L.E.K.

Special Report

Heading East

Biopharma International Expansion to China and Asia

Bio Biotechnology Innovation Organization

Contents

About L.E.K.

L.E.K. Consulting is a global management consulting firm that uses deep industry expertise and rigorous analysis to help business leaders achieve practical results with real impact. The firm advises and supports global companies that are leaders in their industries — including the largest private and public sector organizations, private equity firms and emerging entrepreneurial businesses. Founded 35 years ago, L.E.K. employs more than 1,200 professionals around the world across the Americas, Asia-Pacific and Europe. L.E.K. entered China in 1998 and has since become a leading commercial advisor in life sciences and healthcare services practices, covering all aspects of the industry value chain and life cycle.

For more information, go to **www.lek.com**

Biotechnology Innovation Organization

The Biotechnology Innovation Organization (BIO) is the largest biotechnology not-for-profit trade association in the world, representing over 1,000 biotechnology enterprises, academic institutions and biotech R&D and innovation centers from more than 30 nations. BIO's member companies are involved in the research and development of hundreds of innovative healthcare, agricultural, industrial and environmental biotechnology products, from cutting-edge regenerative medicines and medical diagnostics to renewable fuels and bio-based plastics. BIO also organizes the BIO International Convention, the global event for biotechnology, along with many other industry-leading investor and partnering events held around the world.

For more information, go to **www.bio.org**

Introduction

Asia as a region captures 60% of the global population, which automatically makes it the largest healthcare opportunity in the world. While Japan has been on the industry radar for decades, China, at $123 billion in 2017 Rx market value growing to $160 billion by 2022, is emerging as a growing source of opportunity for the industry.

Driven by pro-innovation and pro-biotechnology policy trends, including drug regulatory reform and intellectual property rights protection, China is becoming a key destination for biopharmaceutical companies globally. Besides being the second largest market in the world, Chinese government's positive policies as well as high levels of public and private financial investments add to the market attraction. Nearly 90% of the biopharmas in L.E.K.'s survey expressed an interest in a China expansion; China-only rights licensed from international biopharmas have tripled in the past five years.

A key phrase being reported throughout news channels proclaims that China is upgrading its pharma industry to enhance innovation. What does that mean for international biopharmas? L.E.K.'s survey suggests that three-quarters of the biopharmas would prefer a partner, as China remains a complicated and unfamiliar market. Those with products in later stages are more inclined than earlier stage companies to consider own operations in China.

The aspirations and challenges for international biopharmas expanding into China and Asia are addressed in this *Heading East* report, the first to tackle these questions for emerging biopharmas looking to expand beyond their home market. Inputs to the report range from the recent L.E.K. biopharma internationalization surveys, analyses of industry data, case studies and experiences from pharmas large and small, advice from industry experts, and on-the-ground experiences from the L.E.K. life sciences team. Find out more about potential opportunities and entry approaches, advice on local partner selection, and suggestions on market acceleration and internationalization in this breakthrough report.

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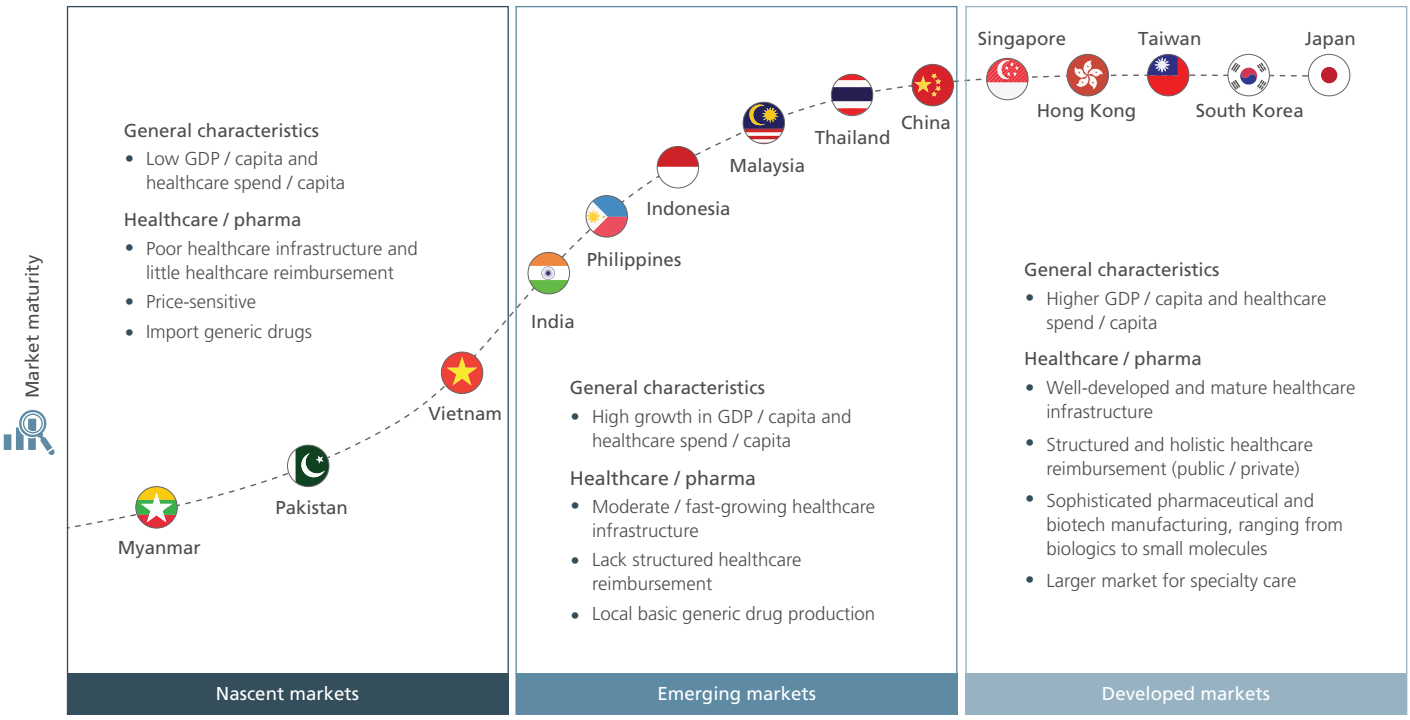
Biopharma opportunities in Asia

Currently, Asia accounts for 30% of all global pharmaceutical spending. That figure is expected to increase as the region's healthcare burden rises, especially with respect to chronic disease treatment. Based on World Health Organization predictions, the cancer treatment market in Asia is projected to reach $150 billion by 2020. This is a 40% increase from the $107 billion spent in 2015. This can be attributed to the five-fold increase in the cancer patient base in India, as well as the nearly 4 million people in China diagnosed with cancer each year. For other chronic diseases, like dementia, 60% of global cases are concentrated in low- and middle-income countries, of which a large portion are in Asia.

The region is complex (see Figure 1) due to the large economic diversity between different Asian countries. Multiple independent factors impact the potential for growth. Population levels and market maturities, varying level of generics and biosimilar adoption, multiple solutions for healthcare reform and cost containment, and significant out-of-pocket or private contributions to finance healthcare all contribute to form a complex healthcare landscape.

Figure 1
Market features of selected Asian markets

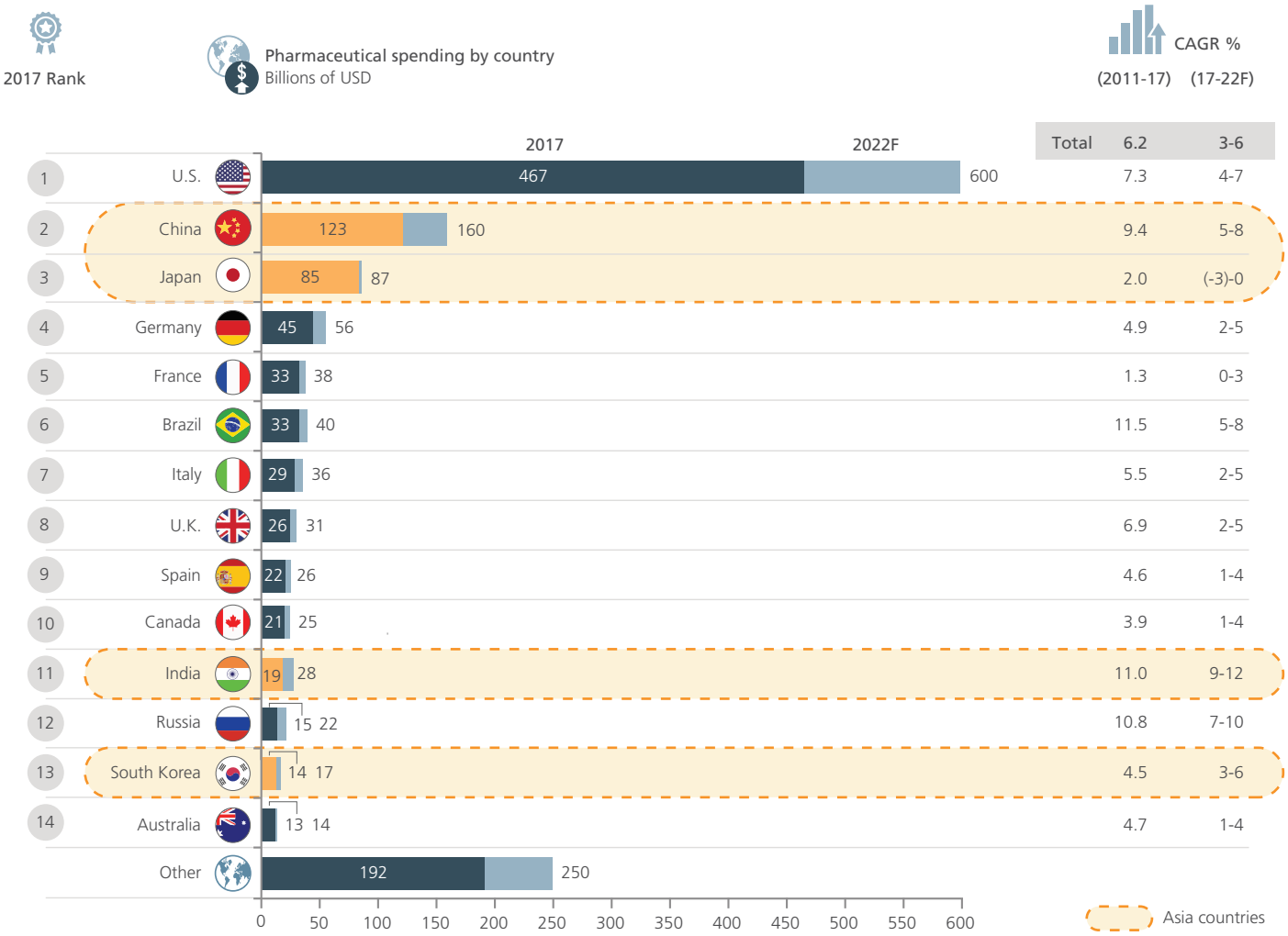


Source: L.E.K. analysis based on IQVIA and IMF

Based on World Health Organization predictions, the cancer treatment market in Asia is projected to reach **$150 Billion** by **2020**. This is a **40%** increase from the **$107 Billion** spent in **2015**.

Within Asia, China and Japan are the two powerhouse economies and prescription markets, accounting for approximately 20% of global pharmaceutical spending. China alone is expected to contribute $37 billion of the global prescription growth in the next five-year period, covering 13% of the growth total (see Figure 2).

Figure 2
Global pharmaceutical spending by country (2017, 22F)



Source: L.E.K. analysis of IQVIA data

China alone is expected to contribute **13%** of the **$37 Billion** in global prescription growth over the next **five years**.

WHO predicts increased healthcare cost in Asia over the next 10 years

Asia has made much economic progress, but also seen social and lifestyle changes such as diet change and increased urban pollution over the years. The World Health Organisation (WHO) predicts healthcare costs will rise exponentially in Asia over the next decade as a result.

CANCER

Cancer + Diabetes + Cardiovascular + Chronic lung diseases

40 million (70%)
56 million total deaths globally in 2015

CANCER DRUGS EXPENDITURE

Year **2015**
USD 107 billion

→ Predicted in Year **2020**
USD 150 billion

WHO ARE HARDEST HIT?

India

Cancer is the leading cause of death with **2.5 million patients**

A five-fold
increase by 2025 is predicted

China

4 million new cancer case were reported in 2016 alone.

The national health bill
predicted to increase four-fold to USD1.84 trillion by 2025

DEMENTIA

Current dementia patient numbers
35.6 million people worldwide

2030
estimate
65.7 million

2050
estimate
115.4 million

60% of cases
are concentrated in low and middle income countries

AIR POLLUTION – RELATED MORTALITIES

Studies have associated high rates of pollution with strokes and dementia, and it has also been significantly linked to an increase risk of cancer.

The primary victims

China

More than a million
premature deaths are seen due to smog during winter season

India

1.2 million
deaths occur each year due to air pollution

CO_2

Japan, Korea & Thailand

These are the countries **closest to China** and are closely affected by pollution

Mortality rates per 100,000 due to air pollution in 2012

India	China	North Korea	Philippines	Singapore	Malaysia	Indonesia
130	163.1	234.1	82.7	20.5	23.4	83.9

Source: WHO,MIMS, https://today.mims.com/infographic--who-says-asia-s-healthcare-costs-will-rise-starkly-over-next-10-years

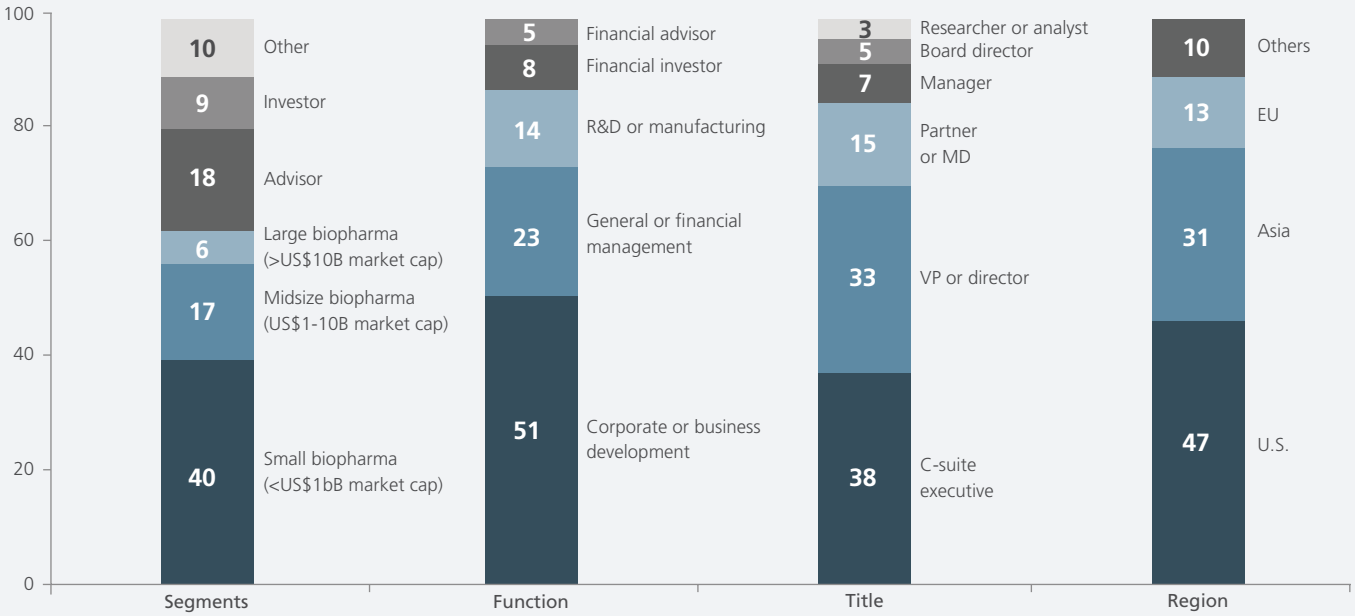
About the L.E.K. Consulting survey on biopharma international expansion into China and Asia

L.E.K. Consulting conducted two rounds of an online biopharma international expansion survey in early 2018 to better understand how biopharmas, particularly those in Western countries, consider international market entry and expansion into China and Asia. Eighty-eight qualified responses were collected and are analyzed in this report. Answers to the responses are included in the Appendix to this report.

Survey respondent background overview

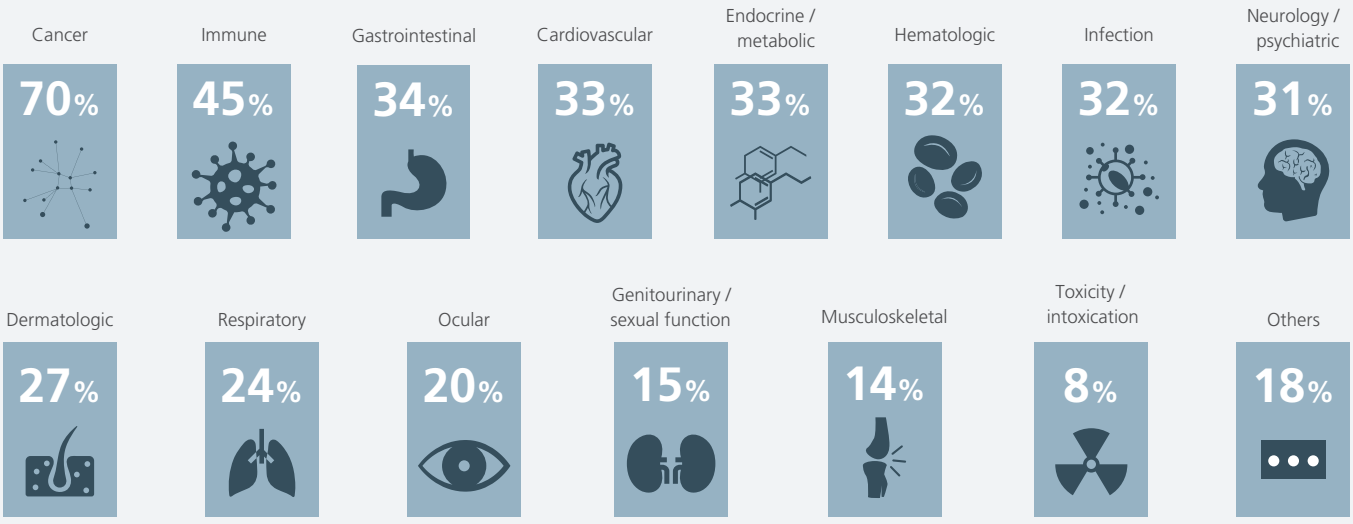
Respondent backgrounds

% of total respondents



Respondent portfolios

% of total respondents



Source: L.E.K. biopharma survey

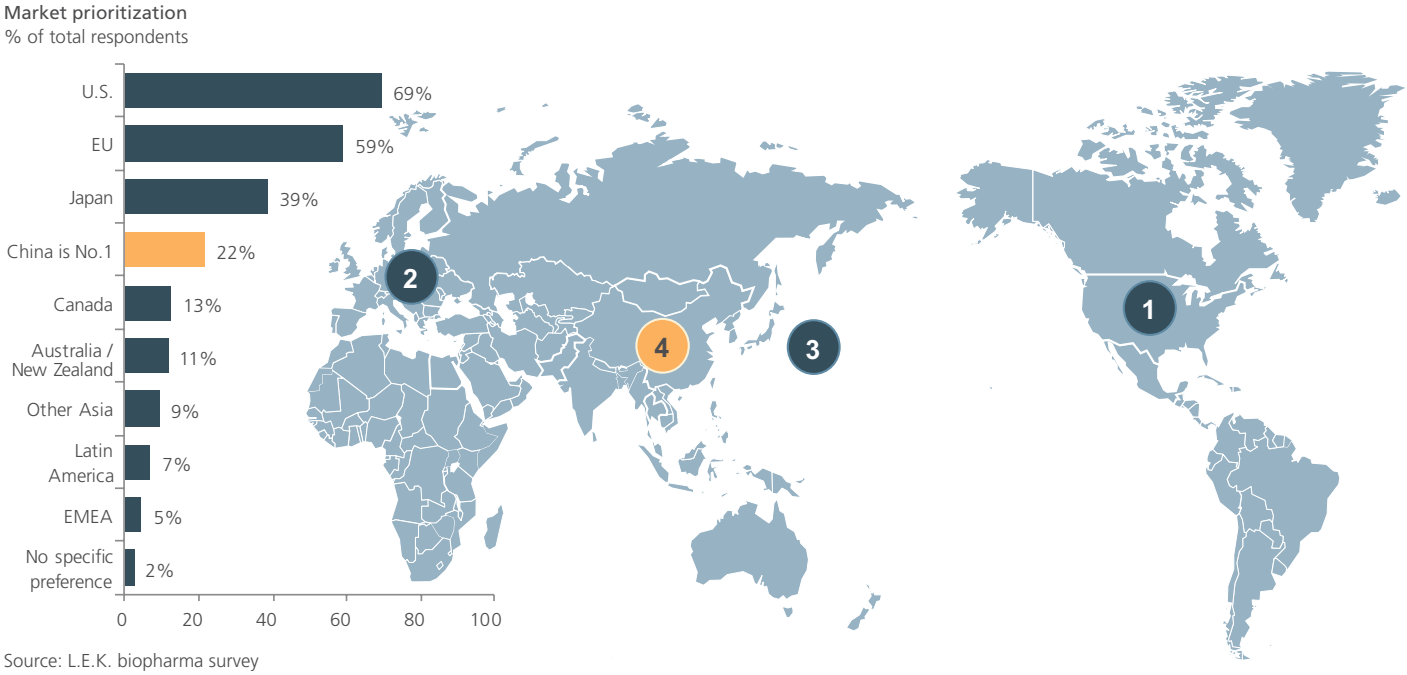
International interest in China and Asia

For the international biopharmas, domestic markets still are the most important. In a survey of international biopharmas, 22% of companies surveyed reported that China is a high priority, making it one of the top four markets for biopharma investment. Nevertheless, most biopharmas remain focused on their home markets in the United States, the European Union and Japan. After establishing the home presence, the U.S.-based principals typically prioritize Western European markets, and vice versa (see Figure 3). This should not be surprising given the relative sizes of the markets and familiarity by the international biopharmas for their home markets.

However, the potential of China is still in industry minds, due to its rapid growth and increased healthcare spending. As one early-stage life sciences investor in the U.S. commented, "For our portfolio companies, it is not necessarily that we require them to consider China, but I want to make sure that they are not overlooking China."

Of the survey respondents, 94% reported an interest in international expansion, with 90% of total companies interested in Asian expansion and 86% in China expansion specifically. The high levels of interest in China are mostly due to the allure of large and emerging market opportunities, but can also be triggered by

Figure 3
Geographic preferences



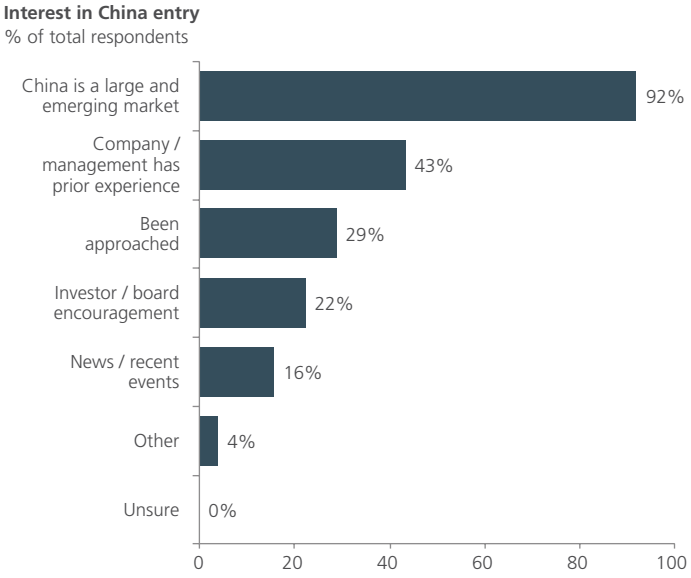
Source: L.E.K. biopharma survey

Of the survey respondents, **94%** reported an interest in **international** expansion, with **90%** of total companies interested in **Asian** expansion and **86%** in **China** expansion specifically.

questions raised by their board of directors or external approaches from outside parties (see Figure 4).

Nearly half of the biopharmas prefer a China or Greater China deal, and another approximately 20% prefer a regional deal that covers China. Biopharmas at all stages of development would consider China entry, with the surveyed biopharmas at phase 2 development being the most interested.

Figure 4
Triggers for interest in China



Source: L.E.K. biopharma survey

China's market opportunity

China has multiple factors that make it a prime area for biopharma growth. It has the world's largest population and 22%[1] of seniors 65 years and older, creating a pharmaceutical market that consumed $122.6 billion of prescription drugs in 2017, with nearly double-digit rates of continued expected growth. A look into China's demographics reveals an already enormous disease burden that will only continue in the coming years.

Board and executive experiences

Biopharmas are sometimes asked by their boards to have a China strategy, given the size of the overall market. If the management team has international pharma experience, they are more likely to think about China proactively.

Approached by Chinese representatives

Smaller or development-stage biopharmas are often focused on their clinical development programs and don't have the bandwidth to look beyond the next milestone, let alone at China or Asia. Two-thirds of the biopharmas have been approached by Chinese biopharmas, investors or their advisers.

China's disease burden

China treats **3-4 million** Cancer patients annually

Accounting for
~37% of lung
44% of stomach
52% of liver cancer patients globally[2]

It has **110 million** diabetics

1/2 of whom have not yet been formally diagnosed

Another **500 million**[3] pre-diabetics

There are **~140 million**[4] hepatitis B patients

of which **30 million** are chronic active

China has **270 million** hypertensives[5]

~100 million chronic obstructive pulmonary disease patients[6]

"The number of pharma companies coming from China for meetings ramped up sharply this year [at the J.P. Morgan Healthcare Conference in San Francisco]. I was surprised by the scale and sophistication of the delegations. In many cases, pharma companies with $1 billion-plus in sales were sending teams of four to six people, attending all the shadow conferences and holding a dozen meetings a day." — Tom Bliss, CEO, Genisphere

Inspired by news and events

The Kite-Fosun deal in January 2017 was considered seminal by many biopharmas: a China deal with terms of $40 million in upfront payments, $20 million to support clinical development, commercial milestones totaling $35 million and single-digit sales royalties. This and other high-profile deals reaffirm that China is a high-growth and high-value market.

"We have recently seen some transactions of U.S. companies having deals with Chinese partners to commercialize products, which triggered us to think about China entry."

— Joe Whalen, Senior Vice President of Business Development and Alliance Management, Horizon Pharma

Chinese innovation and investments

China has fast-evolving needs and expectations from well-informed patients and different clinical capabilities (e.g., a much lower number of healthcare professionals), and has differing tolerance levels for expensive, latest-generation treatments. As a consequence, healthcare innovations that deliver value in developed markets such as the U.S. or EU can still flounder or fail in China, and for over a decade there have been homegrown companies that can build positions despite strong multinational (MNC) company presences in their sectors. Wego, Kanghui and Trauson all built attractive positions in orthopedics, as did Simcere, Qilu and Hengrui in generic drugs.

Healthcare innovation in China often focused on delivering value products, i.e., the development of good-enough quality at a more attractive price point. Now, China's rapid development has brought the country's healthcare industry to be viewed as an emerging global leader closer to the "heartlands" of healthcare innovation. From digital health to immuno-oncology, China is leading in the development areas of healthcare, attracting billions of dollars in investments.

China targets having key medical products accounting for **30%-40%** of international market share.

Step change in indigenous innovation

Since healthcare reform was launched in 2009, and subsequently reinforced in the 12th and 13th Five-Year Plans, China's central planners have provided strong direction and policy support for the development of China's healthcare industry. However, this direction is articulated in the form of far-reaching, and sometimes unachievable, development goals — having key medical products accounting for 30%-40% of international market share, for example.[7] Funding, local policy and regulation enforcement follow along to support movement toward these targets.

China's government has been consistently committed to laying the groundwork for an innovative biopharma industry. Over the past decade, China has launched a number of programs with the goal of building an effective ecosystem in which to develop innovative healthcare products. These include:

- **Better protections for intellectual property.**
- **Repatriating key talent working overseas** (e.g., the Recruitment Program of Global Experts, known as "the Thousand Talents Plan").
- **Funding leading global research and development programs** (e.g., a personalized medicine investment commitment that tops the U.S. federal commitment).
- **Changing regulation to deliver expedited market access for urgently needed or locally developed medical innovations** (e.g., the "Opinions on Deepening the Reform of the Evaluation and Approval Systems and Encouraging Innovation on Drugs and Medical Devices").
- **Investing to shorten and make more predictable China's notoriously long market access pathway** (e.g., three to four times the number of Center for Drug Evaluation reviewers since 2013).

Regulatory support in China

In June 2017, China began a high-profile series of reforms to its clinical evidence approach in order to conform with International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use standards. These reforms have been widely touted as a sign from the Chinese government of interest in mutual cooperation, as the reforms will reduce the cost and time required to bring products to China. The reforms will also better prepare Chinese firms to compete internationally with their own products.

Most important, in 2015, the Ministry of Industry and Information Technology launched the Made in China 2025 (MIC 2025) mega-policy, with the goal of elevating China's pace of innovation and quality of production. The MIC 2025 policy cites both biopharma and medical technologies among 10 strategic industries that will be the focus of continuing government support. These industries have been targeted specifically for domestic innovation, and local policies and initiatives can expect to receive senior-level political support.

Success to date

Despite the high target goals set by the Chinese government, the competitiveness in China's innovation ability in digital health or immuno-oncology is not yet fully pervasive. China's ever-more wealthy and impatient patients are as a result increasingly looking to medical tourism for treatment, which resulted in a nearly doubled outbound investment expenditure from China in 2016-2017 when compared with five years prior. This represents an enormous opportunity for biopharma firms to fill the gap and establish themselves as reliable and trusted partners for Chinese patients.

Japan outbound to China and rest of Asia

The Japanese domestic pharmaceuticals market is expected to decline by as much as 3% annually for the next five years[8], making Japan the only shrinking market among the U.S., EU5, Canada, South Korea and Australia. A reasonable assumption is pricing pressure for both new and long-listed drugs, and the increasing share of generics.

Made in China 2025 (MIC 2025) mega-policy, with the goal of elevating China's pace of innovation and quality of production. The **MIC 2025** policy cites both **biopharma** and **medical** technologies among **10 strategic industries** that will be the focus of continuing government support.

This pessimistic domestic market is forcing many Japanese pharmaceutical companies to look outside Japan for growth, especially to the U.S. and European stars which remain lucrative markets for Japanese companies. That said, these Western entries require substantial investments that not every company will be able to provide. Therefore Japanese companies will potentially turn to the rest of the Asia, especially China, to provide a buffer against the declining Japanese domestic market.

China attraction

China has already proven very attractive for Japanese companies for some time, yet few Japanese companies have successfully established their presence in China compared with the typical Western multinational pharmaceutical companies. Because of unstable government policies and a unique business culture, many Japanese companies have had to adopt conservative strategies in order to make substantial investments in China, where Western MNCs are often making bold movements. Industry research suggests this gap between MNCs and Japanese companies in China has been widening over the past few years[9].

In 2016, the largest Japanese pharmaceuticals company in China was Takeda, though its relative size is changing due to the sale of it its stake in the Chinese joint venture Techpool in May 2018. Among other Japanese companies, Eisai and Daiichi Sankyo are the next tier in China, but they are just a fraction of the revenue that large Western MNCs generate in China.

Despite the general downward trend, not all Japanese companies are fitting this bearish model. Astellas and Dainippon Sumitomo have recently increased the size of their sales forces to strengthen commercial capability in China, showing that these companies are looking to add more Chinese business into their portfolios. While these movements will potentially result in increased revenue from these firms, Japanese companies are notably slow. Western MNCs in establishing R&D engines in China, and this decision widen the gap even further over the long term.

Rest of Asia emerging

The rest of Asia (ROA) is increasingly important for some Japanese companies. Japanese companies have become increasingly active in ROA territories, establishing wholly-owned operations as well as joint ventures with local companies. Because the expected growth in the ROA will be equal to or exceed that of China, the Japanese government has been supporting the companies' moves and creating social infrastructure into the ROA market.

The strategy to expand into China and the ROA market is not just for large-cap pharmaceutical companies. Mid-cap Japanese pharmaceutical companies that have unique niches or serving specialized areas also have much to gain from this regional expansion, as the initial investments into the ROA may not be as high as they are for the major markets.

While the risks of emerging markets cannot be ignored, astrong growth expectations may offset the risk, especially as the Japanese domestic market continues to shrink. Japanese companies with no unique offerings will not be able to compete in these markets; they can neither invest to vie for market share with the large Japanese and MNCs nor drive the focus vs the smaller, niche companies.

It is then critical for companies looking to compete in this space to think carefully examine their offerings, and make an informed decision on their course of action as company in the ROA market.

China aspirations: On-the-ground perspective from Dirk van Niekerk of BI China

Dirk van Niekerk is the president of Human Pharmaceuticals at Boehringer Ingelheim China. He has been with BI for 27 years and has run its China operations since 2016. Dirk shared his perspective as part of a China commercial excellence panel at AmCham Shanghai's healthcare committee event.

I don't think there's any headquarters in the world that dares to say that China is not important. I guess the question is to try and quantify exactly how important. Going into the future I think this is the question on everyone's mind: What can be expected of China? Certainly, on my side, that is the question that comes from my headquarters often.

Key industry developments

There are some nice developments in the industry in China. First, regulatory. We see that the approval timelines of drugs are being shortened for sure, and I believe that there's a willingness and an objective to get it as close as possible to the U.S. Food and Drug Administration time frames. I think they will get there, which is wonderful to see. Also, the government is investing in staff and resources and [the] training of these departments. That, to me, is a beautiful development.

Second is the focus on quality. It's very clear that the government wants to get quality medications to patients in China. We've seen it now with many, many companies, not only local companies but also multinationals, being challenged now on their dossiers, being challenged on their currently registered products — and that they need to do self-inspections on these products — and there are high standards of quality that now need to be adhered to. And we might see some questionable products and/or companies exit the market as a result, which will certainly be in the Chinese patients' interest. So the quality vision is there; we see it already.

And the last thing I would say is innovation. The government wants to innovate, and China will innovate. I believe we'll see a well-established multinational Chinese pharmaceutical company within the short to medium term. The government is intent on doing it; they're investing money in it. The question is, how can multinational industry help, share expertise, share experience? I believe there is a great opportunity for public/private partnerships in this space, to get our scientists into China, to have workshops, to have meetings with scientists in China, to share knowledge, expertise, help … All of this will be good for Chinese patients.

Chinese complexity

I think every market in the world is complex when it comes to healthcare provision. The level of complexity differs and the issues are different. One of my biggest challenges when I arrived [in China] was to align a China strategy with a corporate strategy … given the different [product life cycles]. I've always been a firm believer that structure should follow your strategy. In this case, I've talked about portfolio strategy — we've spent a lot of time, a lot of time, getting the portfolio strategy right, bucketing the different brands in our pipeline and making decisions in terms of what strategy needs to go behind every bucket, and our structure is now in the process of being formed to support those. I don't believe there's one structure, I don't believe there's a silver bullet, but I firmly believe that your portfolio needs to drive your structure.

Competitive home front

Meanwhile, Japanese companies may face fierce competition from Chinese or ROA companies in their own domestic market. In the past few years, Chinese companies such as Luye have been establishing their businesses own operations in Japan. We expect they will actively seek opportunities to enter the market with their wholly-owned or in-licensed marketed products. There may be more promising biotech companies from China and Asia in the next decade while the Japanese biotech industry struggles with technology transfer and funding.

Capturing the expansion upside

There has always been and will always be a rationale for Japanese companies to expand their presence in the China and ROA markets, and also to expand future R&D opportunities, emphasizing long term development over short term gains. This strategy may not work for every pharmaceutical company in Japan, but it can be a viable solution for those that have a strong growth strategy and commitment to the market. This may include large investment decisions in order to capture the future upside of China and the ROA.

Case example: Santen Pharmaceutical

Santen Pharmaceutical, a Japanese firm specializing in ophthalmology, is a successful example of a mid-cap Japanese company competing in the greater Asian market. Santen has acquired Merck/MSD's ophthalmology business in Asia and has been emphasizing the importance of the Asian market as an important growth driver according to its recent company presentation, one their of the five strategic pillars is "Active expansion in Asia and entering the U.S. and European markets," with the goal of becoming the top ophthalmology company in Asia and obtaining 40%-50% of overseas revenue from Asia.

Santen already has a manufacturing facility in Suzhou, and has recently established a joint venture with Chongqing Kerui in China in order to deliver high-quality products at reasonable prices. Santen has enjoyed more than 20% compounded annual growth rate over the past five years in China, compared with the over 10+% growth for the company as a whole.

Santen has enjoyed more than **20%** compounded **annual growth** rate over the **past five years** in **China**, compared with the over 10+% growth for the company as a whole.

Entry approaches: Multiple options

Biopharmas have used a range of options for entry into China and Asia, but most companies think of partnering first. Larger, established companies might be able to establish their own presence outright. Smaller firms might look to China and Asia only as a source of funding or incremental opportunity, and thus would choose to out-license their rights.

Choosing the approach, before discussing partnership strategy, is a critical task.

The choice of entry approach goes beyond simply choosing the right local firm. An effective entry strategy should be geared around the biopharma's overall strategic plan and commercial objectives. These objectives are unique for each firm, and may change depending on specific internal objectives for Asia, the firm's current stage of development, and the willingness to invest financially and operationally on the part of key decision-makers.

Entry strategies can be roughly grouped into four broad categories, each with its own advantages and challenges (see Figures 5 and 6).

Acquisition

Acquisitions provide a jump-start into Asia, with already established infrastructures, supply chains and ready commercial portfolios. This is in addition to, and can work in cooperation with, the acquiring firm's own pipelines. Italy's Menarini entered Asia through the acquisition of Invida in 2011, giving Menarini a commercial presence in 13 Asia-Pacific markets, including China, Australia and major Southeast Asia countries such as Singapore and Malaysia, in a single purchase. Many international generic pharmas, including Teva and Lupin, have chosen to acquire Japanese generics to increase their Asia footprints. Australian CSL acquired 80% of Chinese plasma fractionator firm Wuhan Ruide in 2017 in order to expand into the local market for plasma-derived products.

Greenfield

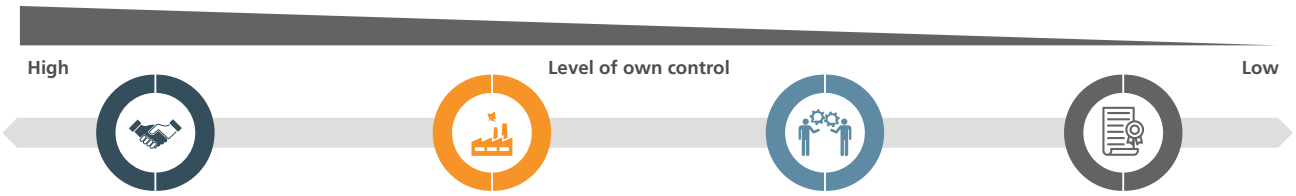
Beginning a brand-new, startup China or Asia business can produce a highly committed organic growth process. The level of upfront investment can be limited to supporting product registration via regulatory consultants and/or contract research organizations, and does not require much direct physical infrastructure. Or this can start with initial setups and product registration preparation, prior to making further decisions on acquisitions or joint ventures later on.

This is similar to FibroGen's, Gilead's (both U.S. companies) and Taiho's (Japanese) approaches to China.

Joint venture

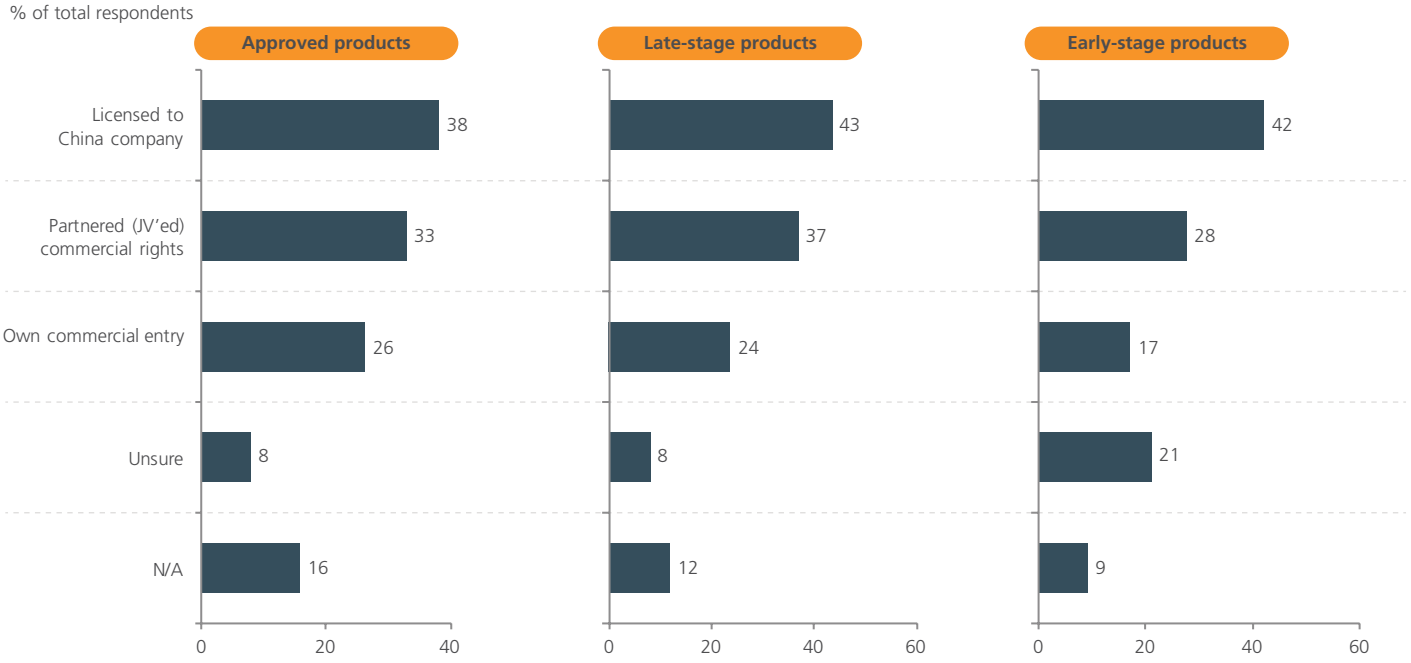
This is the most frequently considered option for those biopharmas on the cusp of becoming international commercial operators. Firms seeking a joint venture have an interest in maintaining some level of their own presence in China and Asia, but are often daunted by the challenge of managing an operation on the opposite side of the globe with different cultural norms. A joint venture is a good choice for executives who feel more comfortable having "locals" navigate the market. Joint venture projects, while maintaining the integrity of both local and international partners, must also navigate steep communication and cultural challenges. Kite (now

Figure 5
Options for China and Asia market entry



	Acquisition Own presence	Greenfield Own presence	Joint Venture Own presence	Out-licensing No presence
Pros	• Immediate access to existing products, talents and other local capabilities. • Full control of business. • Full revenue booking.	• Full control of the business. • Full revenue booking. • Build own brand, capability and network. • Can use support from service partners (e.g., CRO, CSO).	• Leverage external resources to fill in the gap and save time to build by oneself. • Shared investment, risks and upsides.	• Good for company with limited local presence and strength. • Low investment and easy recovery / upside. • Low risk.
Cons	• High upfront investment. • Difficult to find right target. • Risk in business transfer.	• Need to ramp up on full set of capabilities / infrastructure and all fronts from scratch. • Speed to launch may take longer given new to market.	• Require time and effort to identify right partner and negotiate. • Difficulty in JV setup. • Conflicts of interest.	• Limited control over product sales, brand and marketing. • Low profit potential.

Figure 6
Entry preferences by stage



Source: L.E.K. biopharma survey

Gilead) and Juno (now Celgene) both opted for joint ventures in China, with Fosun in 2017 and WuXiAppTec in 2016, respectively.

Out-licensing

The rise of out-licensing to the region has been complemented and facilitated by the rise of the China and Asia startups. Companies such as Aslan, Ascletis, CStone and CANbridge allow international firms to out-license, develop and commercialize for China and Asia with limited direct presence. Out-licensing is often used in Japan. For example, Japan's Ono has the Japanese rights to Proteolix's Kyprolis, KAI Pharmaceuticals' Parsabiv, Servier's Corlentor (Procoralan in Europe) and BMS's Optivo, which it then converted to a deeper collaboration. Smaller biopharmas such as Puma, Mirati, Tesaro and Kolltan have all granted companies exclusive product rights in China in return for upfronts and milestones.

Southeast Asia entry considerations

India and the Southeast Asia region are home to over 1.8 billion people collectively, making them attractive markets for international expansion. Most of these countries are typically considered for entry after or in parallel with China, with the exception of Singapore.

The fragmented nature of the regions, the varying degrees of regulatory barriers (e.g., local production requirements in Indonesia) and the low level of access for novel therapies make the region primarily an out-of-pocket market where entry needs to be planned on a market-by-market basis.

Despite these challenges, markets in Southeast Asia and India are witnessing significant transformations, with most countries establishing universal healthcare schemes. The transition from out-of-pocket to single-payer is long, and budgets can be limited.

Indonesia, the Philippines and now India have nevertheless all announced and are implementing universal healthcare coverage.

"For biopharma companies there has never been a better time to think about entry to Southeast Asia and India, and we are seeing a lot of interest from both new entrants and companies wanting to expand their presence." — Fabio La Mola, Partner, L.E.K. Consulting Singapore

The preferred modes of entry into Southeast Asia and India differ based on the product portfolios of the companies. Companies that work on generics mainly enter the regions via acquisitions, whereas companies that focus on innovative drugs are more likely to out-license their products to partners in the region.

The options for biopharmas entering the Indian and Southeast Asian markets are similar to those for China (See Figure 5).

Acquisition

Biopharma companies often look to boost their generics manufacturing capacity when picking targets in Southeast Asia and India. Mergers and acquisitions seem to be the preferred mode of entry, or to scale up existing operations. However, the fragmented nature of these markets makes it difficult to find deals that include India and all countries in Southeast Asia. Most companies resort to country-by-country deals to overcome nation-specific barriers.

For example, the Indian market is characterized by intense price pressure due to strong competition. Foreign companies, therefore, often acquire local manufacturers to lower manufacturing costs, such as the acquisition of Agila Specialties by U.S.-based Mylan for its injectable manufacturing platform. In Vietnam, multinationals face issues in importing their drugs, as the government sets a pharmaceutical bidding and grading system that is unfavorable to foreign entities. To overcome this hurdle, they acquire local pharmaceutical companies. For example, Abbott acquired the Vietnamese drug manufacturer GloMed in 2016, enabling Abbott to boost its manufacturing capabilities in Vietnam.

In 2014, Actavis (now Teva) acquired the generic pharmaceutical firm Silom Medical to have a more significant presence in the growing Thai pharmaceutical market, where healthcare coverage reaches more than 98%. Similarly, after Indonesia launched its universal healthcare program in 2014, Fresenius Kabi bought a 51% stake in the Indonesian drug maker PT Ethica Industri Farmasi to gain a foothold in the developing market. As universal healthcare coverage reaches 70% in the Philippines and Vietnam, these markets will become increasingly attractive for biopharma expansion. Within the out-of-pocket market, branded generics and novel therapies remain very attractive areas for expansion, though product differentiation is key to penetrating the market.

Joint venture

In countries where there are requirements for a local partner, a joint venture may be a more attractive option. For example, Indonesia's Decree 1010 required foreign companies to manufacture the drugs locally or to form partnerships with local manufacturers in order to register their drugs. In response to that, South Korea-based Genexine set up a joint venture with Indonesia-based Kalbe Farma for biologics research and development in 2015.

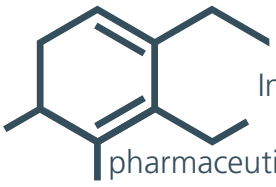
Out-licensing

Companies with novel drug therapies without a presence in Southeast Asia and India often out-license their products to a partner with existing operations in the region. For example, European pharmaceutical company PharmaMar licensed a promising new oncology drug, lurbinectedin, to Specialised Therapeutics Asia to market and distribute the drug throughout Southeast Asia. As midsize companies do not have as much capital to acquire targets in the region, licensing is their preferred mode of entry. Another example is South Korea-based Boryung Pharmaceutical, which out-licensed its antihypertensive drug Kanarb to Zuellig Pharma in 2015 to be launched and marketed in 13 Southeast Asian countries.

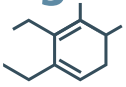
Expansion via technology transfer is also mostly internal to the region, such as India-based BioCon granting Malaysian company CCM Pharma the license for the marketing, sales and distribution of a range of insulin products in Malaysia, Singapore and Brunei.

Universal health opportunities

Southeast Asia and India are rapidly becoming higher on the priority list for entry, as universal healthcare opens up opportunities to reach over 1.8 billion people with lifesaving therapies. Entry remains complex, and the only way to succeed in these emerging markets is to be prepared to invest for the long term.



In 2014, Actavis (now Teva) acquired the generic pharmaceutical firm Silom Medical to have a more significant presence in the growing **Thai** pharmaceutical market, where **healthcare coverage** reaches more than **98%**.

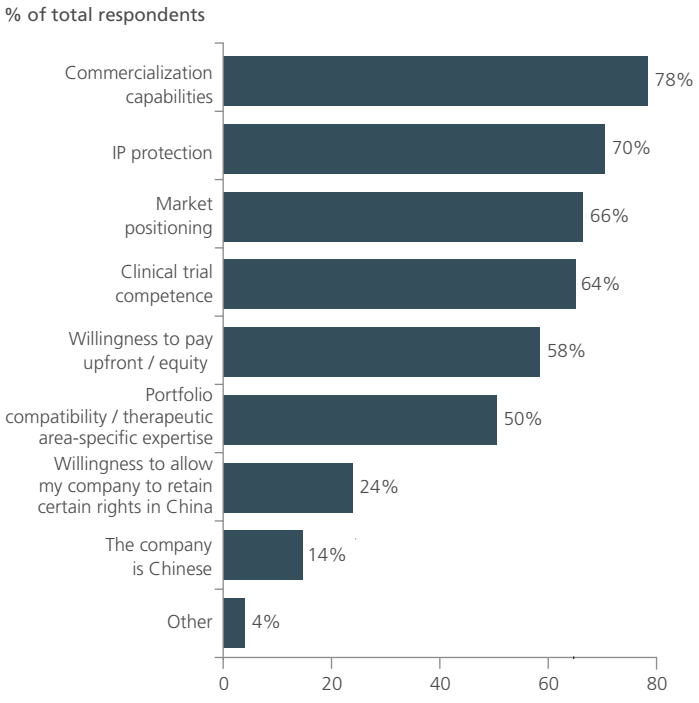


Partner selection: Criteria and negotiations

Once biopharmas start down the path of partnering, selection criteria for suitable China partners are mostly consistent with partner selection patterns in other regions (see Figure 7), and do not necessarily differentiate between multinational / international pharmas in China versus pure domestic Chinese pharmas.

"We will apply the same set of selection criteria for potential MNC and local partner selection. The question is who is going to deliver success." — Joe Whalen, SVP of BD and Alliance Management, Horizon Pharma

Figure 7
Partner selection criteria



Source: L.E.K. biopharma survey

Key selection criteria include:

- **Upfront financials:** A willingness to supply capital is universal to development-stage biopharmas. The injection of cash up front is often necessary for biopharmas to run late-stage trials, and additionally represents a validation of the technology.
- **Clinical trial competence:** Given that both Japan and China require phase 3 clinical trials for product registration, clinical trial competence and access to key opinion leaders are particularly important for innovative companies. This is also reflected in the desire for therapeutic area expertise.
- **Commercial capabilities:** Partners are expected to have demonstrated commercial expertise based on hospital coverage, market access and market positioning. This, for example, means a larger company in China must have, in order to have reasonable coverage, 2,000 large teaching systems out of 20,000 hospitals.
- **Intellectual property protection:** IP protection continues to be a key concern raised by international biopharmas and is often a key selection criterion exclusive to emerging markets. Without enforceable and effective IP protection, biopharmas would either choose not to consider China (or another Asian market with poorer IP records) or would retreat to partners that are considered "safer" from this perspective.

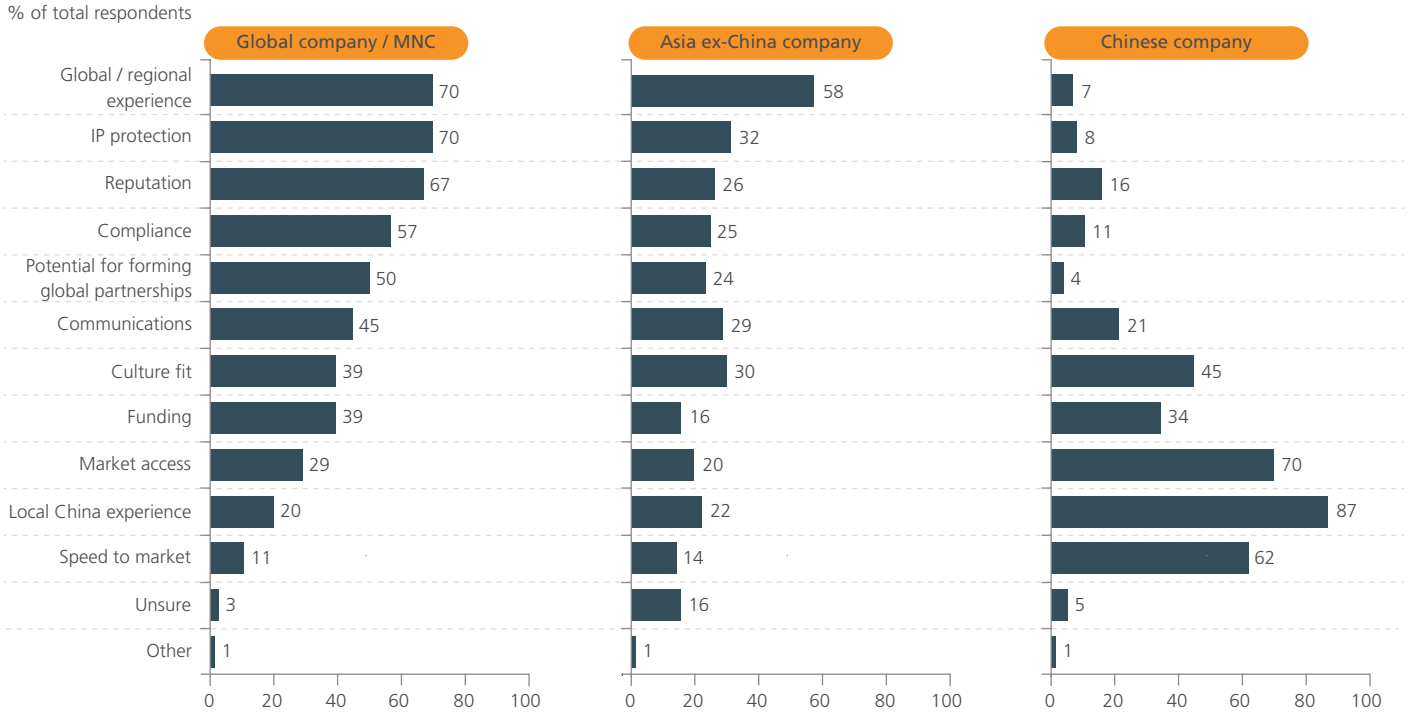
Partner type comparisons

There are vast differences in the perception of the different partner group types by nationality (see Figure 8). Do firms prefer a Chinese partner for China, a Japanese partner for Japan, and so on? For a partner in China, even though less than 15% of the biopharmas surveyed indicated that their partnering firm must be Chinese, half of the biopharmas would prefer the partner to be Chinese. One-quarter preferred regional or global biopharmas as the China partner, and one-fifth remained unsure.

There are significant advantages associated with international pharmas as partners for China as well, especially in perceptions of safety. Three of the top four reasons for partnering with a MNC are safety-and risk reduction-related. IP protection tied with global/regional experience for the top reason are at 70% response, followed by reputation (67%) and compliance (57%). More so than even communication, or being a good cultural fit, MNCs are partnerships valued for their safety and reduction of risk, especially in terms of IP and corporate reputations.

There are **significant advantages** associated with international pharmas as partners for **China** as well, especially in perceptions of safety. Three of the top four reasons for **partnering** with a **MNC** are safety-and risk reduction-related.

Figure 8
Advantages associated with various partner types



Source: L.E.K. biopharma survey

However, MNCs are also beginning to see the value in their own China-related experiences. One large pharmaceutical firm's business development director who was interviewed about China licensing opportunities commented, "It is natural that when talking about China entry, international biopharmas first think of local Chinese companies. But as a top-tier MNC pharma, we have gained deep knowledge of the local market. We can even offer more; we can explore global partnership opportunities with the potential partner that local Chinese companies cannot. We have an excellent local market access team; we are very compliant. So I don't think global biopharmas have to partner with local partners; MNCs can be a choice."

Indeed, MNC pharmaceutical firms have been finding success on their own terms in China:

- 4 out of the top 10 pharmas in China are multinational companies,[10] with Pfizer taking the top spot, ahead of any other domestic or international companies. Others on the list are AstraZeneca (No. 3), Sanofi (No. 6) and Bayer (No. 10).
- AstraZeneca's mereletinib (Tagrisso) for lung cancer had the quickest new drug application (NDA) to approval in the China Food and Drug Administration's[11] history, taking less than two months.
- Merck/MSD's GARDASIL9 (9-valent HPV vaccine) received the quickest conditional approval in CFDA's history in just 9 days based on its significant efficacy breakthrough.
- Of the 260 innovative products granted expedited reviews by the CFDA from March 2016 to December 2017, 99 (38%) are from international pharmas.[12]

China-only or Asia-only development and commercialization deals are part of the global/regional pharmas' business development considerations, or even a key part of portfolio expansion in the region.

Examples of multinational pharmas' in-licenses for China abound: AstraZeneca's 2012 licensing of Ironwood's linaclotide for Greater China, Sanofi's 2013 licensing of a Rituximab biosimilar from JHL, and Mundipharma's 2015 license of Helsinn's anamorelin, for example.

We are a midsize company; we are looking for new products. Our model is actually based on forming partnerships with companies that find the market too complex to get by themselves. We offer all those services, market access, key account strategy, reimbursement, pricing. So choosing the right partner is not always with a local partner; it could also be a midsize energy like us." — Renaud Gabay, General Manager of EPD China, Abbott

Deal types

The number of biopharma deals including the key China and/or Japan territories have fluctuated, falling between 350 and 450 for the past 10 years for each market, according to L.E.K. analysis of the Cortellis deal intelligence database (see Figure 9). The parallel trend lines indicate that many of the deals include both territories. These numbers would be approximately 15% higher if life sciences deals beyond biopharma were included.

Specifically looking at only cross-border deals exclusive to either China or Japan, the China-only deal numbers are twice those of the Japan-only deals, in with 60 plus China-only deals per year compared to roughly 30 Japan-only deals yearly. This reflects the rise of Chinese outbound investment and technology in-licensing from both traditional pharmas and the new startups in China.

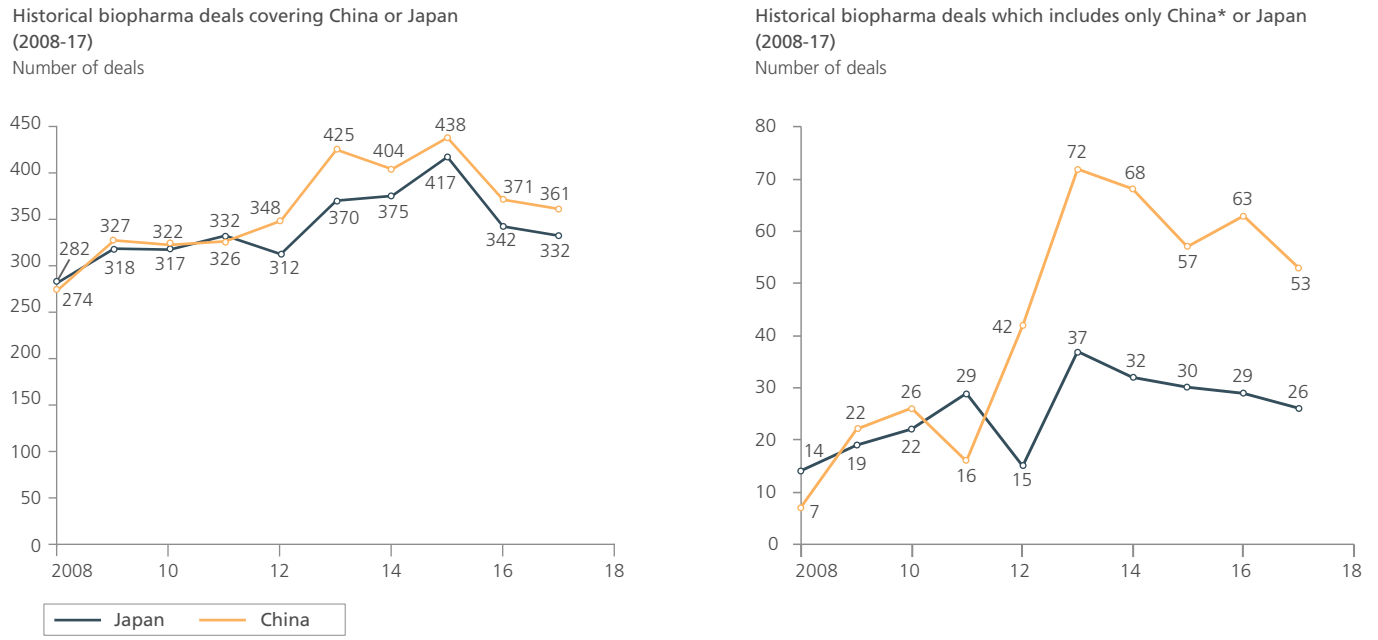
Deal terms

International biopharmas asked for many of the usual terms if given the opportunity: upfront payments (91%), royalties (87%), a variety of milestones (development 71%, sales 70%) and R&D co-funding (55%). Equity investments are sought by only 24% of the biopharmas, though disproportionally by smaller biopharmas who are more likely to seek funding.

Asking for amounts comparable to other China or Asia deals is the most common practice (43%). Just 20% of firms expect investments similar to those of U.S. or EU deals.

On the cross-border biopharma deals, the value of the China deals has increased in the past five years versus historical norms, reflecting the growth of the Chinese prescription market, while those for Japan have remained at similar levels. That said, the Japanese licenses have higher values, as the Japanese market has been a more successful one for high-value therapies.

Figure 9
Biopharma deals covering China or Japan



Note: *Both Greater China and mainland China only deals included
Source: L.E.K. analysis of Cortellis data

Cross-border biopharma deal values for China or Japan rights (2013-2017)

$ millions	China only	Japan only
Deal value:		
Median	$20.0	$70.0
Average	$58.0	$114.2
Maximum	$436.9	$450.0
Upfront value:		
Median	$3.5	$12.5
Average	$18.1	$26.7
Maximum	$310.0	$293.0

Source: L.E.K. analysis of Cortellis data

China negotiations: Across-the-table views from deal maker Andrew Wong

Andrew Wong is an experienced negotiator of US-China biopharma partnerships. He is now SVP of corporate business development at Auransa Inc., and was previously VP of business development at US-a China specialty pharma, SciClone Pharmaceuticals. Andrew shared some of his insights on typical expectations and concerns of Western biopharmas on China deals.

Interest in China

Overall, at least for the U.S. or European companies looking at China, there is increasing sentiment that China is a market they cannot ignore. A number of development-focused firms already have dipped their toes in China in some form–like working with a CRO–to gain some comfort and a sense of China interactions. While these activities alone may not provide enough confidence to establish a presence to conduct their own development in China, there is growing interest to explore partnering there.

The interest level varies with the company size:

- For small and midsize companies, China historically has not generated the type of near-term cash they would desire to support their U.S. development activities. And because of the demands and resources required by U.S. companies in their home territory, China is often quite low in priority. However, with increasing demand from China partners for innovative programs and platforms, a greater number of small and mid-sized companies should consider China collaborative arrangements.
- Larger companies, including biopharmas like my former company, SciClone, are growing their presence and pipelines in China through partnerships. Companies of this size are also regularly conducting or likely to be interested in conducting global studies that include patients from China.

Although the China market as a whole is gaining attention, it has not been a high priority relative to the historically high value markets of the U.S., EU and Japan.

To date Western biopharmas have been quite willing to negotiate a China-only territory deal, and may even include South Korea, Southeast Asia and Taiwan.

Expectations on partnering with Chinese companies

Every partnership deal is different, and should be tailored to address the key objectives of both the U.S. and China partner. These objectives can often be at odds; for example, when the U.S. partner is expecting sizable near-term payments, and the China partner prefers to back-end load a deal because of potential China regulatory delays as well as the evolving process around provincial bidding, hospital listings and reimbursement timing.

If the U.S. partner takes a mid- to long-term view of the China market, there tends to be better alignment with the China partner, who may be concerned that the U.S. partner is principally focused on receiving a substantial near-term payout.

Time is also well spent if both parties can align on a program's value for China, and determine how that value can be allocated over the agreement term. Some deal creativity may also be required to find a mutually acceptable solution between parties. Buy back options, equity investments, and collateralized loans are some example terms that may be incorporated into a China partnership agreement.

Generally speaking, an upfront payment money is more or less essential for the licensor, especially for a smaller or midsize U.S. firms whose strategy is to generate some near-term capital. Royalty rates and milestone payments, in this case, would bear more flexibility during negotiations.

- Western biopharmas often translate U.S. / European deal expectations to China-relevant deals. For a late-stage product, it is not uncommon for a U.S. biopharma to seek a $10+million upfront payment. At SciClone, it was important for us as a result to manage a partner's expectations by explaining a product's market opportunity in China (vs. the U.S.), the likely China development/ regulatory process, and current provincial and hospital listing requirements. These factors provide some rationale as to why proposed terms could be lower than originally expected—lower peak sales and a sales uptake curve that is shifted further to the right.
- China's growing demand for improved treatment alternatives may accelerate the willingness of Chinese companies to spend greater amounts to secure access to originator and first-in-class or best-in-class innovations.

Concerns about entering China

When a U.S. company is not ready to partner in China, some of the common concerns include the following:

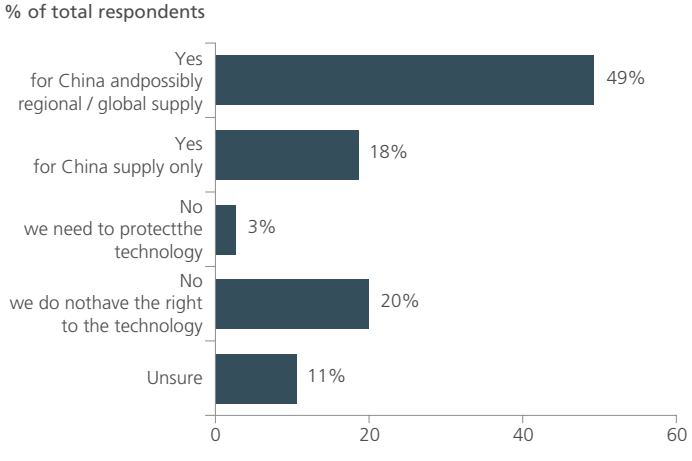
- **Intellectual property (IP) is a principal concern.** For example, once a development collaboration has begun in China, and the China partner is developing the product, what considerations have been given to the additional IP that may be developed? Will this be filed as joint IP? Many western companies feel uncertain how to manage these issues, especially how to enforce their IP under Chinese law.
- **Impact to other territories.** Some companies worry that if they secure a China partnership, and a big pharma subsequently wants global rights, would the China arrangement impact their ability to execute a collaboration for the other major markets (i.e., U.S., the EU and Japan)?
- **Compliance.** Getting comfortable with a China partner who will enforce strict compliance in accordance with applicable regulations is a significant concern. Finding ways to address compliance fears may be possible, however. U.S. companies should not only incorporate into their China agreements strict compliance policy expectations and regular compliance training, but also seek a China partner that is already practicing stringent compliance measures.

Technology transfer

China has a continued focus on manufacturing. Its upgrade of the pharmaceutical industry, beyond breaking through the newest scientific developments, like precision medicine, also includes the upgrading of the baseline manufacturing. The list of priority review's eligible criteria not only includes clinical innovations and treatments for areas of high unmet needs, but also technology transfers and first generics.

International pharmas willing to transfer their technology to China for manufacturing (see Figure 10) give themselves, or their partners, the opportunity to receive expedited review, even when clinical innovation is limited. For the local Chinese partners, the right to manufacture may provide incremental value including employment, company infrastructure, and supporting their local government objectives and obligations, which contribute to their willingness to pay.

Figure 10
Tech transfer willingness



Source: L.E.K. biopharma survey

Partnering with a Chinese biopharma: Suggestion from Bo Tan of 3S Bio

Bo Tan is the president and CFO at 3SBio, an integrated biotechnology company based in China. He has been with 3SBio since 2009 and has extensive experience within the financial and pharmaceutical industries. Bo shared his perspective as part of the L.E.K. Executive Briefing panel in parallel with the 2018 J.P. Morgan Healthcare Conference.

As a China-based biopharmaceutical company, we focus our efforts on researching and developing innovative products that can address unmet medical needs in China. Although our primary focus is the China market, building a global network, as a sub-strategy, is also very important in our long-term vision. In this way we can have a platform to introduce our products overseas and help more international companies bring their drugs into the China market to enlarge the overall portfolio. Going international is very critical to expanding our business volume and strengthening our capabilities.

Nowadays, the hot topic is healthcare reform in China. The regulatory environment is indeed evolving rapidly in China, especially since last year, and the government has released a series of policies aiming to address the underlying issues. I think many of the regulations are positive surprises that could accelerate drug launch and encourage more high-quality products and players participating in the China market. As such, I see current timing as a great opportunity to partner with international companies.

That said, we have applied a very cautious approach when looking at partnerships with international companies. We study our capabilities, from R&D expertise, product pipeline, clinical trial execution and distribution network to sales and marketing coverage, on a regular basis. This could help us understand what we can offer to potential international partners when evaluating the opportunities. Ideally, there should be some complementarity or synergy created for both parties. For example, we have a good lineup of biologic products both in market and in pipeline; it could be even better if we can form partnerships with international companies that can bring our status forward. What we can offer could be local expertise or licensing opportunities of our own products.

I think overall there are a lot of things to be offered by a China-based biopharma in helping international companies entering or expanding to this market. We have spent a lot of time communicating and evaluating these benefits both internally and externally. Once the parties involved have clear views and consensus, I believe it will be a very exciting moment for the China healthcare industry.

Accelerating market entry and access in China

China's rapid development into the world's second-largest economy and pharmaceutical market has created many unique opportunities for growth. Within these opportunities, the Chinese biopharma sector has become a major focus for international firms and investors alike. Despite the recent and rapid advances in the biopharma sector, China is still a complicated market with many conflicting interpretations, and healthcare reform is still a continuing process. Changes in China's healthcare system will bring a number of positive changes, including, regulatory easement, shortened timelines, competitive pricing, reimbursement coverage, and hospital access.

L.E.K.'s Helen Chen hosted a panel discussion on these topics with senior executives at the ChinaBio Partnering Forum in April 2018. Excerpts of the conversation shared by the panelists follow.

China is reforming and opening up rapidly to provide a sound environment for biopharma development, especially for drug registration

The Chinese government's policy reforms in the healthcare industry have taken an upturn over the past decade. As a result, the biopharma industry has advanced rapidly, especially over the past three years with the creation of new policies and regulations to support biopharma companies operating in China. This support from the national and local levels of government provide directional guidance and implementation pathways for biopharma companies. Many of these new initiatives are meant to integrate China into the global pharma market by bringing China's drug regulation standards closer to international norms.

"If you just see the number of drugs approved in China in 2016 and 2017, I am sure you can see the narrower gap of the time taken for the China launch compared to the global launch. And I think that we would not need to wait for another four to five years to see the simultaneous drug development in China versus the rest of the world." — Rae Yuan, Head of Global Drug Development and Vice President, Novartis

"China is now adopting ICH. By definition it doesn't matter where the manufacturing site is, especially for venture capital, virtual funded company. The international company really doesn't have to build up the facility in China to get the drug approval."

— Justin Wang, Managing Director, L.E.K.

"Besides global clinical approval…we are also dedicated to clinical trials in China at the same time. We do perceive China reform is going the right direction even if it is still a long process."

— Renaud Gabay, General Manager of EPD China, Abbott

Biopharma innovation has been a longstanding topic and has a broad range of definition in China

China has been fostering biopharma innovation from a variety of angles, including the implementation of priority review, a faster drug review timeline and protection of innovation outcomes. These initiatives to encourage biopharma innovation can be beneficial to both international and domestic companies seeking market access.

"Even for mature portfolios, you always have ways to innovate. I think the definition of innovation in China is broader than in the Western world. We can innovate through healthcare service delivery or better patient treatment."

— Renaud Gabay, Abbott

"I think the Chinese definition of innovation is not just in real first-in-class products, but also includes first generics. … the definition has a very broad spectrum and as long as you can demonstrate your clinical value to the Chinese patients." — Justin Wang, L.E.K.

Establishing good relations with the Chinese government will bring real value in business dialogue and softer benefits in the meantime

The Chinese government is a critical stakeholder for international and domestic companies doing business in China. Many biopharma companies are concerned about engaging in CFDA dialogue, worrying that such dialogues might bring unexpected delays. However, many Chinese officials now are quite open-minded, as well as willing to learn from the experiences of international producers.

"We are getting better and better relationship with CFDA in regard to introducing product pipeline and designing the best possible practices. To know what the rules and requirements are, you must always have a dialogue with CFDA because guidelines are changing so fast. So it is important to work together in parallel development."

— Renaud Gabay, Abbott

"There is no regulatory discrimination against imports, but commercially there are, I think, some softer benefits of having the

manufacturing presence in China, where you will have a better relationship with the local government that posts your patent, and also have more talking power in dialogue."

— Jun Bao, Chief Business Officer, Shenogen

"If you look historically, not every one of the products that were expedited have local manufacturing, many were imports. … On the intangibles, having a local plant speaks about investment, your presence, your commitment to China. And the facility means bigger employment, better local relationships, higher taxes paid and a number of other things the government values."

— Helen Chen, L.E.K.

On the commercial side, pricing is complex, and China is not yet sophisticated in the use of international tools such as pharma economics

Pricing is never an easy task. For biopharma companies, there are always discussions around what the China prices should be when compared to international products. To apply pharma economics in pricing requires a balance of academic viewpoints versus real-world data. Drug pricing should ideally be set to cover manufacturing costs and be affordable to average Chinese households, while providing sufficient profit margins.

"As for oncology, you can be very flexible to come up with a pricing scheme, and you'd be better off giving a universal price because people do pay a high price if your drug is effective. So I think there is a lot of room to learn from the U.S. on the high-value pricing therapies." — Jun Bao, Shenogen

"It is based on the clinical outcome, on the medical performance, so we need to bring that message to the pricing for sure… We [drug development department] need to work very closely with our commercial colleagues to make sure that everything is aligned and make sure they see the medical value in the early clinical testing stage."

— Rae Yuan, Novartis

China is moving to a rolling system for medical reimbursement, creating more opportunities for biopharma companies to have their products included on the National Drug Reimbursement List (NRDL)

China remains a developing country, given its large population and levels of disposable household income. In such a situation, drug pricing and reimbursement inclusion largely impact patients' affordability and resulting product market share. The NDRL inclusion of 36 high-value drugs through national negotiations in 2017 drove significant price cuts from the producer side, enabled quicker hospital access.

"Well, if you look at the national reimbursement list, a lot of the products are actually imported. So local manufacturing is not a must and it is not going to be a must. That is a simple answer. If you look at the negotiation list, the majority of those products are actually imported."

— Justin Wang, L.E.K.

"In China, national negotiation price is critical because it can give you a short cut to entering hospitals. But this is not the end as the implementation is at the provincial level. Which province will you go first? How do you accelerate the access to the hospital so more and more patient can benefit from the innovative treatment?"

— Renaud Gabay, Abbott

Entry recommendations

While all of the trends and most the policies are pointing in the right direction, China is still a complicated market with many interpretations. Collective recommendations from the experts include:

- Focus on the product
- Have a forward-looking view and game plan
- Don't underestimate the speed of change
- Have a positive attitude and choose partners carefully
- Move forward and be open to options

Broader viewpoints: Expert recommendations on China success factors

The OECD predicted that economies in Emerging Asia (China, India and Southeast Asia) will continue to grow by an average of 6.3% per year during the period 2018-2022, assuming that trade momentum holds and domestic reforms continue.

Given the growth and development in Asia, there are clearly opportunities for biopharma companies in the region. This is especially true of China given its size, population and rapid development. Healthcare generally is seen as a key area for China in the coming decade, and critically as major focus for the government in terms of maintaining social stability.

President Xi Jinping's "Made in China 2025" industrial plan seeks to upgrade China's economy through investment and policy reforms targeting high-technology industries such as pharma and biopharma. in order to address China's reliance on foreign drug imports. In

Economies in Emerging Asia **(China, India** and **Southeast Asia)** will continue to grow by an average of **6.3%** per year during the period **2018-2022**.

addition, China has a large number of able scientists coming out of its universities, and has seen increasing numbers of experts and leading scientists returning to the country from overseas.

With this in mind, it would be prudent for biopharma companies to begin gauging and considering potential opportunities in Asia, if they haven't already.

Matthew Durham is Partner at Simmons & Simmons China practice, where he has been working for over 17 years. David Shen is Partner at Allen & Overy where he leads the IP practice in China. They shared their opinions on some key issues regarding biopharma expansion into China and Asia.

Market overview: increasing market opportunities, but remain complex

"China is a huge potential market for products and offers increasing opportunities for production and R&D facilities. It remains, however, a complex legal and cultural environment; companies should do their homework and determine what is best for them before leaping into the China market."

— Matthew Durham, Simmons & Simmons

Entry strategy: depending on business nature, product line, and objective

"It really depends on the business strategy and its product lines. If a company wants to take advantage of the availability of Chinese capital and government incentives on R&D, then the company should consider entering China pre-commercialization. If the main focus is on sales and marketing, then it should start to enter China post launch or simply out-license its assets to Chinese local players."

— David Shen, Allen & Overy

"There is no 'one size fits all' strategy or preferred entry mechanism. This depends more on the nature of the business and its strategic aims than on the size or origin on the company… Investments should not be made 'at all costs' and opportunities should be explored in line with the nature of the business and its strategic goals."

— Matthew Durham, Simmons & Simmons

Business model for China expansion: depends on the ambition

"I tend to recommend either greenfield operations or license out. Acquisitions or JVs require a good match of culture between the foreign party and Chinese partner, which can be difficult in most cases. Many JVs eventually fail due to irreconcilable culture differences… MNCs tend to favor greenfield operations, while small biopharma should prefer the license out approach."

— David Shen, Allen & Overy

"In some cases licensing or distribution arrangements may be most effective. Or it may be possible to use Chinese CROs rather than to set up a full R&D centre, for example. If a presence is required, the question becomes whether or not a local partner is required or desirable to achieve the strategic aims. If a new state-of-the-art facility is required, a greenfield project may be the best approach, although an acquisition may be a quicker route to obtaining specific regulatory licenses or approvals."

— Matthew Durham, Simmons & Simmons

Key concerns for China expansion: compliance, IP, and personnel

"The number one question I have been asked is 'How is the IP protection environment in China'? My answer generally is: it is improving, but many challenges remain."

— David Shen, Allen & Overy

"Regulatory approvals, compliance, intellectual property, corruption and personnel."

— Matthew Durham, Simmons & Simmons

Selecting partners in China: depends on the asset

"Depending on the assets the biopharma possesses, and the collaboration model. For a long term close collaboration, it may be safer to work with a global partner. If it is a license out case, then local partner may be better because the new product the biopharma provides may become the 'crown jewel' of the local partner and may receive more resources. In contrast, the global company tends to have a large portfolio of innovative products of their own."

— David Shen, Allen & Overy

"This depends greatly on the nature of the business and that of the potential partner. In some cases a global partner with a strong local presence may be most appropriate. In other cases, a more specialized local presence may be preferable to achieve the required goals."

— Matthew Durham, Simmons & Simmons

Upcoming China regulatory changes: positive CFDA reforms

"The upcoming CFDA regulatory reform will make the foreign biopharma's China entry easier and more profitable."

— David Shen, Allen & Overy

"China's government in general, and specifically the CFDA, seems to be committed to continuing legal reforms and speeding up the process for regulatory approvals.

— Matthew Durham, Simmons & Simmons

Key for successful China operation: right people, appropriate localization, and alignment on goals and interests

"Hiring the right senior management, aiming for long term success, localization and seeking supports from your local government…are the keys to commercial success for a foreign biopharma in China."

— David Shen, Allen & Overy

"The single most important factor is probably to ensure that there is a clear alignment of interests between the relevant parties, especially in the case of joint ventures or other partnering… Another key area is people: getting the right people, finding ways to incentivize and retain talent, combining freedom to work and explore ideas with sufficient oversight, structuring agreements and practical arrangements to address intellectual property concerns."

— Matthew Durham, Simmons & Simmons

Building out from China: Global expectations from John Oyler of BeiGene

John Oyler is the Founder, CEO and Chairman at BeiGene, a commercial-stage biopharmaceutical company rooted in China. John has served as CEO and Director since founding BeiGene in 2010. He has robust experience establishing and building companies across various industries and geographies and has lived in Beijing for 12 years. John shared his perspectives as part of the L.E.K. Executive Briefing panel in parallel with the 2018 J.P. Morgan Healthcare Conference

In terms of operating a firm, being local is advantageous in China. This is primarily because developing a strong and executable go-to-market strategy in China is extremely challenging without a deep understanding of the rapidly changing local needs and regulatory requirements. To meet these challenges, a firm needs to have a depth and breadth of talented and experienced people in China.

In-China transformations

Recent changes in the reimbursement landscape, such as the national reimbursement and reasonable pricing initiative for innovative drugs, as well as joining ICH, accepting global data, and removing delays on the regulatory front, have all fundamentally changed China.

Within China, the implications are profound. Reimbursement now requires a broad label, so broad clinical programs must now be run. Much broader coverage is required for a commercial team in order to comply with the reimbursement initiative. The importance and size of the teams required to compete effectively has increased dramatically, and will continue to do so moving forward.

Incorporating China into clinical strategy

External to China, most programs now require a China strategy. With the clinical setting opening up, there is more than a doubling of eligible patients if China is added to the mainstay of today's clinical trial centers in Western Europe and the US.

It is increasingly apparent that over time, China will become one of the most important clinical science centers in the world. In the future, it may be an imperative to be able to operate in China to compete clinically. In the short-term, however, there is a major shortage of talented people and organizations that are capable of running clinical trials at the ICH standard in China. This shortage raises a further risk that organizations or CROs will overcommit to what they are capable of doing well.

Building the China team

On the other hand, building a great team in China is not by itself a guarantee for success. Firms will need to work on frequent communication across the globe to figure out how global and China teams can work most effectively together and leverage each other's strengths while avoiding their weaknesses and helping everyone learn and understand the areas with which they are less familiar.

I think what our leadership team can offer is around the soft part; making processes more efficient or creating an environment that embraces diversified opinion, in additional to providing tangible resources. I think the truth is that we are doing something that is extremely difficult because it is uncharted territory.

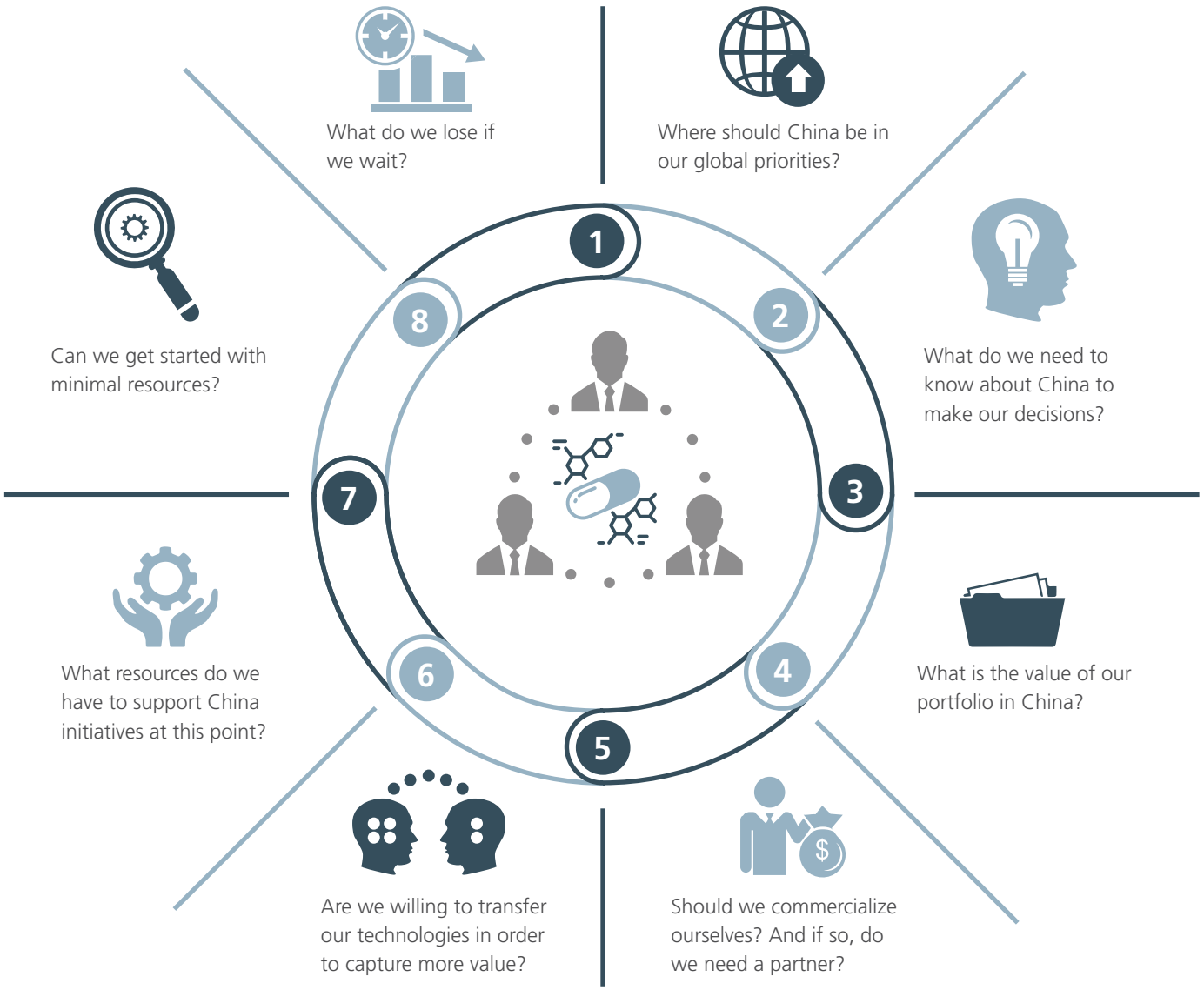
But that is what makes it worthwhile and exciting.

Moving forward

China represents a significant and positively changing opportunity for international biopharmas. While the market remains complex, many of the historical hurdles — lengthy product registration timelines, pricing and reimbursement uncertainties, etc. — are lowering.

Perspectives from biopharma start-ups and the established companies alike are changing from "Should I consider a China entry" to "When and how should I enter China"?

Biopharma boards and senior management should be asking themselves:



There are many ways to tackle the China and the broader Asia region. The geographical distances may be vast, but the regulatory harmonizations and cross-border collaborations are bringing the markets closer.

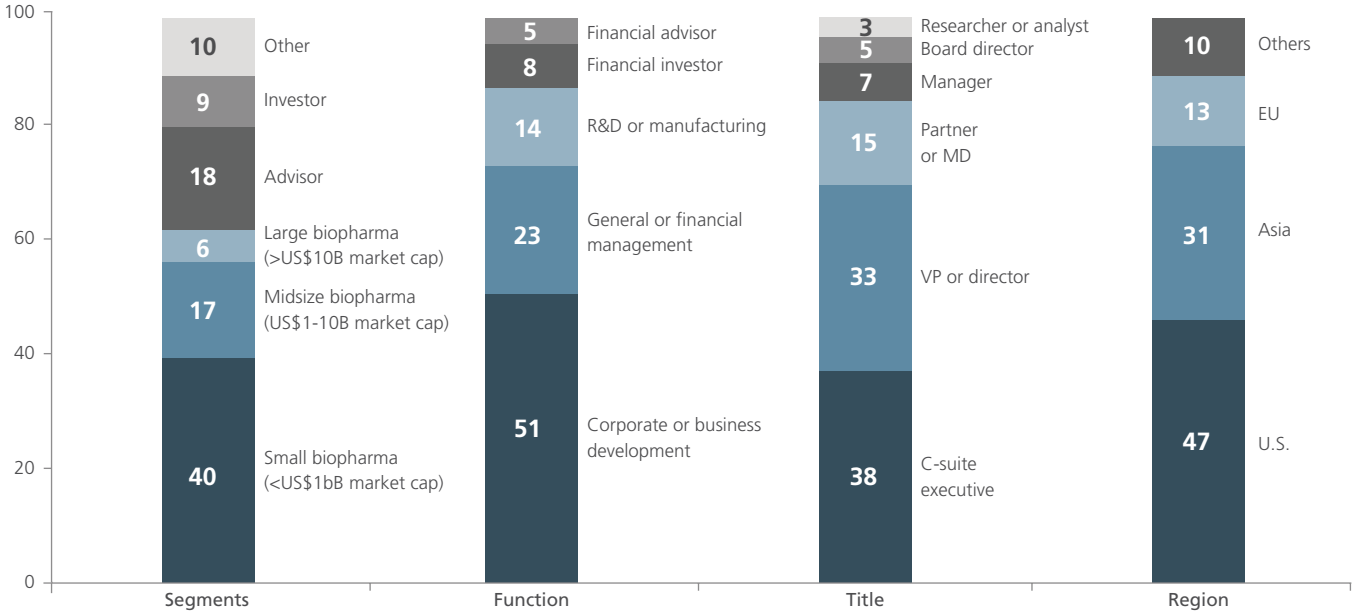
The key is to get started.

Appendix:
Biopharma international expansion survey results

L.E.K. conducted two rounds of an online biopharma international expansion survey in early 2018 to better understand how biopharmas, particularly those in Western countries, consider international market entry and expansion in China and Asia. Eighty-eight qualified responses were collected and are analyzed in this report.

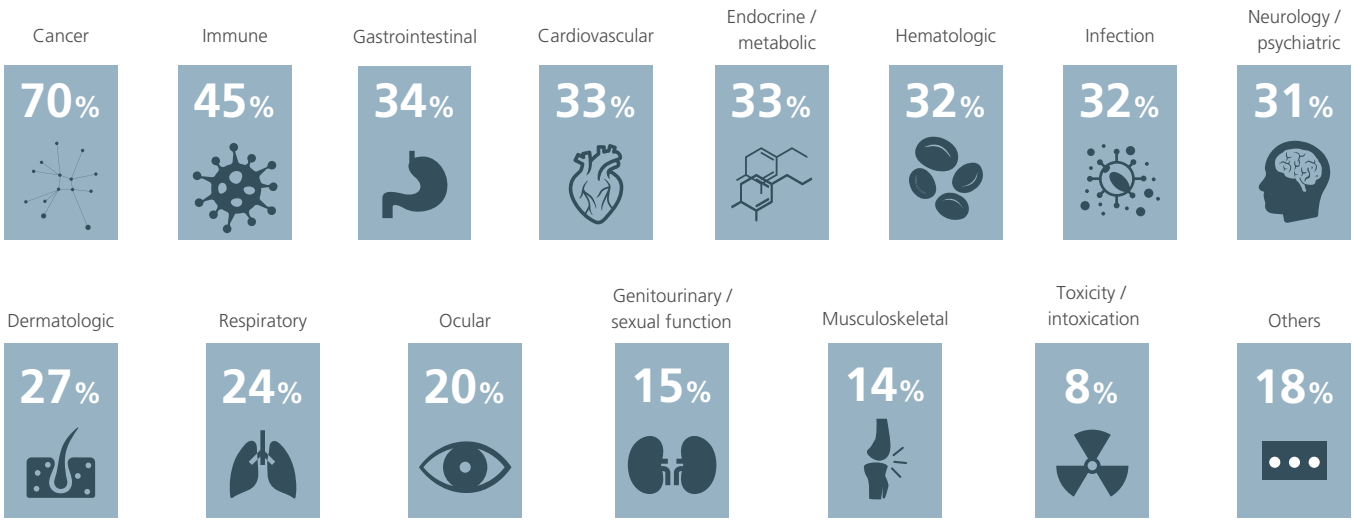
Respondent backgrounds

Respondent backgrounds
% of total respondents

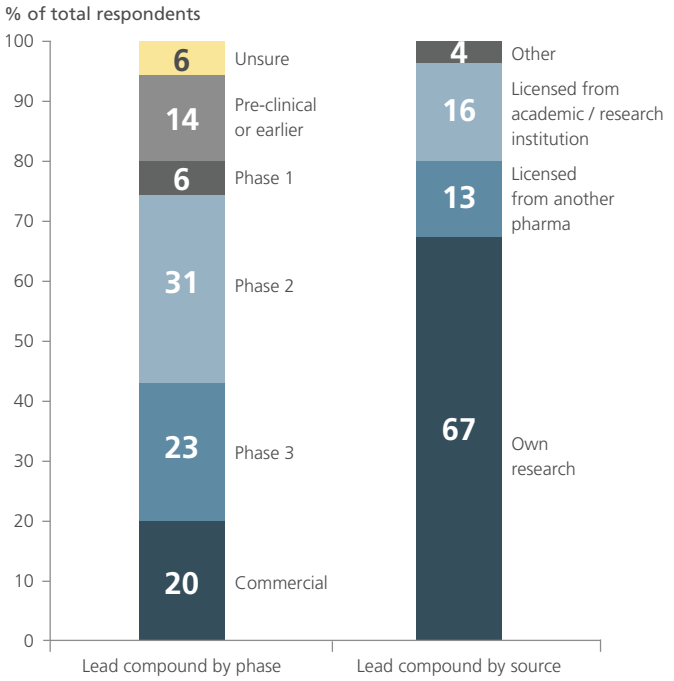


Respondent portfolios

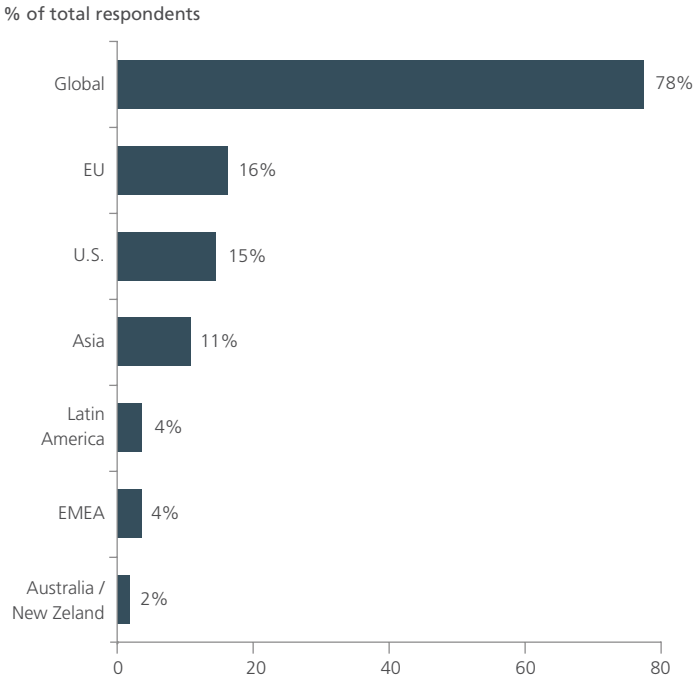
Respondent portfolios
% of total respondents



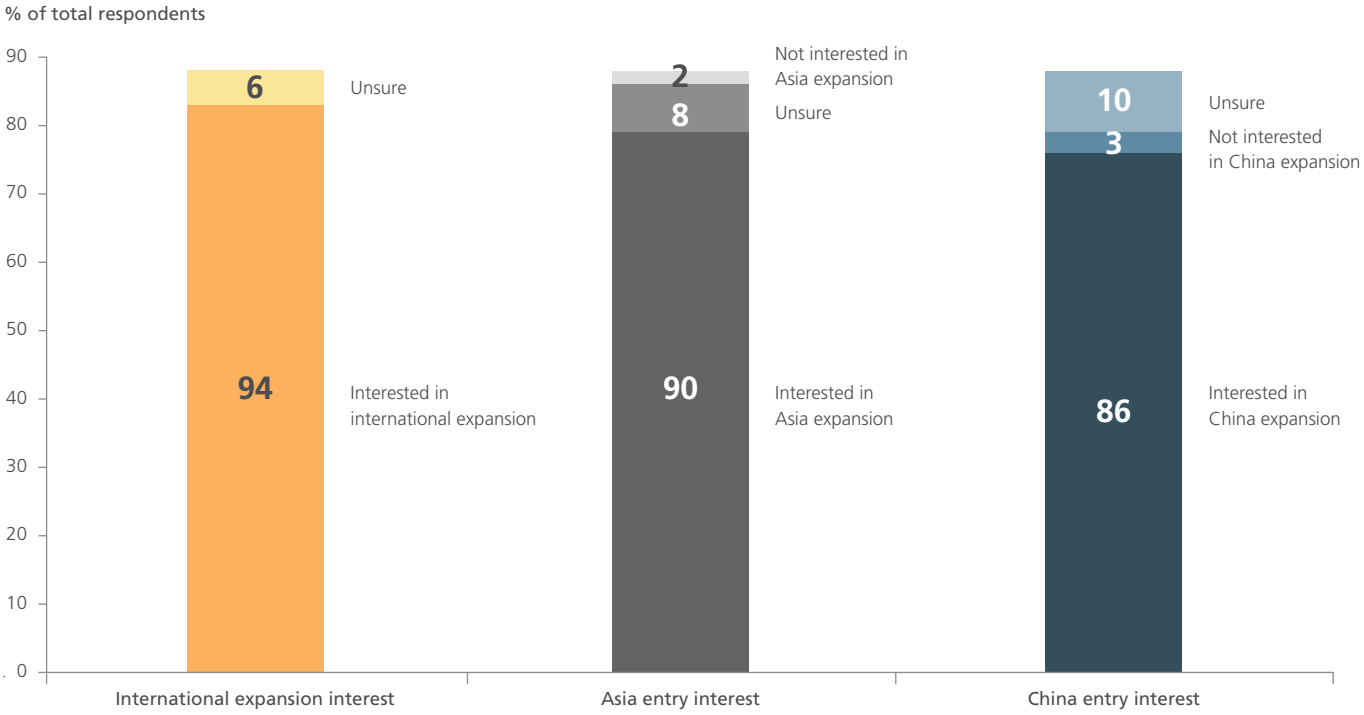
Lead compound information



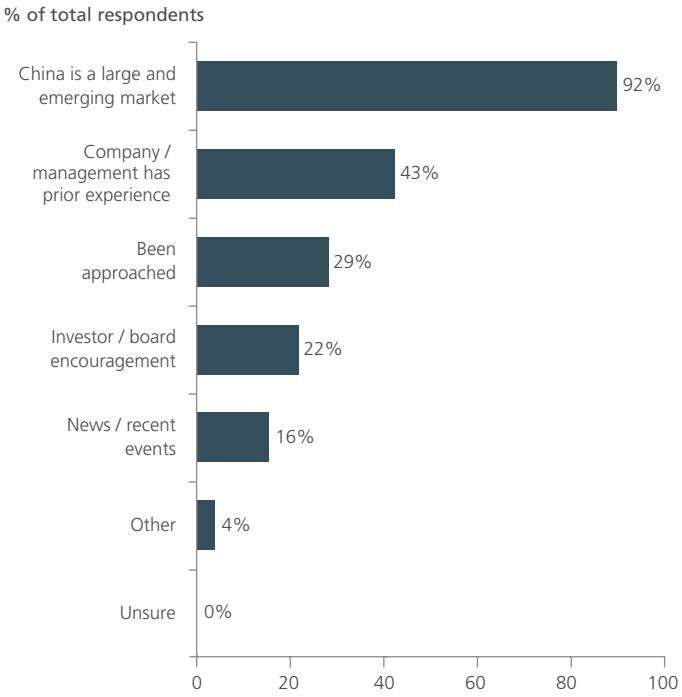
Owned commercial rights



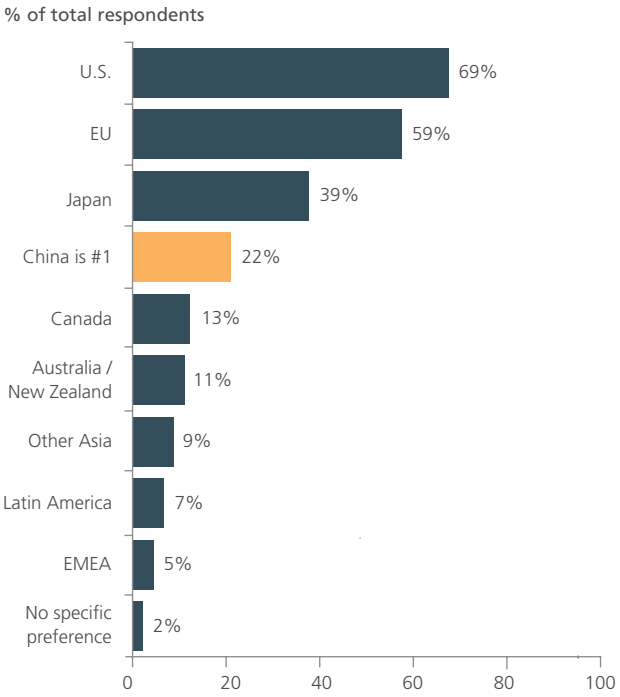
Interest in international markets



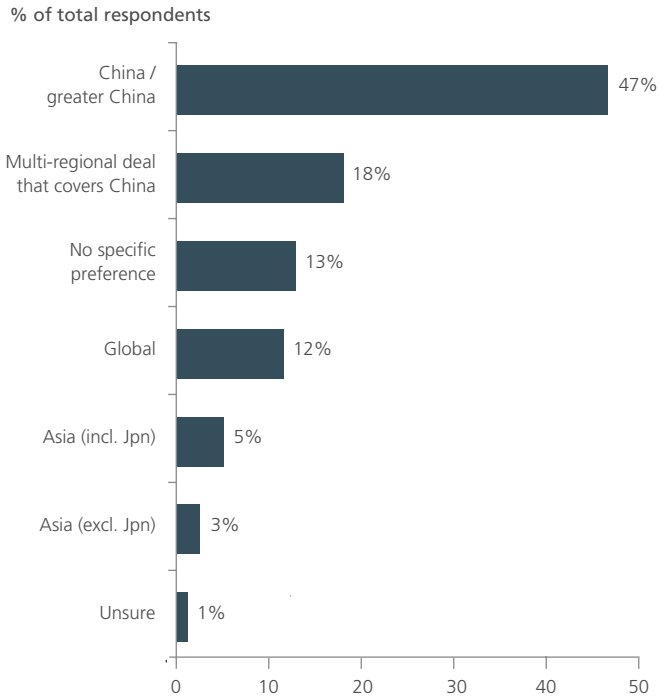
Interest in China entry



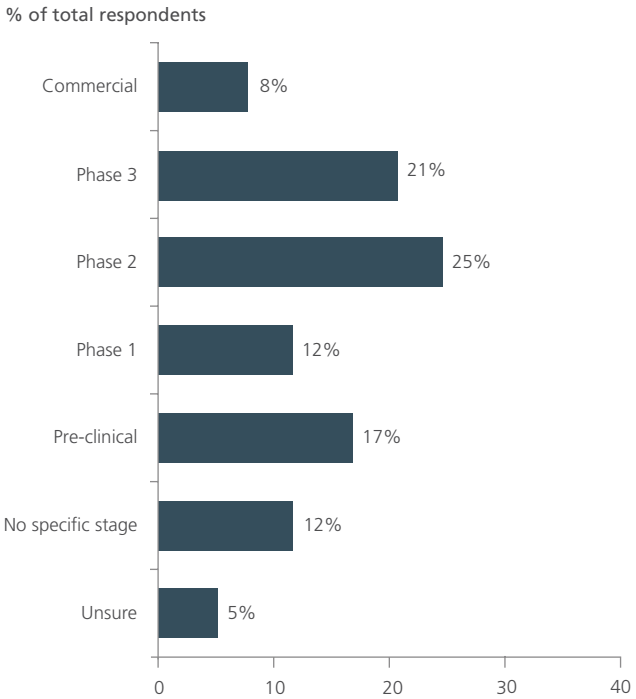
Markets prioritized ahead of China



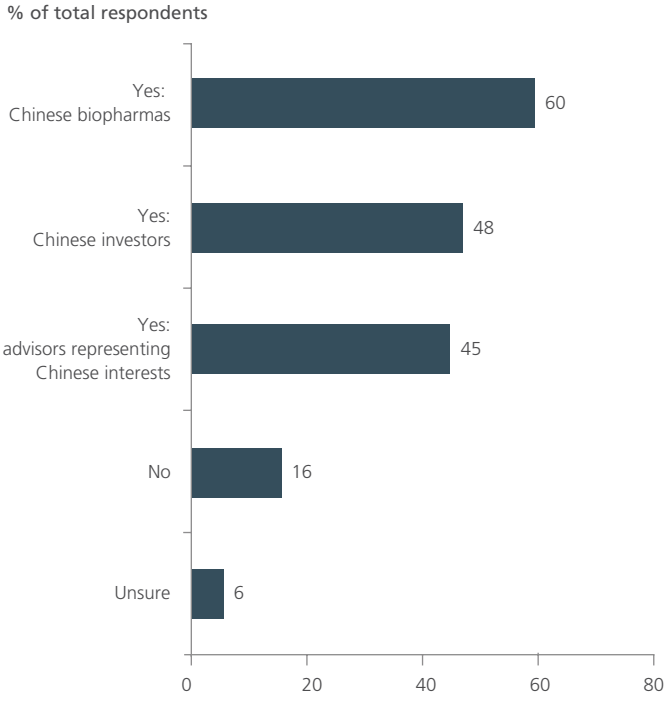
Deal territory preferences



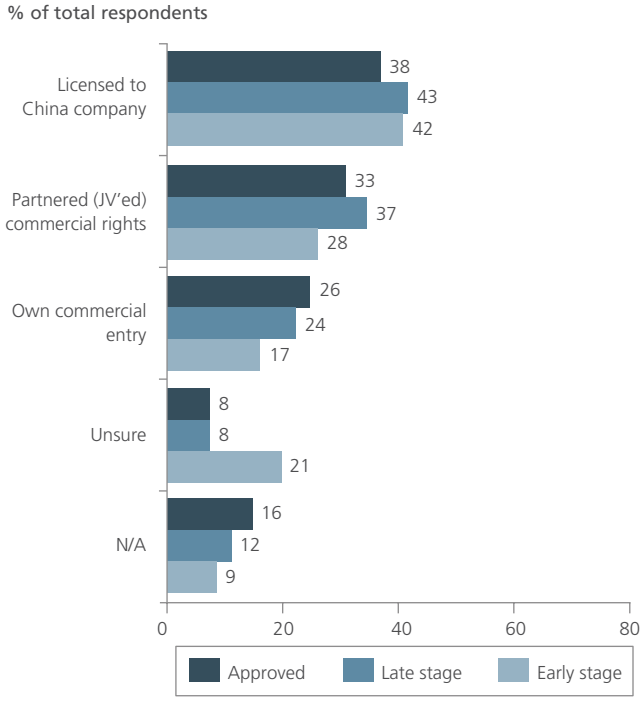
Stage at which began to consider China entry



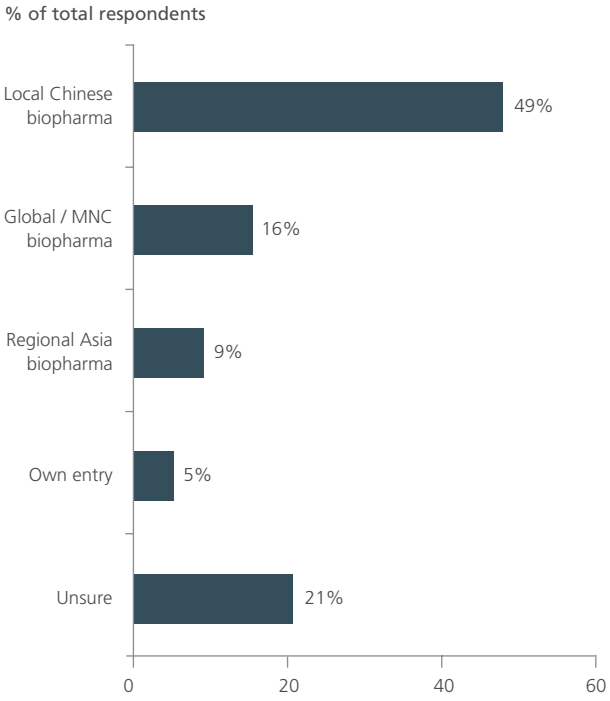
Approached regarding China entry



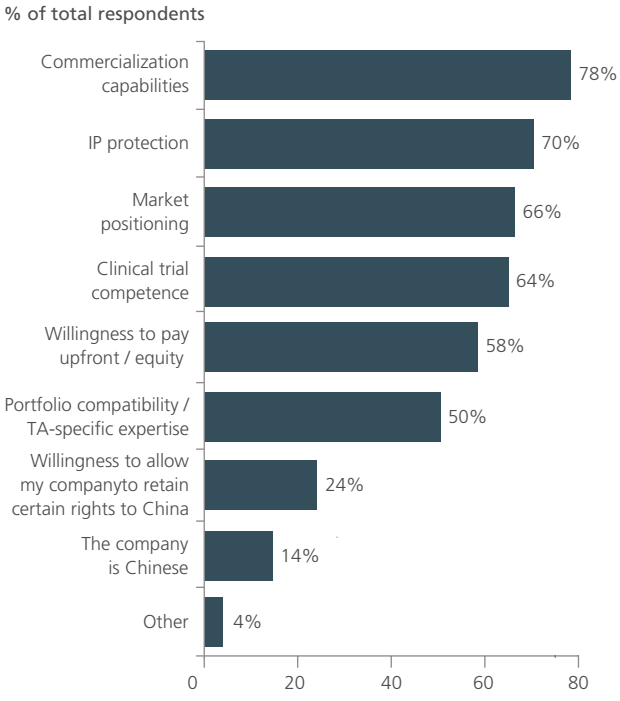
China entry preferences by stage



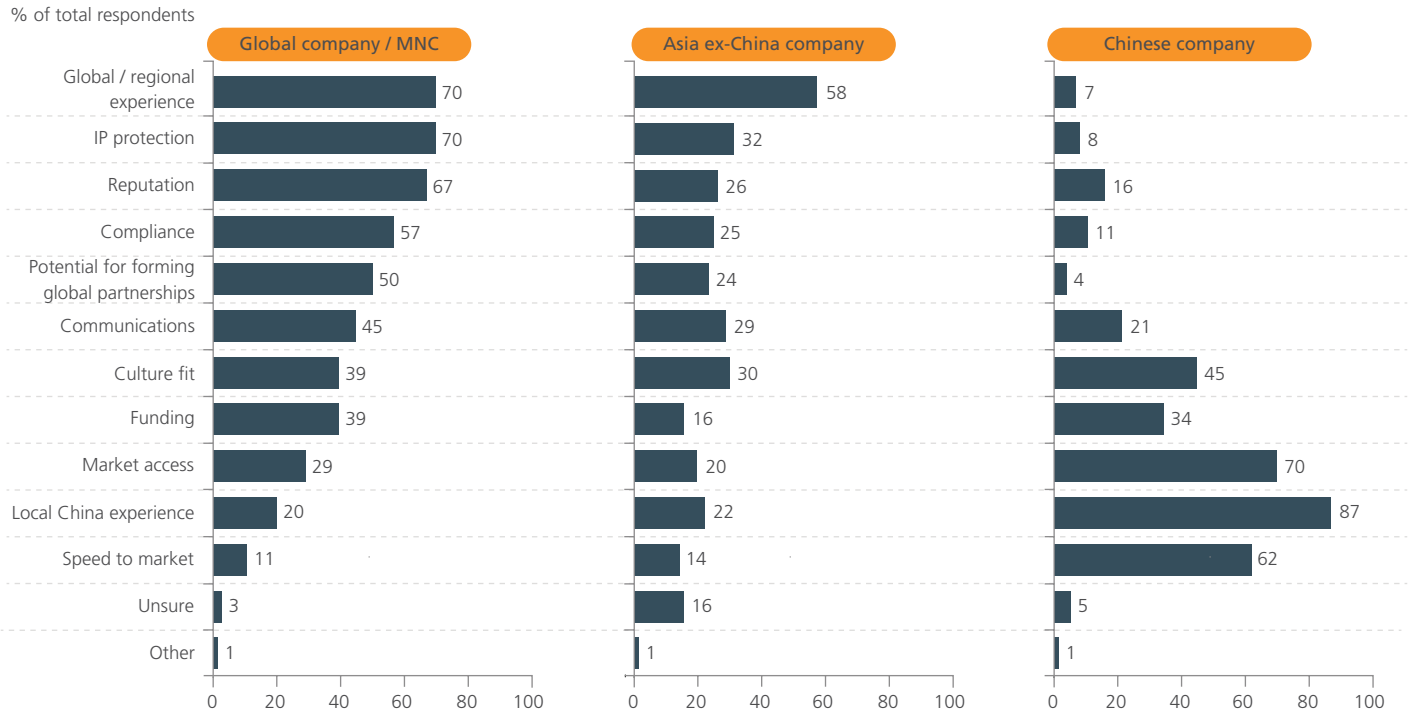
China partnership preferences



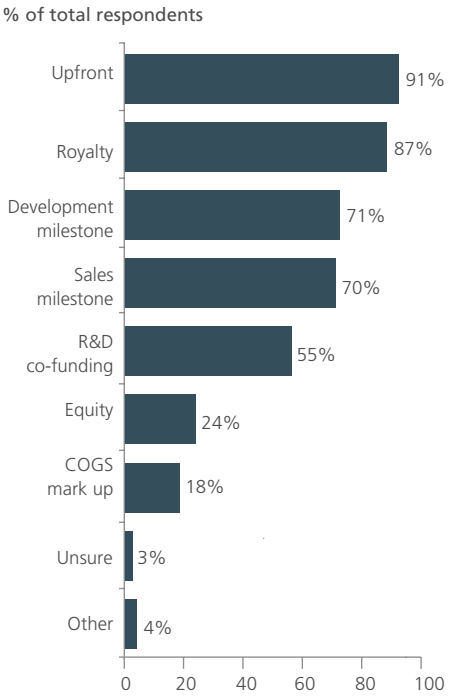
Partner selection criteria



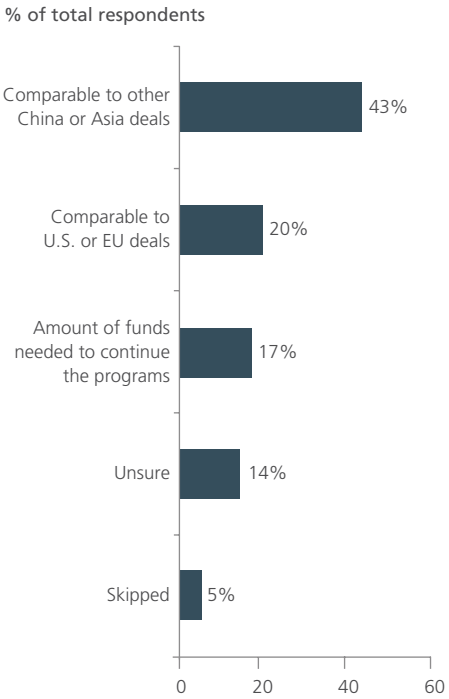
Advantages associated with various partner types



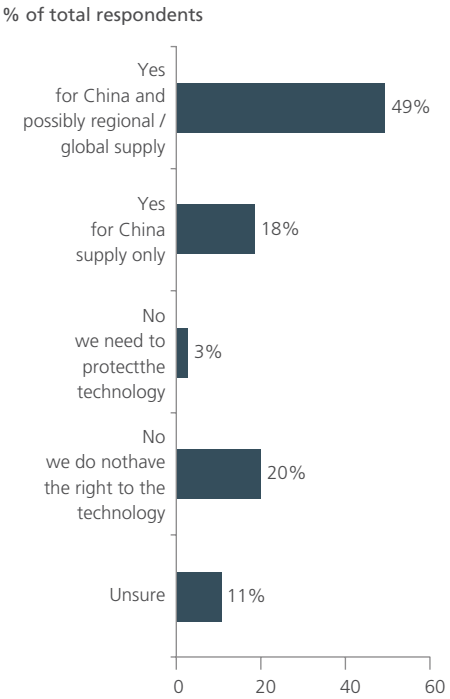
Licensing fee preferences



Equity / upfront expectations



Tech transfer willingness



Endnotes

[1] United Nations.
[2] L.E.K. analysis of Globalcan data.
[3] L. Wang et al., (2017). Prevalence and Ethnic Pattern of Diabetes and Prediabetes in China in 2013. *JAMA* 2017 Jun 27;317(24):2515-2523.
[4] Statistical Yearbook for Health and Family Planning in China.
[5] China National Center for Cardiovascular Diseases.
[6] C. Wang et al., (2018). Prevalence and risk factors of chronic obstructive pulmonary disease in China (the China Pulmonary Health study): a national cross-sectional study; *Lancet*, 2018 Apr 28;391(10131):1706-1717.
[7] 13th Five-Year Special Planning on Medical Device Technology Innovation, Ministry of Science and Technology.
[8] Yakuji Nippo, Issue 12019.
[9] IQVIA.
[10] IQVIA China Pharma Market Outlook, based on 2017 sales.
[11] As of March 2018, China Food and Drug Administration (CFDA) is expected to be renamed to State Drug Administration (SDA).
[12] L.E.K. analysis of CFDA and CDE data.

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