented drugs, a dependence the government seeks to reduce with homegrown and affordable innovative biomedicine. Although China is growing its nascent biomedicine industry from a very low level, it brings its own unique competitive advantages to the table, including fast-growing digitalization across key areas of healthcare like diagnostics and genomics; the ability to leverage big data and rapidly growing AI development capabilities; and the strong backing of big capital and China's largest online corporations.

Regulatory big bang at the CFDA

Crucial regulatory reform by the China Food and Drug Administration (CFDA), which helped streamline clinical trial procedures and grow China's biotech sector, was part of broader sweeping changes introduced to pharmaceutical and hospital sectors in 2015. Three key reforms took place in 2015 that were ultimately transfor-

mative for China's biomedicine industry. First, the introduction of self-checking declarations by drug companies in clinical trials has freed up the CFDA trial pipeline and CFDA resources by eliminating non-starter cases awaiting approval.

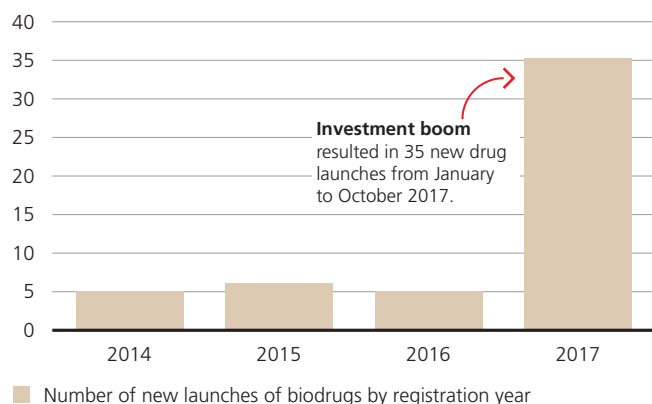
Second, new CFDA regulation modeled after the US Food and Drug Administration's regulatory process requires Chinese generic drug makers (virtually all of China's pharma market at the time) to establish consistent bioequivalence with the innovator product. Drug makers that meet the standards are awarded preferential access to public hospital tenders and prescriptions in China. Although the immediate result of this policy was higher drug manufacturing costs, the Chinese government leveled the playing field by eliminating the 15% markup hospitals earned on dispensing drugs.

Third, the key reform known as Market Authorization Holder (MAH) Law allows drug innovators to hold the manufacturing license for a drug even if the drug manufacturing was outsourced. This supports small-scale drug innovators and reduces manufacturing overcapacity. Because developers no longer have to spend time and resources on drug manufacturing, they are able to devote more energy to developing new drugs. The law has had a particularly beneficial impact on China's developing contract research (CRO) and contract manufacturing (CMO) organizations, as highlighted by Dr. Zhang, CEO of FMD, on page 9.

With China's pharma sector upended by these three reforms, the final game changer was announced two years later: the addition of 340 drugs to China's National Reimbursement Drug List (NRDL), including many novel and high-priced biologic drugs. This has had a profound impact on the drug industry, as it communicated that the Chinese government was prepared to subsidize high-priced, innovative therapies. It also broadened the scope of therapeutic area coverage. The announcement led to a wave of Chinese capital investment in R&D and manufacturing for innovative, biosimilar and generic drugs, as well as contracting companies (CROs and CMOs). Reflecting the efficacy of the CFDA reforms, 35 new drugs launches took place from January to October 2017 based on registration year (see Fig. 1), compared to just five in 2016.

Fig. 1

Surge in new biologic drug launches in China in 2017 after CFDA reform



Source: McKinsey & company, October 2017

Originally, it took drug applicants 8–10 years to launch a new drug, up to 5–7 years longer than the US. This was an area the CFDA was keen to reform, as well as to use the reform to direct innovation in strategic therapy areas. It especially sought to shorten clinical trial periods for investigational new drugs (IND) in therapeutic areas such as immunology (checkpoint inhibitors and

CAR-T). According to McKinsey, 177 molecules were granted priority review by the CFDA in 2017, 40% of which was in anti-infectives and oncology. Similarly, nine of the 35 innovative drugs approved for launch in 2017 (between January and October) had their launch times reduced dramatically (see Fig. 3).

China's biotech boom

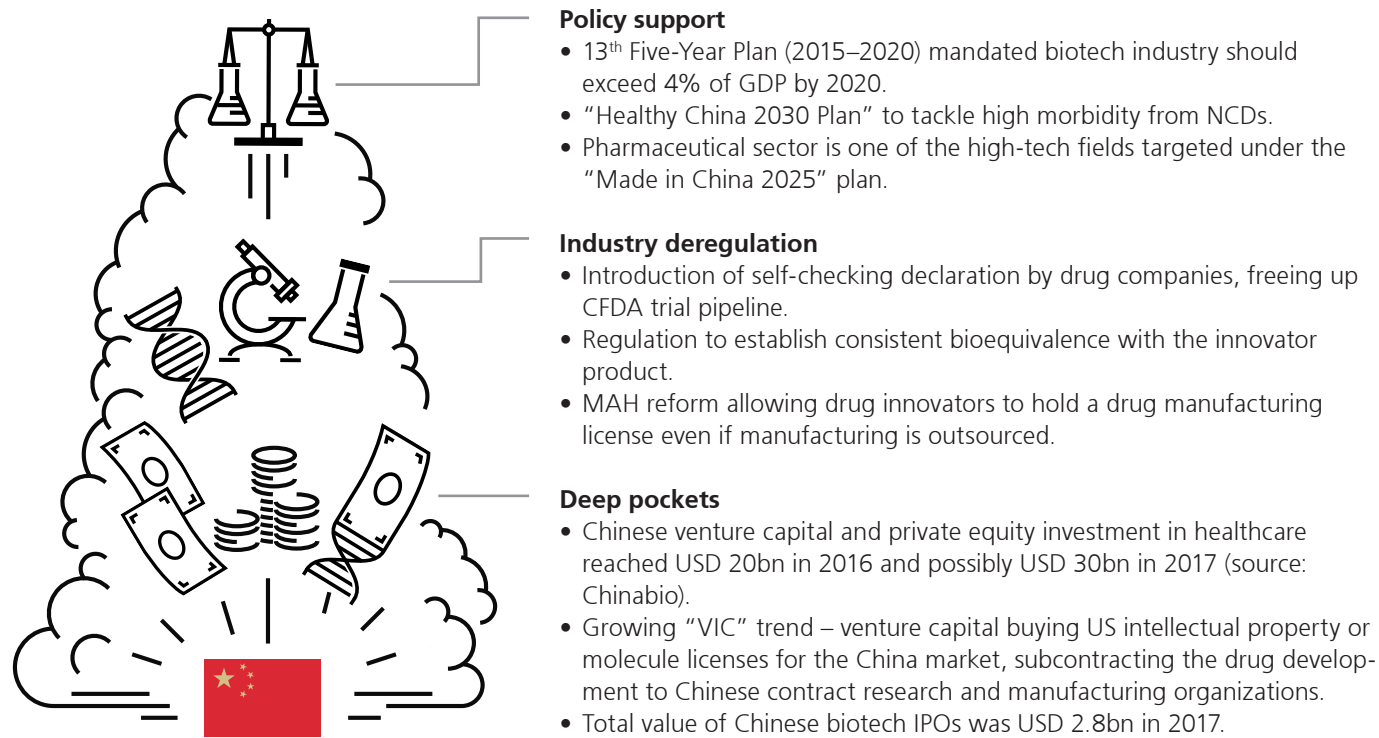


Fig. 2

China's CFDA clinical testing process is closely modeled on the US FDA's

	Phase I	Phase II	Phase III
Definition	Test how the drugs interact with body and decide dose range	Assess efficacy and adverse effects of the drugs	Further assess efficacy and safety, determine the therapeutic effect
Participants	Healthy people, small group (10–50)	Patients with the disease, larger group (100+)	Patients with the disease, larger group (100+)
Years needed	0.5–1	1–2	2–3+
Average cost	USD 1–20m	USD 5–50m	USD 10–300m
Success rate	63.2%	30.7%	58.1%

Source: Tufts Center for Drug Discovery Research; Biotechnology Industry Organization, UBS as of 2016

Anti-infectives: Drugs that are capable of inhibiting the spread of an infectious organism by killing it.

Genomics: A field of science focusing on the structure, function, evolution, mapping, and editing of genomes – an individual's complete set of DNA. Genomic analysis can identify an individual's predisposition to certain diseases, allowing them to take preventive steps.

“China has an insatiable appetite to access the biotech area...I don't think there's going to be any shortage of Chinese capital...”

— Joel Marcus, CEO of Alexandria Real Estate Equities

Deep pockets for Chinese biotech

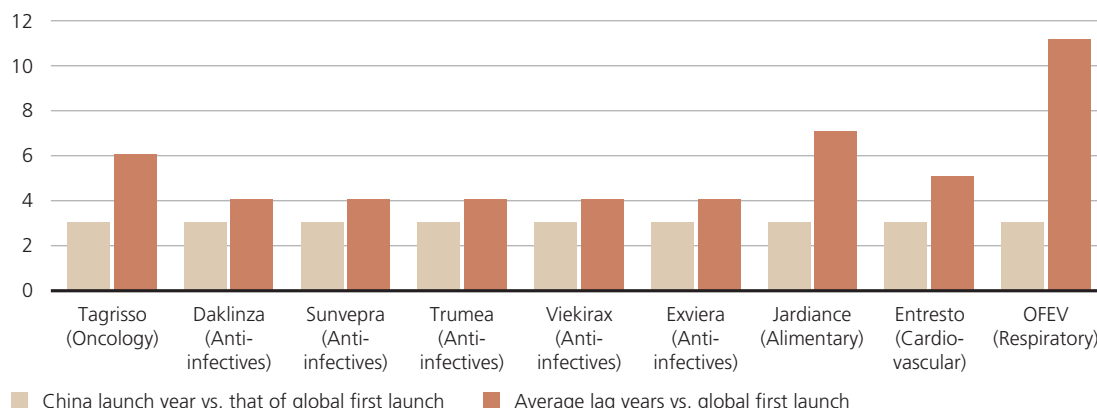
The third key pillar helping to grow China's nascent biotech sector is the ready availability of capital in China for investment in the sector. According to Chinabio, Chinese venture capital and private equity raised USD 45bn for investment in life sciences from January 2015 to June 2017. Only one-third of this sum was reportedly invested due to a dearth of innovative investment targets. Chinese venture capital and private equity investment in healthcare doubled to USD 20bn in 2016, possibly reaching USD 30bn in 2017. Outbound Chinese M&A in biopharm also reached USD 3.9bn in 2017, the bulk targeting US companies. According to Dr. Zhang Dan of FMD (interviewed on page 9), Chinese investment into the US biotech sector in 1Q18 was 10-fold higher than the same period in the previous year, reflecting the growing “VIC” (venture-IP-contracting) trend – venture capital buying US intellectual property (IP) or molecule licenses for the China market, and then subcontracting the drug development to Chinese CROs and CMOs.

The combined value of Chinese biotech IPOs globally reached USD 2.8bn in 2017. While the previous trend has been for Chinese biotech companies to list overseas, we expect this to gradually shift as Chinese bourses relax listing regulations to accommodate the biotech sector. The implications are that local biotech companies will find it increasingly easier to raise equity funding through domestic public markets rather than having to go overseas.

China's giant internet and fintech platforms (Baidu, Alibaba, Tencent and Ping An Insurance, which have a combined market capitalization of USD 1.3trn) are also active investors in China's biotech sector. They often provide seed capital focused in areas that can be leveraged through artificial intelligence or in areas that can be commercialized through digitalization like genomics, diagnostics and telemedicine.

Fig. 3

Innovative drugs approved by CFDA in 2017 by therapeutic area and by launch lag years



Source: CDE, GBI, October 2017

Interview with Dr. Dan Zhang of FMD



Dr. Dan Zhang
Executive chairman of FMD

Dr. Dan Zhang is the executive chairman of Fountain Medical Development Ltd, a clinical contract research organization (CRO) with 1,700 employees operating in China, Hong Kong, Taiwan, South Korea, Japan, UK, India, Philippines, Armenia and the USA. Dr. Zhang received his pre-med training from Peking University, received his M.D. from Peking Union Medical College, and received a Master's of Public Health from the Harvard School of Public Health. He obtained a master's degree in healthcare management in 1998 from the Wharton Business School of the University of Pennsylvania.

Can you talk about your background studying, researching and working in the US and what brought you back to China? What led you to decide to found FMD?

I originally started my medical training at Peking University and then went on to obtain a Master's of Public Health at the Harvard School of Public Health in the US. After graduating, I received a master's degree in healthcare management from the Wharton Business School in 1998.

When I completed my studies, I started to work for Quintile, a US-based CRO. Quintile subsequently asked me to head up their greater China operation in China, so I returned to Beijing where I worked for five years. I was then approached by Italian pharmaceutical company Sigma Tau Development to head their US clinical development, so I returned to the US. I worked for them for five years and was also their head of safety. I was then approached by China's Ministry of Science and Technology to return to China and set up a CRO. This was before the Thousand Talents initiative and was rather unusual, and was how Fountain Medical Development (FMD) was founded. It is now a 100% private entity, following a management buyout.

How did the Market Authorization Holder Law of 2015 benefit CROs in China, and what do you think motivated the government to pass this law?

This was tremendously beneficial for Chinese CMOs, and immediately spawned the creation of contract development and manufacturing organizations (CDMOs). It encouraged all biologic developers in China to take advantage of the opportunity to outsource to CDMOs. However, CROs like us also benefited because biologic devel-

opers found themselves with more time and resources at hand to develop new programs and molecules, all of which required research capabilities. One of the reasons the government pursued this policy was because CMOs, which were likely to be more focused on manufacturing, could pursue clinical trials more efficiently and faster. At the time, the regulator was trying to streamline and improve the entire clinical testing system. China learned about the contracting manufacturing industry from the US and Europe but had been concerned about quality standards, believing that a developer that also manufactured its own drugs was more likely to maintain quality standards to guarantee its supply.

What's your view on the trend of technology transfers and Chinese firms' licensing of molecule rights from MNCs? How about on Chinese companies developing their own molecules?

Technology transfers are very popular in China at present. In fact, in 1Q18 Chinese investors put 10 times more money into the US biotech sector than the same period of the previous year. A lot of the spending targeted technology transfers. Chinese investors are starting to buy the rights to molecules developed overseas, particularly in the US, for launch in China. It is a rapidly growing trend, especially now that CROs and CMOs can do all the "heavy lifting" for the China licensee. It's a model known in China as the VIC model. Venture capital (V) buys the intellectual property (I) and then contracts (C) out the domestic licensing to CROs and CMOs. The VIC model will be the main trend for some time to come in my view. China has begun to attract talent back under its Thousand Talents program, however I believe it will be at least 10 years until we truly start to develop our own intellectual property capabilities.

What type of biologics is FMD most involved in developing (which therapeutic area?) and what are the trends you see in the Chinese biomed market going forward?

We tend toward more oncology product development. This is not just a trend in China but also in the US, Europe and Japan where oncology is a hot area. With new policies in China and the US, particularly with the US adopting real-time reviews of oncology products, the entire oncology industry is on the rise globally. China is also part of this global oncology product development drive, as it has the highest incidences of cancer in the world.

Is the biosimilar market in China a potentially attractive one in your view?

China has huge market potential to develop biosimilars, as its own ability to develop bio-origins is currently limited and biosimilars are a good way to follow and slowly build its own capabilities.

Would you say that there is a sufficiently strong culture of innovation in China? What is changing and what do you think is driving the change?

Chinese culture has traditionally not been a very supportive one for innovation. However, over the last 10 years, the central and regional governments have made innovation a top priority. A lot of encouraging policies have been put in place to drive innovation in the biotech sector; for example, allowing research scientists to set up commercial operations without losing their academic posts. The government is also investing more to encourage innovative research and to encourage companies to pursue innovative product development.

How does China source the talent and technology to grow biotech?

"Biotech is people, people, people."

– Qinwei Zhou, COO of Innovent Biologics



The common perception within China's largely generic pharmaceutical sector is that the mindset, talent and culture to create an environment for innovation, which is necessary for a successful biotech industry, is absent within China. The CFDA recognizes the dearth of innovative local companies and the key role that MNCs play in nurturing local talent. It is no accident that the CFDA's big bang made it easier for MNCs to apply for multi-regional clinical trials and launch drugs by removing the pre-requirement that new foreign drugs be registered outside of China and be in phase II or III trials overseas. The reaction to this regulatory shift was immediate, with 34 of

the 35 new drugs launched in China in 2017 from MNCs. The CFDA also made the approval process faster for priority therapeutic areas and INDs. AstraZeneca's lung cancer treatment pill, Tagrisso, made headlines in 2017 for achieving clinical launch approval in China within just three years of application. In April 2017, China's Finance Ministry announced it would remove tariffs on imported anti-cancer treatments and potentially on all imported therapies. While a key reason behind this was to improve local affordability of critical drugs, the government also hopes it can encourage homegrown drugs to be price competitive.

The search for biotech expertise has not only targeted MNCs but also the large pool of Chinese PhD researchers working at post-graduate research institutes and foreign companies. Chinese students in the US, for example, currently number 352,000 and make up the largest foreign student group at almost one-third of the foreign student population. Most study chemistry and engineering. Over the last six years, 250,000 of the 2 million returnees, known as “sea turtles” (haigui), are estimated to be working in China’s life sciences industry. They have been lured back to China by new regulations allowing research professors to hold positions at private companies. China’s “Thousand Talents Plan,” designed to recruit overseas talent, confers prestige, attractive remuneration and career enhancement opportunities to researchers or employees poached from high-profile overseas R&D institutions and companies. Moreover, a surplus of local venture capital looking for innovative ideas, coupled with new start-ups’ access to local equity funding, makes China an attractive environment for Chinese returnees. Significantly, many Chinese biomedic professionals (including some of our interviewed panel) have migrated to Chinese start-ups from MNCs, another channel of technology transfer.

There has been a small number of cross-licensing deals that have emerged in recent years between US companies (Celgene, Lilly) and Chinese biotech companies, with the latter (Hengrui, Beigene) having licensed Chinese development and commercial rights to US companies. We expect the emerging trend toward exclusive licensing of molecules developed by US and other foreign companies to Chinese companies to grow strongly in the wake of CFDA regulatory reform. Besides the aforementioned VIC model, as existing Chinese biotech companies become more profitable and enjoy increasing local access to public equity markets, they will be in a position to buy or pay more for licenses, in our view. Licensing molecules in China and producing them through CMOs is an effective channel of technology transfer and future biosimilar development. Conversely, while out-licensing of Chinese biotherapies to the US market is likely to continue, we expect to see an increasing trend of Chinese companies pursuing their own clinical trials in the US and other markets despite the higher costs involved, a point highlighted by Dr. Tong, CEO of Kintor (interviewed on page 18). This may partly reflect better local funding prospects for Chinese biotech firms, but it is also likely to occur when the risks of clinical test failure are perceived to be lower.

Fig. 4

China is a leading source of international students at US universities

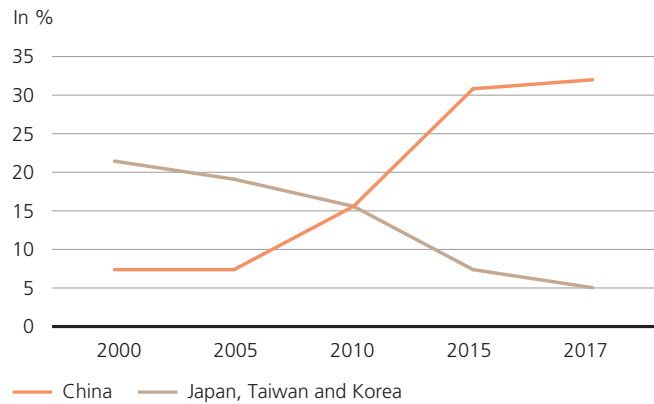
	2000	2005	2010	2015	2017
China	11%	11%	18%	31%	32%
India	8%	14%	15%	14%	17%
South Korea	8%	9%	10%	7%	5%
Saudi Arabia	1%	1%	2%	6%	5%
Canada	5%	5%	4%	3%	3%
Vietnam	0%	1%	2%	2%	2%
Taiwan	6%	5%	4%	2%	2%
Japan	9%	7%	4%	2%	2%
Mexico	2%	2%	2%	2%	2%
Brazil	2%	1%	1%	2%	1%
Int'l students in US	514k	563k	692k	977k	1.1m
US enrollment	14.8m	17.3m	20.4m	20.3m	20.3m
% int'l in US	3.5%	3.3%	3.4%	4.8%	5.2%

Source: UBS, Institute of International Education, Open Door Report, November 2017

A third key channel for technology transfers has been overseas M&A. Chinese M&A involving US biotech reached an all-time high of USD 2.8bn in 2017 (source: McKinsey & Company) through five deals, of which Sanpower's acquisition of Dendreon Pharmaceuticals was the largest at USD 820m. According to the South China Morning Post, Chinese venture capital invested USD 1.4bn in US biotech in the first quarter of 2018, 40% of the total USD 3.7bn that had been raised over the period. While Chinese government capital controls and greater scrutiny of overseas M&A have impacted Chinese M&A growth, investment in biotech receives full government support as it falls into the politically important category of "high tech and advanced manufacturing investment, overseas R&D centers." Still, biotech is often a sensitive and strategic national sector; delays in China's largest overseas acquisition of Swiss agricultural biotech firm Syngenta for USD 43bn are a reminder of this.

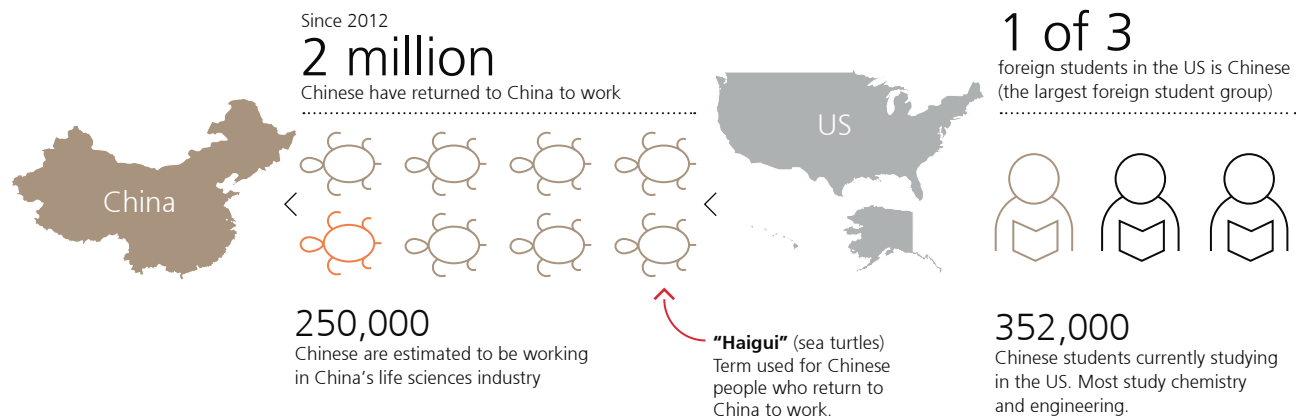
Fig. 5

Chinese vs. other Asian students as a share of US international students



Source: UBS, Institute of International Education, Open Door Report, November 2017

Chinese students foreign education



Source: UBS, Institute of International Education, Open Door Report, November 2017.

Oncology: A driving force for innovation in Chinese biotech

"I want to see cancer cured in my lifetime. It might be."

– James D. Watson



Oncology: A branch of medicine that deals with the prevention, diagnosis and treatment of cancer.

China suffers from an unusually high incidence of cancer, which has been the country's leading cause of death since 2010. The country recorded 3.8m new cancer cases in 2014, accounting for 27% of new global cases even though China claims 20% of the world's population. For some cancer types such as lung cancer, China's share of global incidences is even higher: there were 730,000 cases of lung cancer in 2015, accounting for 36% of the global total. High lung cancer rates in countries like China have been linked to air pollution (source: WHO). The World Health Organization forecasts that demographic effect alone will result in China's total new cancer cases (ex-melanoma) almost doubling to 5.5m cases per year by 2035 from 2012. Meanwhile, the WHO expects total deaths from cancer will rise 80% to 4.3m per year in China over the same period. And the share of patients over 65 years old developing cancer will rise from 60% of the total in 2012 to 75% of the total in 2035, reflecting the relationship between China's rapidly ageing population and cancer incidence.

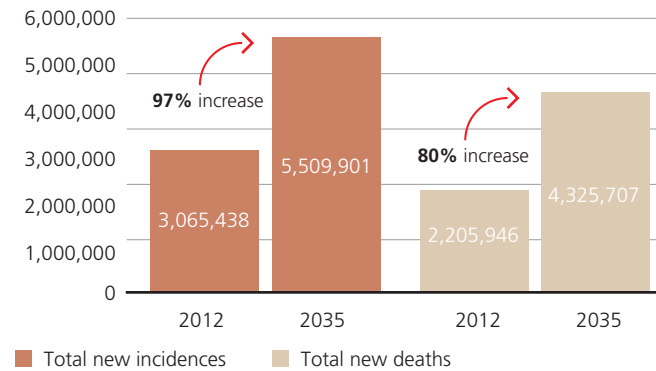
Despite China's high cancer mortality rate, which is forecasted to rise 80% by 2035, China represents just 4% of the global oncology drug market and oncology drugs only represent 9% of total domestic drug sales. Affordability is one reason, and the low quality of treatment is another – it drives many patients to seek treatment overseas. Every year over 1.1m Chinese spend an aggregate USD 8.8bn on overseas medical treatment, often to treat NCDs at advanced stages. The business case for offering effective, affordable and quality oncology therapies at home to remedy the country's leading killer is significant; IMS Global Oncology reports a growth rate of 10% for Chinese oncology sales over the last five years, outpacing the global sector. Indeed, anti-cancer drug research and treatment are the leading drivers of innovation in China's biological drug industry, where oncology claims over half of total sales value, ahead of the global average.

Chinese biologics – the world's fastest-growing biotech market

Biopharmaceuticals, or biological drugs, which are made from living organisms rather than chemical syntheses, are currently the fastest-growing sector in global healthcare. Only 2% of Americans use biologics, even though they make up 40% of pre-

Fig. 6

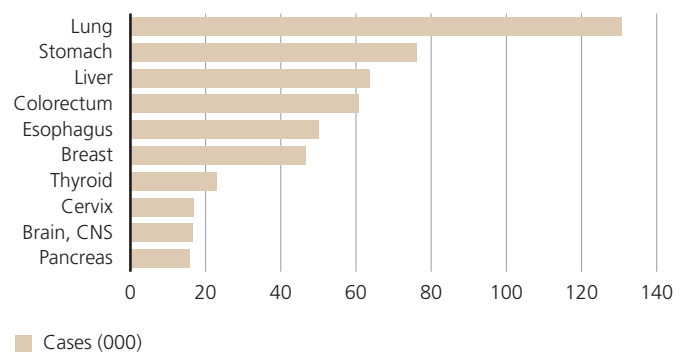
China's estimated cancer incidence and mortality from 2012–2035



Source: GLOBOCAN 2012: Estimated Cancer Incidence Mortality and Prevalence Worldwide in 2012, WHO, June 2017

Fig. 7

Annual new incidences of cancer in China by type

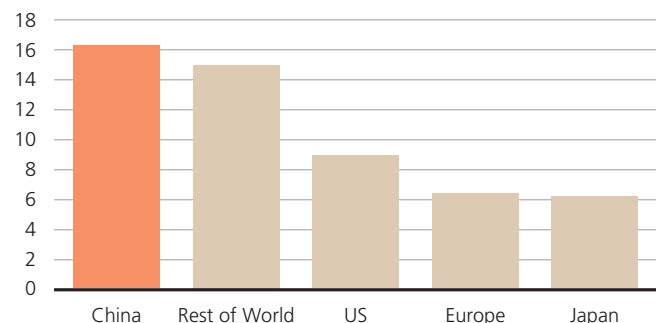


Source: WHO, Cancer Incidence and mortality in China in 2013

Fig. 8

Comparative forecasts for global biologics market growth

CAGR from 2010–2021E, in %



Source: Frost & Sullivan

Immuno-oncology: An innovative approach that uses the body's immune system to help fight cancer. Applications include the use of monoclonal antibodies to improve or restore immune system functions, which have broken down due to the cancer cells.

scription drug spending in the US. Biologic treatments cost on average 22 times more than traditional therapies. Their premium prices are the key reason they attract higher R&D spend by pharmaceutical companies.

According to Frost & Sullivan, Chinese biologic drugs make up 12% of China's total drug market, compared to a global penetration of around one-quarter – yet it's the fastest-growing area in China. China's biologic drugs market expanded from CNY 62.7bn in 2012 to CNY 152bn in 2016, an annual growth rate of 25%, ranking China as the world's fastest-growing biologics market. Frost & Sullivan forecasts the market's total value at CNY 326bn by 2021, implying an annual five-year growth rate of 16.4% (see Fig. 9).

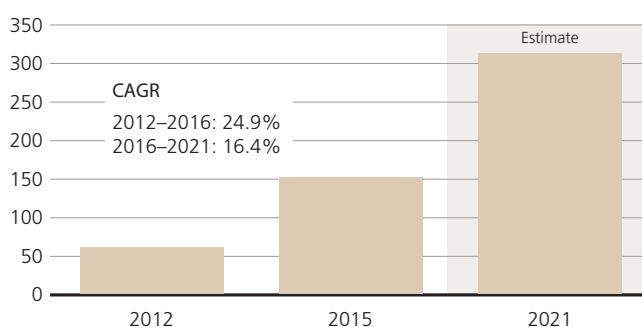
Unsurprisingly, China's fast-growing biologics market is making important early breakthroughs in therapies derived from advanced treatments for cancer. Predominant examples include advances in monoclonal antibodies (mAbs), which are proteins

that mimic a body's immune system to attack foreign objects; immuno-oncology, which leverages the patient's natural immune system to kill cancer cells; and CAR-T, a type of gene editing of the body's T-cells to attack cancer cells.

Fig. 9

China biologics market size (2010–2021)

CNY billion



Source: Frost & Sullivan

Fig. 10

China's domestically produced antibodies and fusion proteins

Generic name	Company	Indication	Year	Technology
Etanercept	CP Guojian Pharma	Rheumatoid arthritis, ankylosing spondylitis	2006	Fc fusion protein
I131-labeled human-mouse chimeric mAb	Shanghai Meien Biotech	Late-stage lung-cancer	2006	Chimeric mAb
CD3 murine mAb	Wuhan Biopharma	Organ transplant	2010	Murine mAb
Anti-human Interleukin-8 mAb	Asia Space Pharma	Psoriasis, eczema	2010	Murine
Anti-rh-TNF II antibody fusion protein	Celgen Pharma	Moderate to severe spondylitis ankylosans	2011	Fc fusion protein
Humanized anti-CD25mAb	CP Guojian Pharm	Organ transplant	2011	Humanized
I131-labeled metuximab	Huasun Pharma	Liver carcinoma	2011	Murine
Humanized anti-EGFR mAb	Biotech Pharma	EGFR+ stage III/IV nasopharyngeal carcinoma	2012	Humanized
Conbercept	Kanghong Pharma	wet AMD	2013	Fc fusion protein
Anti-rh-TNF II antibody fusion protein	Hisun Pharma	Rheumatoid arthritis, spondylitis ankylosans, Psoriasis	2015	Fc fusion protein

Source: CFDA, J.P. Morgan, 2018

Monoclonal antibodies (mAb): The immune system attacks foreign substances in the body by producing and releasing antibodies, which attach to the intruders. Cancer cells develop from normal cells, making them difficult for the immune system to spot. Monoclonal antibodies are designed to target specific cells or proteins that are relevant to the disease being treated. MAbs are used to treat cancer, cholesterol, rheumatoid arthritis, pain, etc.

Monoclonal antibodies leading China's biologics growth

Monoclonal antibodies are key therapies for many types of cancer, psoriasis and auto-immune diseases like rheumatoid arthritis. They have become the leading segment within global biologics, with a value of USD 100bn in 2017 – over 40% of the biologics market (source: Kalorama). In 2017, following its regulatory big bang, China launched 22 mAbs, of which 12 were imported and 10 developed locally. Although this first wave of Chinese domestic mAbs was of variable quality, Conbercept, used for the treatment of wet AMD, an eye disease affecting the elderly, is considered an innovative domestically developed therapy. Development of mAbs in China has faced the challenges of high costs and a lack of recognition by the medical establishment. However, this has improved in recent years, with more efficient clinical trials,

improved reimbursement by the NRDL and better pricing. China now has 171 mAbs under development (source: CFDA), over one-fifth of total mAbs under development globally.

Immuno-oncology

Immuno-oncology uses a patient's own immune system to kill cancer cells, rather than directly attack cancer cells itself. This therapy has the advantage of being longer lasting with fewer side effects and is often combined with other cancer therapies. China is currently developing at least 16 checkpoint inhibitors, known as PD-1 and PD-L1, a type of mAb that blocks proteins that are preventing an immune system from attacking cancer. This development compares with around 50 candidates being developed globally that are undergoing phase II or III testing. Many checkpoint inhibitor developers in China are prominent domestic biotech compa-

Fig. 11

Summary of PD-1/PD-L1 development in China

Company	Candidate	Target	Stage
MSD	pembrolizumab (Keytruda)	PD-1	Phase III (in China)
BMS	nivolumab (Opdivo)	PD-1	Phase III (in China)
Hengrui	camrelizumab (SHR-1210)	PD-1	Phase III (multiple trials in phase I and II for different indications)
Innovent	IBI308	PD-1	Phase III
Beigene	BGB-A317	PD-1	Phase II (expected to start phase III soon)
Junshi biopharma	JS001	PD-1	Phase II
Genor biopharma	genolimzumab	PD-1	Phase I
Gloria pharma/Wuxi App tec	GLS-010	PD-1	IND approved
Akeso biopharma/Hanzhong biopharma/Hanzhou hansi biopharm	AK-103	PD-1	CTA in review
Bio-Thera Solutions	anti PD-1 mAb	PD-1	CTA in review
Henlius	anti PD-1 mAb	PD-1	CTA in review
Livzon	anti PD-1 mAb	PD-1	CTA in review
Alphamab/3dMed	KN035	PD-L1	Phase I
Hengrui	SHR-1316	PD-L1	Phase I
Kelun	KL-A167	PD-L1	CTA in review
Cornerstone/Tuoshi pharma	anti PD-1 mAb	PD-L1	IND approved

Source: ClinicalTrial.gov, GBI, Berstein analysis

Interview with Dr. Youzhi Tong of Suzhou Kintor



Dr. Youzhi Tong
CEO of Suzhou Kintor
Pharmaceuticals

Dr. Youzhi Tong is the founder and CEO of Suzhou Kintor Pharmaceuticals, a biotech company focused on developing novel medicines for treatment of oncological diseases. Dr. Tong received his B.S. and M.S. in chemistry from Peking University, his PhD. in pharmacology from Cornell University / Memorial Sloan-Kettering Cancer Center, and completed his postdoctoral fellowship at Cornell Medical School. Dr. Tong has 30+ years of academic and biotech industrial experience, with specialties in pharmacology and exploratory R&D. Dr. Tong was assistant professor at Albert Einstein Medical School, served as director of the radiation oncology laboratory at North Shore-Long Island Jewish Health System laboratory, and was vice president of Angion Biomedica Corp., a clinical stage organ restoration biopharmaceutical company.

As a small molecule chemical drug developer, why is Kintor moving into biodrug development?

Instead of categorizing our product strategy by small and big molecules, we prefer to define ourselves by our core target therapeutic areas. Our strategy is to primarily focus on select major therapeutic areas, such as prostate cancer and triple negative breast cancer, to serve the unmet medical demand with a full solution, ranging from small molecules to large complex biologic drugs and combination therapies. Compared to the reliance on single drug therapy of either small or big molecules, we view combination therapy as a major trend for cancer treatments going forward.

What do you think of China's biosimilar market? Do you think there will be a lot of patent infringement in this market?

Given the large Chinese cancer patient base and the need for more affordable medicines, the addressable biosimilar market should be very big. However, the intense competition within the industry has resulted in significant pricing pressure, which could be a major challenge for most companies, especially for domestic biosimilar players. The differentiation in biosimilar players remains in their capabilities in cell-line development and manufacturing process that ensure quality and consistency of products, as well as regulatory strategy to become among the first-to-launch.

With China joining the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use, we expect there will be more patent-related

lawsuits happening in the near term. While China will continue to push toward international quality standards, there will be a significant variability of quality for biologics and biosimilars as competition intensifies.

What do you see as the future industry trend for biologics?

In my opinion, as we advance our understanding of human drug targets through scientific research, we should expect the number of effective targeted drugs being launched in the market to increase dramatically. Particularly, current and future research shall provide a much more insightful dissection of the mechanisms of action of a variety of drugs, thus revealing details around the interconnectivity between drug targets. Another important trend should be an increased availability of combo therapies, providing efficacious treatments due to synergies realized through acting on multiple targets. This may act in concert through the combination of more established and standard treatments and those addressing novel targets. Testament to this success would likely require better coordination between domestic and overseas companies, bringing together know-how and capabilities in the years to come.

What are the trends you see in the Chinese bio-med market?

Lung, breast and liver cancers have the largest number of patients currently in China. Prostate cancer has been the fastest-growing but the most under-diagnosed cancer in men in the past decade, as 40% of patients undergoing treatment develop metastatic or late-stage prostate can-

cer. The market for major cancers is facing intense competition from both overseas and domestic players. Overseas companies' products are able to enter China at a faster pace due to the introduction of new CFDA policies that expedited the approval process of qualified therapies. Most have attempted to address the mass China market by lowering their drug prices relative to their home markets. On the other hand, domestic companies have focused on a few "hot" therapeutic areas, resulting in significant over-competition in crowded markets.

How does being a "haigui" (returnee) benefit you in developing and launching drugs overseas?

The Chinese government has been actively supporting overseas experts to return to China, and we are very grateful for all the governmental support we have received since the inception of our company. Such a supportive environment has also attracted more and more returnees to come back and make contributions to our country in their respective fields.

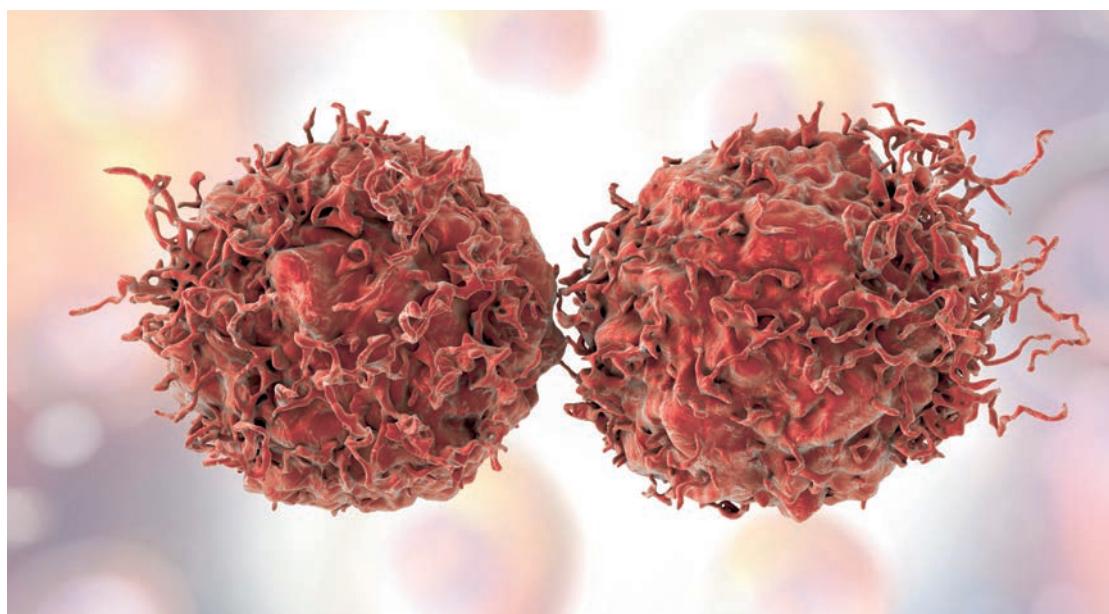
nies, with at least two candidates being developed by MNCs for lung cancer treatment. In fact, one of them produced the first PD-1 inhibitor to be approved in China (on 15 June) (see Fig. 11). Checkpoint inhibitors have become an active and competitive space in China because the CFDA prioritizes these drugs as INDs and therefore facilitates accelerated market launches based on phase II clinical trials.

China's CAR-T success

Isolated cases of real innovation are starting to emerge in several categories of Chinese biologics. One therapeutic area that has achieved a measure of local success is CAR-T (Chimeric antigen recep-

tor) treatment, a complex and personalized treatment for blood cancer. With CAR-T treatment, cell-killing T-cells are removed from the body and engineered to recognize the relevant cancer target. After the edited T-cells (CAR-Ts) are reintroduced to the patient, they multiply and attack the targeted cancer cell. CAR-T is a last line of defense against cancer, but can have serious side effects and is prohibitively expensive at a cost of USD 500,000 a treatment in the US.

Because CAR-T clinical trials have "orphan designation" in China, companies enjoy streamlined and accelerated clinical trials, which lower costs. They can also enjoy tax breaks. At least four other



Prostate cancer cells.

Biologics: Unlike regular drugs, which are manufactured through chemical synthesis, biologic drugs, or biologics, are pharmaceutical drug products synthesized from biological sources. Producing biologics is a far more complex (and costly) process than manufacturing regular drugs, yet they have been efficacious in treating certain medical conditions where regular drugs have failed.

Originator biologics (bio-origins): Approved biologics, whose molecules are used to form biosimilar products and are protected by patents.

“We’re still in the very nascent stages of the biosimilar story...it’s in a state of flux right now, and that’s why it’s interesting.”

— *Asthika Goonewardene, Bloomberg Intelligence*

Chinese biotech companies have IND filings for CAR-T that are under development. Notably, outside of China there are only two approved CAR-T treatments, which are developed by Gilead and Novartis. This is a considerable milestone for China because it demonstrates that Chinese researchers repatriated from the US can innovate in the home market, and then proceed to develop the therapy globally through their overseas networks. By leveraging China’s mid-stream genomics sequencing capabilities (see next section), the hope is to build on China’s nascent CAR-T technology and move on to other gene-editing therapies, including those that can tackle solid tumors, which are currently beyond the reach of existing CAR-T treatments. Select Chinese biotech companies like Hengrui are already starting to explore a more advanced form of CAR-T therapy that can be mass produced at lower costs, although this technology is still at an immature stage.

Biosimilar drug growth potential

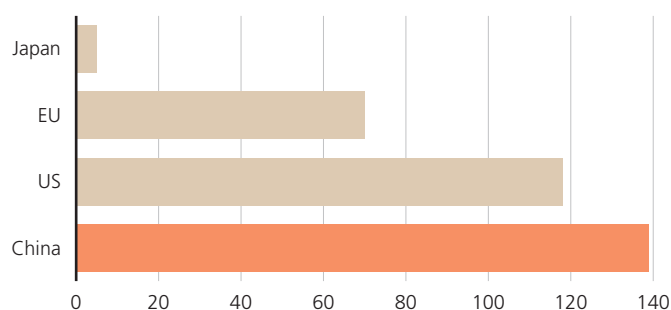
The Chinese government has prioritized certain therapeutic areas in part because of the growth potential of the biosimilar (the biologic equivalent of a generic chemical drug) market, given the number of expiring blockbuster biologics patents. Although only 1.3% of the global market is comprised of biosimilars, this sector is expected to reach USD 21bn in value by 2025, growing at a compound annual growth rate of 30%, according to Sandoz forecasts. One reason the biosimilar market is so undeveloped compared to generics is because as living systems, biologics do not tolerate changes to the manufacturing process. This also complicates IP protection and regulation due to the dynamic nature of living organisms compared with the fixed structures of manufacturing small molecule drugs.

Many originator biologics were developed in the nineties, with the equivalent of USD 65bn in sales of protected drugs, almost one-third of the entire global biologics market, set to expire in

Fig. 12

China emerging as a growing force in CAR-T clinical research¹

Number of trials



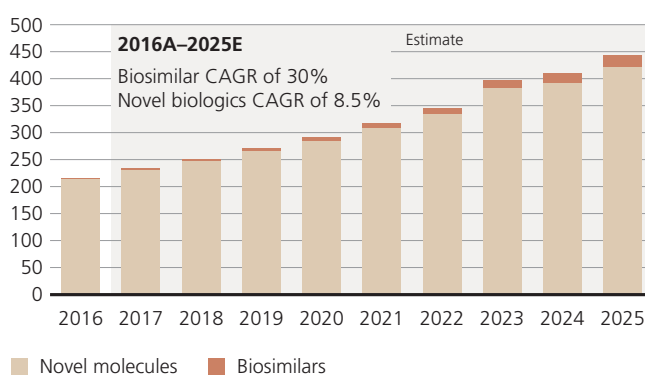
¹ Number of clinical trials of CAR-T cell therapy by 2 Oct 2017

Source: McKinsey and Company, November 2017

Fig. 13

Superior growth prospects of global biosimilar drugs

USD billion



Source: Frost & Sullivan, EvaluatePharma, J.P. Morgan

Europe and the US from 2015–2020 (refer to Fig. 14). Although China has its own patent system, most MNCs typically register their patents in China at the same time as they do in the US or Europe. China’s signing of the International

Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use now exposes Chinese companies to litigation if registered patents are not honored – a point raised by Dr. Youzhi Tong in the previous interview. By 2030, the patents for several blockbuster biologics including, Humira, the world’s bestselling biologic, will expire. Humira, the trade name for adalimumab, an anti-inflammatory TNF inhibitor, is used to treat rheumatoid, psoriatic arthritis and Crohn’s disease. The drug generated sales of USD 16.4bn in 2016 and doubled in price between 2012 and 2017. With its patent in the US and the EU expiring in 2016 and 2018 respectively, there are currently 15 biosimilars being developed by MNCs. The huge advantage of biogenerics to treat critical or essential diseases in China is that they can often be produced at much lower costs and at starting price

discounts of 25% to bio-originals and potentially much higher once more players have entered the market (source: J.P. Morgan). With the annual cost of treatment of a top biologic like Humira running at USD 38,000, biosimilars are potentially much more affordable solutions for Chinese consumers while the cost savings for the Chinese government, which now reimburses up to 100% of specific NRDL biologics, could be considerable. Two cancer treatment biologics, Herceptin and Avastin, added to the NRDL in 2017, are examples of expensive cancer treatments that will see their patents expire in 2019 (see Fig. 14). Earlier this year, new NRDL regulations stated that any approved new generic or biosimilar of an existing NRDL original drug is guaranteed automatic inclusion in the list, serving to further incentivize growth of this sector.

Fig. 14

Blockbuster biologics’ patents set to expire from 2015–2025E

2015	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Lantus	Rituxan	Novomix	Remicade	Herceptin	Lucentis	Soliris		Stelara	Aranesp	Prolia
Neulasta	Humira		Erbitux	Avastin						
Epogen			Xolair	Levemir						

Source: Company data, J.P. Morgan Research, 2018

Interview with Ruilin Zhao of Illumina



Ruilin Zhao
Vice president and
general manager of
commercial operations for
Greater China at Illumina

Ruilin Zhao is the vice president and general manager of commercial operations for Greater China at Illumina, a US-listed company. In his role, Zhao is responsible for the development and implementation of the company's overall China strategy for sales, services and marketing in mainland China, Hong Kong and Taiwan. Before joining Illumina in 2014, Zhao held several leadership positions at Thermo Fisher, including China head of corporate marketing and commercial operations. Prior to Thermo Fisher, Zhao held roles as vice president of finance at OrbusNeich and vice president of business development at Microport Medical (Group) Co. Zhao received his doctorate in medical engineering and medical physics from the Harvard-MIT Division of Health Sciences and Technology, a Master's of Business Administration from the Wharton School at the University of Pennsylvania, a master's in electrical engineering and computer science from Massachusetts Institute of Technology, and a bachelor's in biomedical engineering from Xi'an Jiaotong University.

What is Illumina's China strategy in general?

Illumina is a gene-sequencing machine maker that provides technology for the publication of genomics data. We hope to continue to build long-standing relationships with world-leading researchers. This will maintain the historical core of our business while we continue to develop our partnerships with innovators in the clinical space. China has a huge population with a long history of interest in medicine, health and wellness. From traditional Chinese medicine to the cutting-edge early diagnosis of cancer, Illumina is teaming up with leaders in the space to provide genomics tools that are tailored to the Chinese population.

Beyond health, China has a proud history and one of the longest-surviving cultures on Earth. The history of the Chinese people can be traced through changes in their DNA and mapping back to specific areas and families. We expect this to be a big area of growth in the near future.

How do you see the increasing competition from local sequencing machine producers?

We deal with local competition in the same way that we deal with all competition – by focusing on our customers and providing what they need to accomplish their research or business goals. Competition keeps us sharp, but doesn't distract us from working closely with our customers to deliver the best experience. We never get complacent and are always seeking to better our products and

services within China. We also partner with key opinion leaders and businesses to make sure that we are addressing the largest portion of the market that we can.

What domestic health policy changes do you expect on the horizon?

The Chinese government cares a lot about its people and their health. We expect to see increased reimbursement for sequencing-based diagnostics in areas from oncology to reproductive health. The government is ambitious about making China a place where new technologies are quickly, but safely, adopted and they will likely be putting more drugs and therapies on a fast track to approval.

What is your future expansion strategy?

Beyond the biggest cities in China, second- and third-tier cities are also taking an active interest in increasing their population's welfare as well as encouraging business development. So we are engaging actively with local governments and their partners to make sure they're equipped to meet their goals. As we expand in China, we are also making sure we are developing solid partners with Chinese companies to develop China-specific assays. This allows our sequencing technology to gain faster uptake in the market while complying with all local laws and regulations. We expect, like in other global markets, that the direct-to-consumer business, such as Ancestry.com and 23andMe in the US, will be of interest to Chinese customers whether it's a lifestyle or genealogical interest.

China's great genomics advantage

"The superior doctor prevents sickness; the mediocre doctor attends to impending sickness..."

– Chinese proverb



The global genomics market is forecasted to grow by an estimated 10.3% per year over the next two years and estimated to reach a total value of USD 27.6bn by 2020, according to Grand View Research. Genomics is one branch of biotechnology in which China enjoys an important competitive advantage, positioning it for dynamic growth. Aside from the essential role gene sequencing plays in creating biologics, genomics receives strong government backing in China as part of a drive to promote preventative medicine in order to reduce the incidence of NCDs. Preventative medicine uses genomics – the study of genes within DNA – to profile individual dispositions to

certain diseases. This allows people to take steps to prevent sickness.

This form of precision medicine has become a major focus for the Chinese government since 2016, when it launched a USD 9.2bn 15-year China Precision Medicine Initiative. Indeed, the funds that China is investing in the sector, together with the scale of its population, place it in a position to become a global leader in this field. China has spent the equivalent of USD 43 for every dollar spent by the United States Precision Medicine Initiative started in 2016. This has transformed China into the world's second-larg-

Diagnostics: The procedure of testing for medical conditions.

Biomarker: A naturally occurring molecule, gene or characteristic by which a particular pathological or physiological process, disease, etc. can be identified.



China's DNA repository of over 40m individuals, which targets 100m by 2020, dwarfs that of any other country, including the US's DNA database of over 9m and the UK's 6m

est sequencing market, and made the Beijing Genome Institute (BGI), with its gene bank of over 500m genetic sequences, the world's single-largest gene sequencer. China's DNA repository of over 40m individuals, which targets 100m by 2020, dwarfs that of any other country, including the US's DNA database of over 9m and the UK's 6m. Scale brings a clear competitive advantage to genomic clinical study in China because the larger the genomic database, the easier it is to establish patterns.

Alongside building enormous genomic databases from millions of samples, China is also stepping up research into genetic biomarkers. While clinical genomic study identifies genes involved in a large number of diseases, genetic biomarkers indicate disease severity or susceptibility to treatment. They are key in assessing a patient's response to particular treatments, paving the way for personalized medicine like CAR-T therapies. Biomarker research is still in its infancy in China, indeed globally, but Chinese firms are exploring the application of artificial intelligence to process large genomic databases in order to recognize

disease pathology and to identify new patterns and new biomarkers. The CFDA has also created new standards for this field, encouraging transparency and planning. The key listed genomics companies in China are upstream gene-sequencing machine makers and mid- to downstream gene-sequencing service providers. The entry barriers are especially high in the upstream sequencing machine-making industry.

Diagnostics

Several Chinese sequencing service providers have been particularly quick to commercialize clinical genomics for diagnostics. The key application has been non-invasive pre-natal testing (NIPT), which avoids using a syringe on an expectant mother to test for Down's syndrome (DS). The popularity of NIPT is due to the high incidence of babies born with DS in China and its ability to lower miscarriage risk for advanced-age child-bearing mothers. Other genetic-related diseases can also be screened by NIPT. Costs of NIPT in China vary from CNY 855–2,400 (USD 133–375) depending on province, with national insurance providing partial reimbursement. DPI Research reports that 300,000 NIPT tests were carried out in China in 2016 and forecasts 1.7m by 2024.



Telemedicine: The remote diagnosis and treatment of patients by means of telecommunications technology like smartphone apps.

While growing exponentially, this is still a small drop in the ocean and, in our view, should present significant growth potential as prices fall and affordability and awareness rise. With Chinese companies now launching their own proprietary gene sequencers, sequencing costs are expected to decline and reimbursement coverage should improve as test prices fall. As Dr. Zhao of Illumina points out (refer to interview on page 22), the Chinese government is expected to increase reimbursement coverage of sequencing-based diagnostics. We believe the Chinese government would like to see pre-birth genome sequencing for every baby at under CNY 100, ensuring an early establishment of healthy lifestyle practices to reduce NCD morbidity. Gene editing to create personalized cancer vaccines and gene testing for early cancer detection should be one of the leading growth areas within China's genomic industry, in our view.

Connecting the dots with digitalization: the rise of China's telemedicine market

Although not generally regarded as a field for biomedicine, the growth of telemedicine in China is creating a new platform for diagnostics, spurring the rapid development of the digital healthcare market in China¹. In the longer term, telemedicine diagnostics have the potential to leverage future genomic databases to offer personalized diagnostics and treatment. The rapid growth of telemedicine, or online medical services, in China has emerged largely because of elevated broadband/

mobile internet penetration, demographic dispersion and the idiosyncrasies of China's medical system. The latter includes a lack of general practitioners (as most medical doctors are specialists) and problematic access to doctors, drugs and hospitals for residents in more rural or remote parts of China. Telemedicine, which can leverage artificial intelligence through the use of bots to collect basic medical information prior to diagnosis by a live doctor, receives strong policy support from the Chinese government, as it can potentially cut healthcare costs. It also strongly benefits the consumer, as online diagnostic costs at this stage are free. According to Frost & Sullivan, China's online consultations grew 49% to 148m between 2012 and 2016, and are forecast to grow at a compound annual rate of 40% over the next decade. By 2026, almost one-third of all consultations will be online.

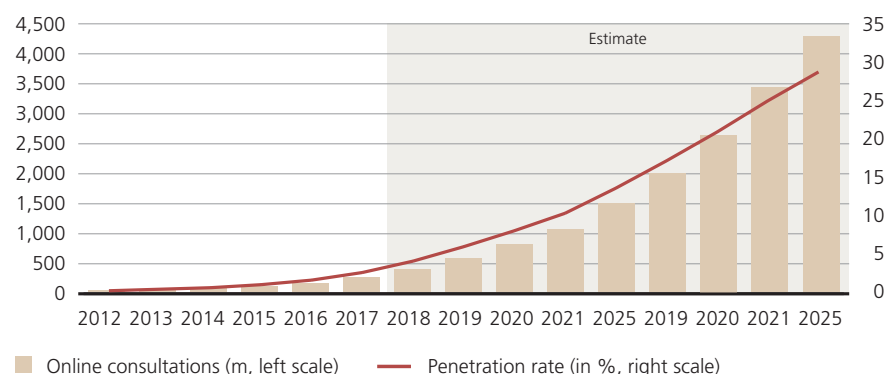
China's telemedicine market is currently led by Good Doctor, a subsidiary of life insurance company Ping An Insurance. Two other key players are Wedoctor, operated by China's largest online messaging platform (Tencent), and Alihealth, operated by China's largest e-commerce platform (Alibaba). While the business models of the three leading



By 2026, almost one-third of all consultations will be online.

Fig. 15

Online medical consultation growth trend in China



Source: Frost & Sullivan, April 2018

¹ For a broader insight of the global and Chinese telemedicine market outlook, refer to UBS Long Term Investments series publication on Healthtech (dated 28 June 2018).

Interview with Yingrui Li of iCarbonX



Yingrui Li
Co-founder and chief scientist
of iCarbonX

Yingrui Li is co-founder and chief scientist of iCarbonX. In 2006, he joined BGI and became chief scientist in 2010. He led the BGI research team to initiate and engage a number of national projects, including the Yan Huang Project, 1,000 Genomes Project, Yan Huang Whole Genome Methylation and Cancer Genome Project. He has more than 130 papers published in high-impact journals like Nature and Science. His own research interests include algorithms and data structures, computer programming, mathematical statistics, modeling methods, data mining techniques and genomics analysis. In 2015, He left BGI and co-founded iCarbonX, a new data-driven healthcare platform company, as chief scientist. He was featured as Thomson-Reuters' "Highly-cited Researchers" in 2014, 2016 and 2017, and included in Forbes' "30 under 30" list for healthcare sciences in 2015.

How do you see the digital healthcare market developing in China? Can it be a blueprint for Asia?

We should note that the digital transformation of an industry, healthcare specifically in our discussion, has to be based on standardization and informatization. It has been many years since China started to build information infrastructures from scratch in its hospitals and other medical service centers. Many software companies have therefore emerged from this trend. Frankly speaking, great efforts have been made. We also see a lot of cross-disciplinary collaborations that are advancing digital healthcare, empowered by IoT (Internet of Things), internet and artificial intelligence at different levels. Such topics include but are not limited to advanced clinical decision support systems, remote vital sign monitoring and caring, artificial intelligence in imaging analysis, assisted diagnosis and transaction optimization, online patient engagement and prescription, IoT applications in chronic disorder management and medical insurance, etc.

Obstacles do remain in this field, and some are really hard to resolve. Data flows are very fragmented and interoperability is highly limited, which constrains the power of big data. Even if an administrative bureau can gather data from all sources, data curation could be impossible, which would slow down insight discoveries. In short, there is a long way to go. Mobile healthcare applications and smart devices tried to solve part of the problem, and some companies have even opened or bought their own clinics to implement digital healthcare in a so-called "closed-loop," where all roles in the stakeholder chain become one entity. But they are far from achieving a scale comparable to the population of China.

Being a highly populated nation, we should keep in mind that China has a vast spectrum of development statuses across the country. Districts in well-developed areas could have advanced systems that implement real-time remote monitoring, while parts of western China may only have very basic medical devices. There are certainly valuable experiences to be leveraged in China's digital transformation, such as the application of mobile internet technology to improve the quality of community healthcare and to optimize the utilization of medical resources. However, I think it is quite early to judge whether it could be a "blueprint" for Asia.

Is health data in China sufficiently protected in your view?

I would say data access is strictly controlled. That is, access is very difficult and has to go through a long administrative check. In the meantime, awareness of the importance about personal healthcare records in the public has dramatically increased. Potential data leaks or misuse of information is now heavily punished by the government. In this way, the data is "protected." However, the use of data, such as for clinical studies or basic research, is hindered by such regulation. Personally, sufficient protection means advanced implementation of technical infrastructure and regulatory practices that promote research for good and prevent potential misuse and manipulation. While the infrastructure and practices are still far from perfect, the best option for health data management is to get rid of any risks and say no to most data access applications.

iCarbonX was originally designed as a data analytics company aggregating molecular profiles, conventional medical records, general wellness behaviors and environmental/social factors to model human individuals and therefore provide insights in healthcare management for more precise and personalized experiences. It is an “enabling” company rather than a product company. However, to demonstrate the complete picture of its concept, iCarbonX and its collaborators have developed various home-based data collection tools such as smart toilets, smart mirrors, continuous vital sign monitoring systems, etc. We also packaged these tools as well as analytics into wellness services to transform our collaborators into digital healthcare providers, including personalized skincare, diets, supplements, workout plans and medicines.

What is iCarbon X’s vision for the future?

We truly believe that in the future, a person will have the right to choose his own “healthy” way of living in which “healthy” is defined from his unique profile, which can be very different from what is recommended as generally good for the average population. We believe the onset of most chronic NCDs could be significantly postponed and their prognosis improved as a result, helping people to live longer with a superior quality of life.

players differ, it is significant that China’s leading life insurance and internet platforms lead the tele-medicine segment. By leveraging their existing information infrastructure, AI technologies, logistic channels and large captive online audiences, these companies offer consumers free diagnostic, appointment and drug-delivery services. They are also able to partially monetize these services

through their respective core businesses – i.e. health insurance, online advertising, merchandising, etc. In the long term, as online consultations become more scalable and grow from a current low base, we believe they will be able to generate fees in their own right, and at a later stage potentially be covered by China’s primary national medical insurance.

How to invest in China's medical biotech revolution

"Biotech investment is not for the faint-hearted investor."

– Charles Li, Chief Executive Officer, Hong Kong Exchanges & Clearing Ltd.



Publicly listed equities of Chinese companies engaged in medical biotech offer a direct means to gain exposure to China's medical biotech boom, in our view. These include legacy listed Chinese generic chemical drug companies that are moving into biologics, as well as a new wave of recent biomedicine listings of both drugs and equipment makers. Material exposure to biomedicine through legacy Chinese generic drug makers can vary greatly, despite almost all having ambitious biomedicine drug portfolio targets. Healthcare companies are still a relatively small part of

benchmark indices in China – in terms of market cap, they make up around 7% of main and SME A-share boards and around 11% of China's ChiNext bourse (a Chinese equivalent to NASDAQ). In comparison, healthcare stocks account for around 18% of the NASDAQ's total market cap.

Historically, financial requirements to list on Chinese and Hong Kong boards have not accommodated biotech companies that have neither profits nor sales. This has driven many new Chinese bio-



Around 250–300 Chinese biotech companies operate in Hong Kong.¹

tech start-ups to list overseas on boards like the NASDAQ or AIM (a sub-market of the London Stock Exchange that features small-cap investments). More recently, there have been initiatives to attract local biotech listings in China by loosening listing requirements; for example, on

China's National Equities Exchange and Quotations (NEEQ) board and on the Hong Kong Stock Exchange (HKEX). The HKEX introduced a major overhaul of listing regulations for biotech companies in early 2018, effective 1 May 2018. The new rules, combined with the perceived attractiveness of a USD-pegged currency, may well transform Hong Kong into the preferred destination for Chinese biotech companies seeking to list. According to Baker McKenzie Hong Kong, between 250 and 300 Chinese biotech-related companies operate in Hong Kong¹.

Private equity (PE) and sustainable “impact investing” in specialized areas of Chinese biotech, including oncology, offer early opportunities to invest in Chinese innovation, in our view. Many PE investors in private start-ups seek to exit via IPOs, and the aforementioned changes in HKEX regulations are likely to tap into this pent-up onshore demand for listings. With one in four global cancer cases in China, and given China's dependence on MNC biotherapies, developed-market oncology PE will likely be indirectly exposed to Chinese therapy demand². However, over the longer term, the global market share of Chinese-produced cancer therapies should rise, and Chinese oncology growth looks set to outpace the global sector. As biotech represents the higher-value and higher-growth segment of China's healthcare sector, investors gain indirect exposure to the sector by proxy when investing in broader Chinese healthcare and emerging-market healthcare³ mutual funds or exchange-traded funds. However, direct exposure in these cases is likely to be more diluted.

¹ South China Morning Post, 28 January 2018

² Refer to UBS Longer Term Investments: Oncology, dated 25 January 2018

³ Refer to UBS Longer Term Investments: Emerging market healthcare, dated January 2018

Risks

Biotech is an industry with high sensitivity to risk appetite and often experiences boom-bust cycles. It is regarded as a high-risk industry for investors due to high failure rates owing to strict regulation in clinical testing, given the repercussions for human health. In the US, less than 10% of drugs are successful from phase 1 to clinical approval, according to the Biotechnology Industry Association.

The biggest industry risk for biotech in China relates to price cuts of biologic drugs. In China, most companies need to list on the NRDL to be commercially successful, as the NRDL has considerable pricing power. Indeed, following the recent restructuring of the Chinese Reimbursement Bureau, with the centralization of both funding and payment arms, we believe the NRDL's bargaining power will further strengthen. NRDL's superior bargaining power, coupled with shrinking central government funding and pressure to improve reimbursement coverage for a broader range of therapies, will likely put downward pressure on Chinese biologic drug prices in the future.

Another major and currently topical risk to China's biotech sector is the violation of drug safety standards due to weak implementation, a risk that surfaced recently with the vaccine scandal linked to Changsheng Biotechnology Co. Although China now has among the highest standards in the world for drug manufacture and safety, implementation of central government policies and standards at the provincial government level can often be lax or weak.

Intellectual property and patent disputes are areas of risk for the pharmaceutical industry globally. Such cases are likely to increase now that China has joined The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use. While most major MNCs and foreign drug companies register their patents in China as well as in the US and Europe, there are cases where the patent may not be registered in China. Additionally, biologics' patent expiry dates can vary by country.

In China we see a higher risk of IP disputes in the development of biosimilar drugs, where it may be easier to bypass patents. In addition, quality issues for a biosimilar versus its bio-original, even though the new CFDA regulations seek to control quality standards, could result in legal disputes. The chances of legal disputes are also higher when a molecule has been licensed out to multiple companies instead of a single Chinese licensee. Litigation aside, US IP issues in this field could trigger broader retaliation and protectionism in the sector from the US government. This could also impact Chinese M&A activity in US biotech.

Another area of potential risk is MNC molecules that have been licensed out to Chinese companies or venture capital firms, rather than developed and launched in China by their own local

subsidiaries. Reasons for out-licensing can range from limited patent life to failed launches overseas or an overly competitive or crowded therapeutic area. Still, there can be sound commercial cases for Chinese companies to buy the licenses of molecules even under the above circumstances. Smaller overseas companies are also more likely to license out to Chinese companies because they lack subsidiaries or infrastructure in China to do so.

Healthcare is normally regarded as a defensive sector across economic cycles. However, biotech, as mentioned, is vulnerable to boom-bust cycles and is also sensitive to rising interest rates. This is because the terminal value of a biotech company is a major part of its valuation, making it sensitive to changes in the discount rate applied.



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