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SPECIAL REPORT

China Market Opportunities for International Pharmas

An extract from "Life Sciences Unicorns: From a China Investment Perspective"

Contents

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1. Introduction

China's pharmaceutical market presents an immense opportunity for pharmaceutical companies from home and abroad. With a vast population, significant unmet clinical needs, and a rapidly improving regulatory and market access environment, international pharmas have strategically expanded to China to invest in this dynamic market. Over the past four decades, these companies have made substantial investments, introduced hundreds of innovative medicines, and played a pivotal role in advancing the Chinese pharmaceutical industry.

This L.E.K. Special Report explores the strategic opportunities available in China for international pharmas. It explores the changing landscape of the pharmaceutical market, examining how MNCs (Multinational Corporations) have adapted to the "new normal", fueled innovation, and embraced digital transformation. Additionally, the report sheds light on China's increasing contributions to global innovation, offering a compelling reason for international pharmas to explore partnerships and collaborations in the country.

The report, 'China Market Opportunities for International Pharmas' is written by Justin Wang, Partner at L.E.K. Consulting, China. It is an extract from the book 'Life Sciences Unicorns: From a China Investment Perspective' written by Mr. Da Liu and published by The Commercial Press (Singapore) Limited in June 2023.

2. Strategic Opportunities in China

China's pharmaceutical market is characterized by the sheer size of its patient base and by significant unmet clinical needs, as well as by the rapidly improving regulatory and market access environment. These factors have long been the key drivers for international pharmaceutical companies (or "pharmas") that made strategic decisions to enter China and invest in the Chinese market.

In 1981, Japan's Otsuka was the first international pharma to enter the People's Republic of China, through a joint venture (JV) with the local government of Tianjin. Together with the establishment of Sino-American Shanghai Squibb (SASS), Xi'an Janssen and a few other entries, this marked the start of a new era for the Chinese pharmaceutical industry. Over the past four decades, these international pharmas have invested more than US$20 billion in the Chinese market[1], contributing to the development of commercial infrastructure, manufacturing, and advanced research and development (R&D). International pharmas have introduced more than 350 innovative medicines[2] for the benefit of Chinese patients, and trained hundreds of thousands of technical and commercial talents for the Chinese pharmaceuticals and biotech industry.

Data published by IQVIA shows that as of 2021, hundreds of international pharmas are operating in China, contributing to about 30% of the Chinese in-hospital pharmaceutical market.

- In 2021, five of the top 10 pharmas by hospital sales are international companies, with AstraZeneca taking the top spot ahead of any other domestic or international peers. Others on the list are Pfizer (No. 4), Roche (No. 5), Bayer (No. 9) and Novartis (No. 10).
- AstraZeneca's osimertinib (Tagrisso) for lung cancer attained the fastest new drug application (NDA) approval in the history of the National Medical Products Administration, or NMPA (then China Food and Drug Administration, or CFDA), taking less than two months.
- Merck & Co./MSD's GARDASIL9 (9-valent HPV vaccine) received the fastest conditional approval in NMPA/CFDA history, in just nine days, on grounds of its significant efficacy breakthrough.
- Of the 59 innovative products that were granted expedited reviews by the NMPA in 2021, 29 (49%) are from international pharmas.

Over the past decade, as mentioned in other chapters of "Life Sciences Unicorns," Chinese pharma companies have begun to accelerate their investments and R&D

activities in innovative therapies, moving rapidly from generics to fast followers to their present position: leading global development in certain therapeutic areas and modalities. This — in parallel with evolving policies, expedited regulatory pathways, expanded reimbursement coverage, centralized procurement and pricing pressures in China — has fundamentally changed the market environment and competitiveness for international pharmas in the country, posing challenges yet also presenting new strategic opportunities.

China provides not only a sizable and growing pharmaceutical market but also strategic value for companies operating a global business. As an increasingly important source of innovation for the global pharmaceutical and biotech industry, China generates first-in-class and best-in-class assets that represent significant, global commercial opportunities. At the same time, it offers world-class clinical development capabilities and resources, with a large patient population — backed up by abundant funding from both public and private institutions that place biotech and life sciences at the top of their investment priorities.

Despite recent geopolitical tensions and market fluctuations, most multinational corporations (MNCs) within the pharma sector remain committed to the Chinese market, with continued presence and investment in the country. These MNCs show great confidence in the future of the Chinese pharma market and its role as a critical, integral part of the global industry.

"Greater China is an important region for global pharmaceutical products broadly, and specifically for medicines that treat cardiovascular and metabolic diseases."[3]

CEO, Arrowhead, April 2022

"The one thing I'll say about China is that, going forward, and given the fact that the country is now so open to innovation, we are now thinking about China as we think about any other country."[4]

President, Novartis, February 2022

"[China serves] not only as a market but [to a great extent] as an innovation hub. That's also the reason why we are present in China across the full value chain, from research, development [and] manufacturing to distribution."[5]

CEO, Roche, February 2021

"Tremendous patient need and a fast-developing healthcare infrastructure make China a strategic priority. We are eager not only to expand late-stage therapies to the broader patient population there, but also to accelerate our clinical development efforts in Asia and [to] better understand and address the needs of patients there."[6]

CEO, BridgeBio, August 2020

3. MNC Pharmas: Adapting to the New Normal

China's pharmaceutical market has evolved significantly since the first MNCs came to China in the 1980s, and the speed of change has only accelerated in the past few years. Facing this reality, and in order to adapt to this "new normal," MNC pharmas have been called to make bold transformations in their China strategies.

Accelerated path to market

Over the past six or seven years, China's NMPA has made continuous efforts to standardize product registration processes and introduce expedited registration pathways for innovative therapies. China also, in 2017, joined the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), aiming to upgrade the nation's drug regulatory system to international standards. As a result, the development and launch of new drugs has been expedited through China's early involvement in international multicenter clinical trials (IMCTs). This has led to more rigorous and globally recognized clinical trials, and to the use of Chinese patient trial data to support global registrations.

In 2017, the NMPA (then known as the CFDA) recorded a mere 82 IMCTs — a figure that nearly tripled in 2021, including more than five times the Phase I and II trials, contributing to 37% of the 302 IMCTs recorded that year. Over 80% of these IMCTs were carried out by international pharmas.

Table 1
Launch lag between China and global first launches (2016 vs. 2021)

2016: 4 products in total	Launch lag (years)
Sirturo (bedaquiline)	3.9
Prevnar13 (pneumococcal conjugate vaccine)	6.9
Cervarix (HPV vaccine)	8.8
Zavesca (miglustat)	14.0
Average lag (2016)	**8.4**
2021: 32 products in total	**Launch lag (years)**
Gavreto (pralsetinib)	0.5
Enspryng (satralizumab)	0.7
Qinlock (ripretinib)	0.8
Evrysdi (risdiplam)	0.8
...	...
Xenazine (tetrabenazine)	12.8
Average lag (2021)	**5.7**

Source: NMPA, FDA, European Medicines Agency, L.E.K. analysis

As a result, the lag between the first global launch (excluding China) and China's launch for innovative therapies is rapidly narrowing (see Table 1). In 2016, only four new international pharma drugs were approved in China, with an average lag time of 8.4 years after their first global launch. In 2021, the NMPA approved 32 NDAs by international pharmas, with an average lag of 5.7 years. Notably, Blueprint Medicines' pralsetinib (Gavreto®), which was licensed to CStone, obtained approval in China just six months after its first ex-China approval by the U.S. Food and Drug Administration (FDA).

In addition, starting in 2020, within designated hospitals in several locations (namely Boao Lecheng International Medical Tourism Pilot Zone in Hainan Province and the Greater Bay Area in Guangdong Province), China has allowed importation and clinical usage of innovative drugs and medical devices that have already been approved in a developed market but are not yet approved domestically. Real-world data generated from these designated hospitals can now be used to support NMPA registrations in China, creating an opportunity for Chinese patients to access innovative therapies from abroad much earlier than would otherwise be possible. Almost all MNC pharmas in China have established an "early access" task force to fully leverage this opportunity.

Faster to peak, faster to cliff

In terms of pricing and reimbursement, China established the National Health Security Administration (NHSA) in 2018, consolidating the administration of all drug pricing, procurement and reimbursement into one central government agency. Upon inception, the NHSA initiated a series of drug pricing and reimbursement reforms that have profoundly changed the commercial life cycle of pharmaceuticals and hence the pricing strategies of all pharma companies.

NRDL negotiations

For international pharmas, newly approved innovative drugs are now eligible for annual negotiations to enter the National Reimbursement Drug List (NRDL) as early as the same year of receiving NMPA approval — no more yearslong waits for the next round of NRDL review, as in the pre-NHSA era. In exchange, however, for international pharmas looking to list an innovative therapy on the NRDL, the NHSA is one of the toughest negotiators and demands a steep price cut, usually in the range of 50%-60%. Each negotiated contract is valid for two years before a mandatory review for renewal, at which time pharmas usually can expect a further (but more moderate) price cut of around 10%-20%. Drugs negotiated onto the NRDL are eligible for approximately 70% reimbursement, i.e., the patient co-pays 30%, reducing their out-of-pocket expenditure on a therapy by 80%-90%. As a result, prescription volume typically increases significantly after

an NRDL listing, requiring the pharma company to invest quickly and heavily in commercialization efforts in order to achieve this very steep ramp-up curve.

Listing on the NRDL through negotiation at low but acceptable prices thus remains the key strategic objective for international pharmas when it comes to most innovative therapies. For those whose products are already commercialized in the U.S., Europe and other markets, the marginal costs of serving the Chinese market may justify price compromises in exchange for significant volume upsides. To protect pharmas from potential challenges from payers in other markets on international reference prices, the NHSA also provides the option of not formally disclosing the negotiation results.

According to NHSA data, in the five rounds of annual negotiations from 2017 to 2021, international pharmas chose to cut prices on 140 imported drugs in order to be listed on the NRDL, representing about 50% of all successful negotiations. It is widely understood that there is an annual cost ceiling of approximately RMB300,000 (or US$45,000) for what the NRDL could accept. The government believes that the NRDL should cover drugs that are, post-negotiation, affordable to ordinary Chinese families whose annual household disposable income (according to data published by the National Statistics Bureau) was RMB92,000, or approximately US$13,500. Therefore, ultra-high-price drugs and therapies such as CAR-T or those for rare diseases are yet to benefit from the NRDL. The NHSA stated in October 2020 that it "attaches great importance to medical security for patients with rare diseases, and constantly explores the establishment of drug security mechanisms for rare diseases, including critical disease insurance, medical assistance, special funds, charity projects and commercial insurance,"[7] and thus would aim to develop a "multi-layer co-funding" mechanism to support payment for rare-disease drugs.

Volume-based procurement

In addition to expanded spending on reimbursement for innovative therapies, the NHSA aims to save money on older and genericized drugs. Many observers see this structural change in spending as a chance to "vacate the cage for a new bird," and it is a critical piece of the puzzle in terms of China's healthcare and pharma market reforms. With volume-based procurement (VBP), first introduced in 2018, manufacturers of originator and generic drugs with the same molecule name bid for a committed volume through the government's centralized procurement process. Incumbents typically face a 60%-80% price cut in exchange for committed volumes in the selected jurisdictions; companies that give up or lose the VBP bid are eligible for only a small fraction of the hospital prescription volumes. A series of strict hospital prescription monitoring measures ensures compliance with the volume commitments.

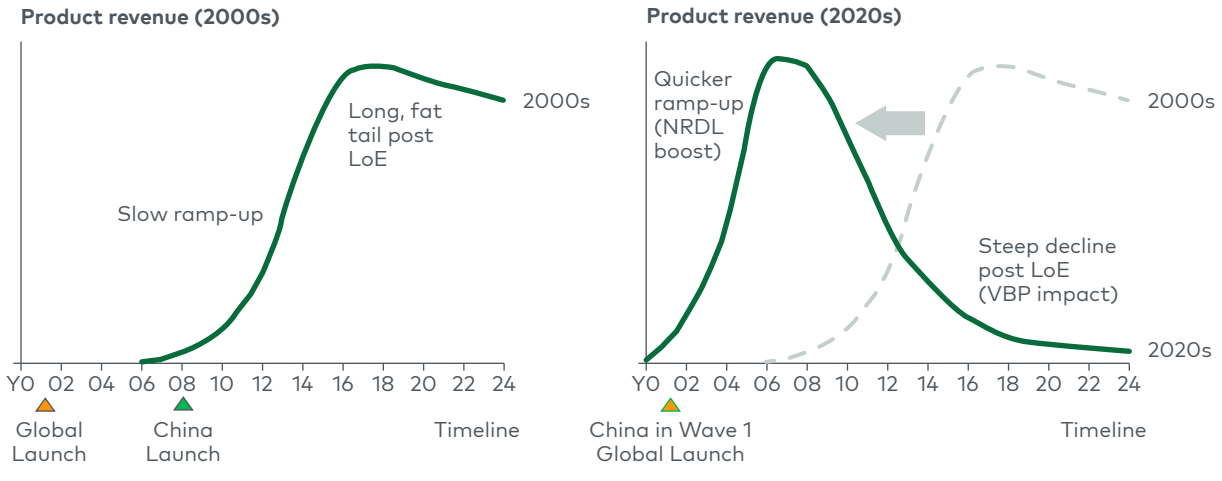
Between November 2018 and November 2021, six batches of national VBP were carried out, covering 234 drug varieties.[8] According to the NHSA, VBP savings on drug spending between 2019 and 2021 potentially reached RMB260 or US$36 billion. Only a small number of international pharmas were willing to offer products (mostly originators) with a large enough price cut to win VBP, leading to an average success rate of approximately 12% (compared with more than 50% for domestic pharma products, mostly generics).[9] Those who bid aggressively expected volume gains to partially offset the price reduction, so their revenues would resume growth from a lower base after the "VBP reset." The majority of international pharmas chose to walk away from VBP to maintain high prices despite the cost of losing committed volumes in their core hospital markets.

Until the introduction of VBP, off-patent originator (OPO) products had long been the "cash cow" for many international pharmas. With continued investment in clinical education and branding, the majority of these OPO products were able to demand a much higher price than generics while still capturing dominant market share. Although some pharmas were able to maintain or even increase sales volumes, for many — win or lose — VBP resulted in a sharp revenue decline. To mitigate their losses, many MNC pharmas reduced sales and marketing investment in the hospital channel; shifted resources to market access and hospital listing efforts (to minimize obstruction in the distribution pathway); and increased efforts in private hospitals, retail pharmacies and ecommerce channels, all of which are not subject to VBP procurement rules.

Shifting product life cycle

The typical product life cycle in China for innovative drugs has fundamentally shifted (see Figure 1), with the ramp-up in the initial years after launch accelerating

Figure 1
Illustrative drug lifecycle shift in China (2000s vs. 2020s)



Source L.E.K. analysis

now that drugs have much earlier access to the NRDL, and with the post-LoE (loss of exclusivity) decline likely becoming much steeper as the launch of generics triggers VBP. For international pharmas, reconsidering their commercialization strategy in China and reshaping their go-to-market model have been on top of their agenda.

Going digital

In the "pre-digital era," international pharmas helped shape China's pharmaceutical commercialization model with an approach focused on academic promotion. Today, they are also pioneers embarking on a digital journey.

The early movers are more focused on ecommerce and social media coverage, as well as online conferences and events. Fundamentally, as in any other country (and even more so in China), digital channels have become a critical means of accessing information. Gradual easing of governmental restrictions on online drug sales and increased scrutiny over sales rep visits to hospitals and physicians have been important external forces behind continued investments in these digital efforts. The rapid expansion of VBP, too, has driven the pharmas to significantly reduce commercialization investments and, as a result, turn to online and digital tools to maintain their reach to a broad customer base while controlling costs. Furthermore, the COVID-19 pandemic and the Chinese government's strict movement control policies accelerated the challenges involved in providing patients with access to hospitals, and pharma reps with access to healthcare professionals (HCPs).

According to a 2021 Yibai (100doc) survey, more than 80% of international oncology pharmas spent approximately 30% of their marketing budget on digital channels, compared with less than 20% for the majority of the Chinese oncology pharmas.[10] WeChat is a critical tool for disseminating medical information to target HCP audiences, through pharmas' own official accounts as well as third-party channels that publish proprietary articles sponsored by, in many cases, pharma companies. Conferences and events are also moving online, saving on costs for the host and significantly removing constraints on audience size. This trend is particularly helpful in reaching the large number of HCPs in lower-tier markets (such as county and community health centers), who are rarely invited to the live events.

International pharmas are also working closely with the leading third-party digital health platforms (such as JD Health and AliHealth) and internet hospitals (innovative approaches similar to telemedicine services) in connecting the dots between diagnosis, treatment and patient disease management. Leading MNC pharmas such as AstraZeneca, Novartis and Sanofi have all established partnerships in China on this front, with dedicated internal digital or innovation

teams steering their efforts, often led by senior talent with extensive internet or digital experience outside the healthcare/pharma industry. Certainly, a key challenge to overcome is payment, as the current reimbursement policies are still shy of providing full coverage for digital services.

In the 2022 APAC Hospital Priorities Survey by L.E.K. Consulting, one-third of senior managers from the 120 Chinese public and private hospitals surveyed reported currently using some form of digital tool, with the remainder either experimenting with or exploring digital solutions. The importance of investing in digital health capabilities has increased significantly compared with the previous year, ranking fourth among all strategic priorities of Chinese hospitals (see Table 2). This trend is anticipated to continue on a steep trajectory, offering tremendous opportunities for Chinese and international pharmaceutical companies alike to help shape — and improve — hospital and patient experience in the digital era.

Table 2
Chinese hospitals' strategic priorities over the next three years (ranked by importance)*

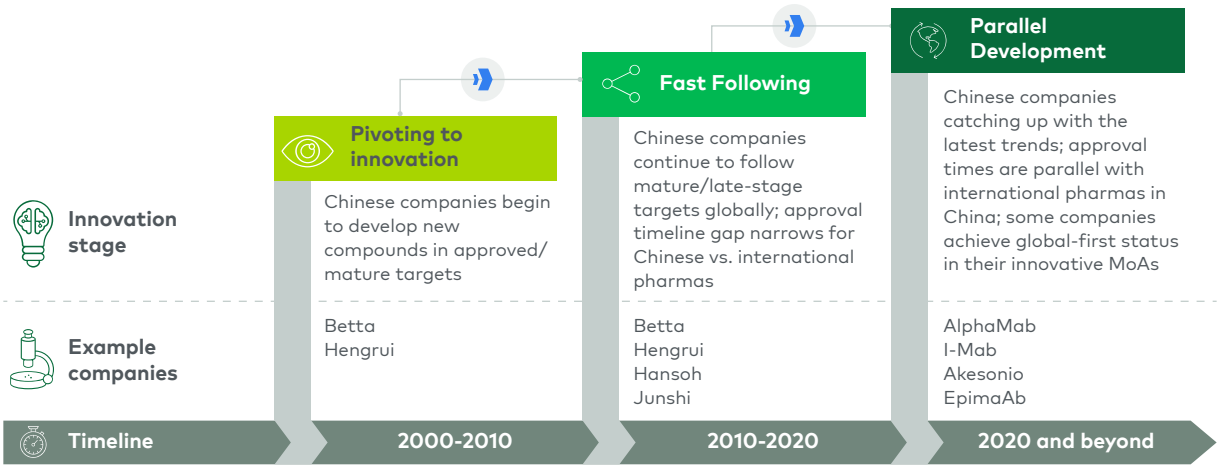
2022 rank	Top strategic priorities	2022	2021	Percentage point change
#1	Improving clinical outcomes	76%	53%	+23
#2	Standardizing clinical care protocol within and across hospitals	72%	53%	+19
#3	Improving healthcare worker safety	70%	48%	+22
#4	Investing in digital health capabilities	66%	39%	+27
#5	Investing in new IT systems	66%	55%	+11
#6	Reducing acquisition costs of capital equipment	63%	49%	+14
#7	Reducing cost of medical supplies	63%	52%	+11
#8	Improving labor efficiency/workflow optimization	58%	50%	+8
#9	Recovering from financial impact of COVID-19	58%	48%	+10
#10	Working with other sites of alternative care	58%	51%	+7

*Survey question: How important are the following strategic priorities for your hospital over the next three years?
Source: L.E.K. 2021, 2022 APAC Hospital Priorities Surveys

Sourcing innovation from China

Another key mandate for many international pharmas is to scout for innovation originating in China. As local Chinese pharmas and biotech companies accelerate their R&D efforts, they are quickly catching up and (in some areas) are on the cusp of innovations parallel to their counterparts' in the developed markets (see Figure 2).

Figure 2
China: Innovation stages and timeline



Note: MoA=mechanism of action
Source: L.E.K. analysis

Gaining global recognition

Over the past few years, numerous Chinese pharmas and biotech companies have enriched their pipeline by moving from "China first" products to "global first" molecules. In 2021, according to the U.S. FDA records, a total of 26 drugs received a breakthrough, fast-track or orphan drug designation, exemplifying the quality of innovations coming from China now (see Table 3).

Table 3
Example first-in-class* drugs under development in China (August 2022)

Company	Product	Therapeutic area	Mechanism of Action	Clinical stage
Remegen	Telitacicept	Autoimmune	BLyS/APRIL fusion protein	Approval
Alphamab	KN046	Oncology	PD-L1/CTLA-4 bispecific antibody	Phase III
Ascletis	ASC40	Oncology	FASN Inhibitor	Phase III
Generon	F-652	Hepatitis	IL-22 agonist	Phase II
Junshi	JS-004	Oncology	BTLA4 antibody	Phase II
Jacobio	JAB-3068	Oncology	SHP2 inhibitor	Phase I/II
Fosun	ORIN1001	Oncology	IRE-1α inhibitor	Phase I

*First molecule globally within a specific mechanism of action
Source: Pharmaprojects, NMPA/CDE, L.E.K. analysis

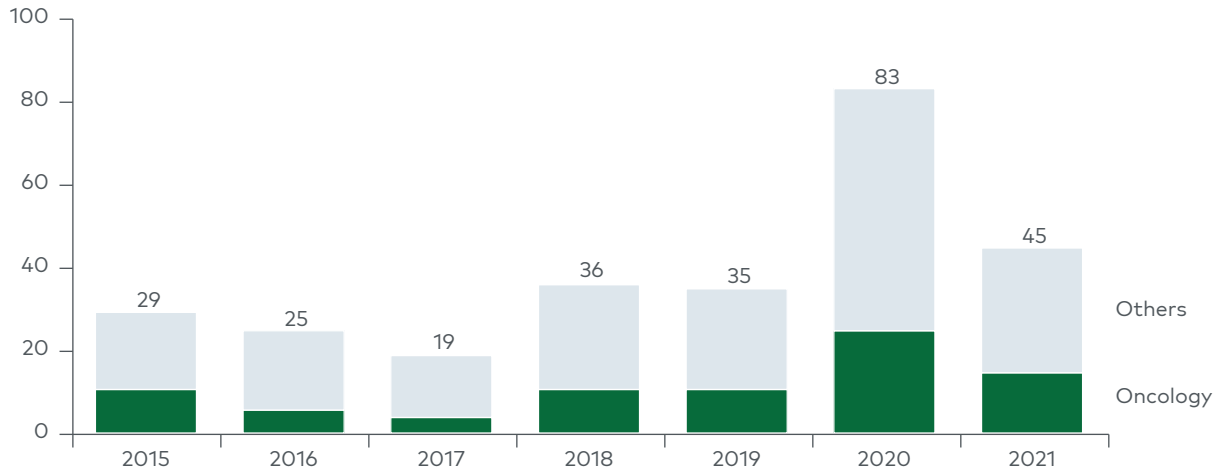
Many of these Chinese biotech companies have a clear ambition to become a full-fledged pharmaceutical company and commercialize these products in China on their own. At the same time, the strategic importance of opportunities outside the Chinese market is rising, especially given the low prices currently resulting from NRDL negotiations, which limit revenue potential within China. However, very few Chinese biotech companies have the confidence and appetite to set up their own commercialization capabilities in the developed markets. This presents an

opportunity for international pharmas to realize commercial value outside China by enriching their global portfolio with innovative assets originating from China.

China-to-international deals

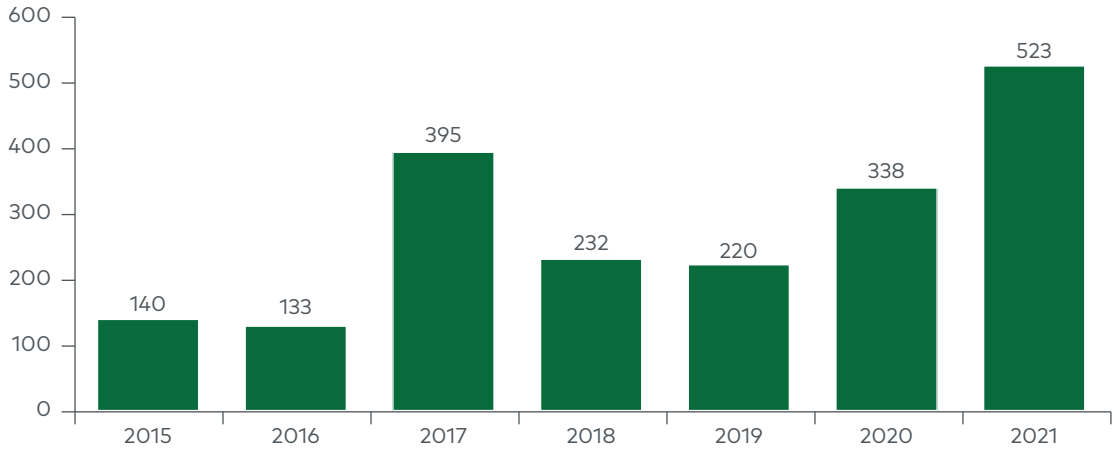
China-to-international licensing deals have increased remarkably in both volume and value recently, especially over the past two years (see Figure 3). In 2021, about 45 deals (totaling more than US$10 billion) were disclosed where a Chinese organization licensed ex-China rights to an international licensee, with an average deal size of more than US$500 million (see Figure 4).

Figure 3
China-to-international licensing deals (2015-2021, Number of deals)



Source: Cortellis, L.E.K. analysis

Figure 4
Average size of China-to-international licensing deals (2015-2021, US$million)



Note: Includes only deals with value announced
Source: Cortellis, L.E.K. analysis

Novartis, AbbVie, Lilly and Seagen are among the international pharmas that have struck major deals, which undoubtedly demonstrates continued global confidence in the high quality and strong commercial appeal of Chinese innovation (see Table 4). The Chinese government's efforts over recent decades in building and cultivating a healthy biotech innovation ecosystem are now bearing fruit. International pharmas view China no longer as a source of mere "me too" followers in the pharma industry, but as a powerhouse supplying truly innovative pipelines of products that will require heavy bids.

Table 4
Top oncology out-licensing deals (>US$500 million) by Chinese pharmas (August 2020-August 2022)

Date	Licensor	Licensee	Product(s)	Deal size* (US$,million)	Territory
Aug. 2022	Jemincare	Genentech	JMKX-002992	650	Global
July 2022	CSPC	Elevation Oncology	SYSA-1801	1,245	Global ex. Greater China
June 2022	Henlius	Organon	HLX-11, HLX-14	644	Global ex. Greater China
May 2022	Kelun	MSD	Undisclosed	1,363	Global ex. Greater China
May 2022	LaNova	Turning Point	LM-302	1,100	Global ex. Greater China and South Korea
Mar. 2022	Adagene	Sanofi	Masked monoclonal and bispecific antibodies	2,518	Global
Dec. 2021	BeiGene	Novartis	Ociperlimab	2,900	Canada, EU, UK, U.S., Japan and six other markets
Aug. 2021	RemeGen	Seagen	Disitamab vedotin	2,595	Global ex. Asia, plus Japan and Singapore
June 2021	Allist	ArriVent	Alflutinib mesylate	805	Global ex. Greater China
Feb. 2021	Junshi	Coherus	JS-006, JS018-1, toripalimab	1,110	Canada, U.S.
Jan. 2021	BeiGene	Novartis	Tislelizumab	2,200	Canada, EU, UK, U.S., Japan and six other markets
Nov. 2020	Henlius	Binacea	HLX-35	768	Global ex. Greater China
Oct. 2020	CStone	EQRx	CS-1003, sugemalimab	1,300	Global ex. Greater China
Sep. 2020	I-Mab	AbbVie	Lemzoparlimab	1,940	Global ex. Greater China

*Includes upfront and milestone payments
Source: Cortellis, L.E.K. analysis

In 2021, more than 60% of the approximately 400 pharma collaborations in China were cross-border.[11] Beginning in late 2021 and continuing into 2022, the Chinese biotech market plunged amid ongoing concerns over geopolitical tensions, forced delisting from the U.S. stock exchanges and a slowdown in China's macroeconomic growth, casting shade on cross-border deal-making. Despite such volatility, long-term confidence in China remains the mainstream view among investors. In 2022, international pharmas continued to invest in sourcing innovation from China, with Sanofi, Turning Point, Merck (MSD) and Elevation Oncology, among others, striking licensing deals of more than US$1 billion each with Chinese innovators.

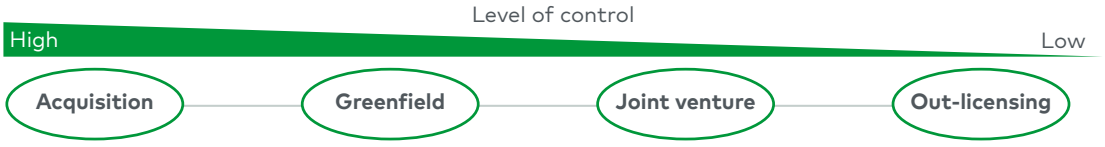
4. New Entrants: Options & Trade-offs[12]

International pharmas have employed a range of options to enter China, but most companies, especially biotechs, take partnering into consideration first. Whereas larger, established companies mostly invested in their own presence outright, smaller firms might look to China only as a source of funding or incremental opportunity, and thus would choose to out-license the rights to their products.

For those that are not yet operational in China, choosing the right approach before discussing partnership strategy is a critical task. The choice regarding method of entry goes beyond simply locating the right local partner company. An effective entry strategy should be geared around the pharma's overall strategic plan and commercial objectives. These objectives are unique for each firm and may change depending on internal objectives specific to China (and more broadly to Asia), the firm's current stage of development, and the key decision-makers' willingness to invest financially and operationally.

Entry strategies can be grouped chiefly into four broad categories as described below, each with its own advantages and challenges (see Figure 5).

Figure 5
Options for Chinese market entry



	Acquisition	Greenfield	Joint venture	Out-licensing
	Presence	Presence	Presence	No presence
Pros	• Immediate access to existing products, talents and other local capabilities • Full control of business • Full revenue booking	• Full control of business • Full revenue booking • Build own brand, capability and network • Can use support from service partners (e.g., CRO, CSO)	• Leverage partner resources to fill in gaps and save time • Shared investment, risks and upsides	• Good for company with limited local presence or strength • Low investment and easy recovery/upside • Low risk
Cons	• High upfront investment • Difficult to find right target • Risks from integration	• Need to ramp up on full set of capabilities/ infrastructure at all fronts from scratch • Speed to launch may be slower given newness to market	• Requires time and effort to identify right partner and negotiate • Difficult to set up • Potential conflict of interest	• Limited control over product sales, brand and marketing • Low profitability potential

Note: CRO=contract research organization, CSO=contract sales organization
Source: L.E.K. analysis

Acquisition

Acquisitions provide a jump-start into a new market, with already established infrastructures, existing supply chains and ready commercial portfolios. This is in addition to, and can work in cooperation with, the acquiring firm's own pipelines. By entering Asia through its acquisition of Invida in 2011, Italy's Menarini achieved a commercial presence in 13 Asia-Pacific markets (including China, Australia, and major Southeast Asian countries such as Singapore and Malaysia) with a single purchase. In another example, Australia's CSL acquired Chinese plasma fractionator firm Wuhan Ruide in 2017 in order to expand into the local market for plasma-derived products.

Greenfield

Starting a brand-new business in China 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 it does not require much direct physical infrastructure. Alternatively, the greenfield approach can start with initial setups and preparation for product registration, with an eye to making further decisions about acquisitions or joint ventures later in the game. This method was used by FibroGen, Gilead, Biogen (all U.S. companies) and Taiho (a Japanese company) to enter the Chinese market. Alternatively, U.S. pharma Biohaven (acquired by Pfizer) established a new entity in China, Bioshin, to develop and commercialize its pipeline products in China and other Asia-Pacific markets.

Joint Venture

A JV is the most frequently considered option for biotech companies on the cusp of becoming international commercial operators. Firms seeking entry through a JV have an interest in maintaining some level of their own presence in China yet are often daunted by the challenge of managing an operation on the opposite side of the globe, where cultural norms are unfamiliar. A joint venture is a good option, therefore, for executives who feel more comfortable having "locals" navigate the market. JV projects must navigate steep communication and cultural challenges while maintaining the integrity of both Chinese and international partners.

Kite (acquired by Gilead) and Juno (acquired by BMS) both opted to setting up a joint venture in China, with Fosun in 2017 and WuXi AppTec in 2016, respectively, to develop and commercialize their CAR-T and other cell therapies. Both JVs had their first CAR-T product approved in China in 2021. More recently, Allogene formed a JV with Overland (backed by Hillhouse Capital) in 2020 in order to operate in China and other Asian markets, and Arrowhead formed Visirna with Vivo Capital in 2022 for the Greater China market. The participation of private equity and venture capital funds provides alternative sources of funding and a greater degree of managerial flexibility.

Out-licensing

The rise of biotech startups in China has complemented and facilitated the rise of out-licensing to Chinese firms. Companies such as Everest, CStone and CANbridge allow international firms to out-license, develop and commercialize in China with limited direct presence. Smaller pharmas such as Puma, Mirati, Tesaro and Blueprint have granted companies exclusive product rights in China in return for upfronts and milestones (see Table 5).

Table 5
Examples of in-licensed drugs approved by NMPA (non-exhaustive)

Product	Therapeutic area	China approval date	Licensor	Licensee
Ramucirumab	Oncology	March 2022	Lilly	Innovent
Ivosidenib	Oncology	February 2022	Servier (Agios)	CStone
Dinutuximab beta	Oncology	August 2021	EUSA	BeiGene
Carfilzomib	Oncology	July 2021	Amgen	BeiGene
Avapritinib	Oncology	March 2021	Blueprint	CStone
Pralsetinib	Oncology	March 2021	Blueprint	CStone
Ripretinib	Oncology	March 2021	Deciphera	ZAI Lab
Niraparib	Oncology	December 2019	Tesaro	ZAI Lab

Source: NMPA, L.E.K. analysis

5. Partnership Considerations[13]

Once international pharmas start down the path of partnership, the selection criteria for identifying suitable Chinese partners are mostly consistent with partner selection patterns in other regions. The approach to partnering with multinational/international pharmas in China versus domestic Chinese pharmas does not necessarily differ.

Key selection criteria include the following:

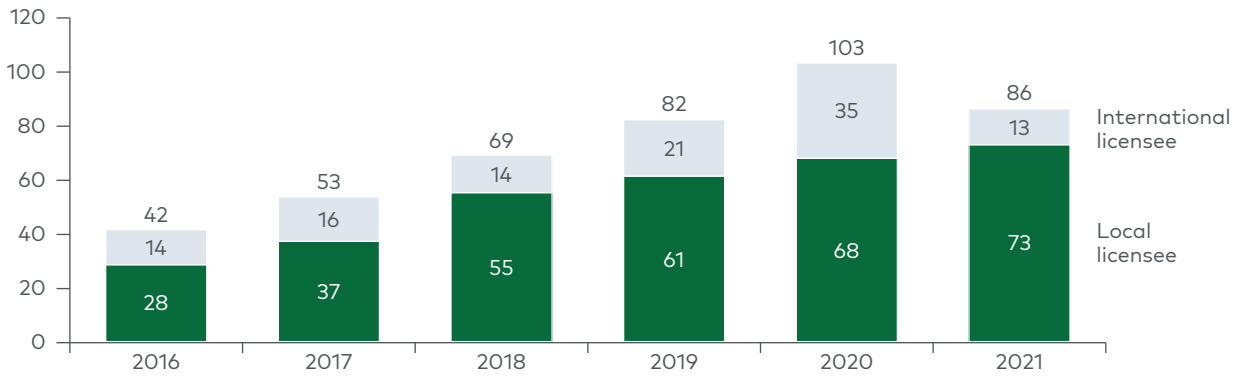
- **Upfront financials.** A willingness to supply capital is a universal requirement for biotech companies in the development stage. The injection of cash upfront is often necessary so these firms can run late-stage trials. Plus, it represents validation of the technology.
- **Clinical trial competence and access.** Given China's requirement of Phase III 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 of the potential partner.
- **Commercial capabilities.** Partners are expected to possess demonstrated commercial expertise based on hospital coverage, market access and market positioning. This means, for example, a larger company in China must have at least 1,000 large teaching systems (known as "Level 3A hospitals") out of the 20,000 hospitals nationwide in order to have a reasonable coverage.
- **Intellectual property (IP) protection.** IP protection continues to be a key concern raised by international pharmas and is often a key selection criterion exclusive to emerging markets. Without enforceable and effective IP protection, pharmas either would refuse to consider China (or any other markets with an underdeveloped IP protection system) or would seek out partners that are considered "safer" from this perspective.

Over the past five years, international pharma out-licensing deals in China continued to grow at 13% compound annual growth rate, with more than 100 deals reached in 2020 and close to 90 in 2021 (see Figure 6). Among such deals, approximately 80% are licensed to a Chinese partner and the remaining 20% to international peers already operating in China — a ratio that has remained largely stable over the years. Yet vast differences exist, typically by nationality, in the perception of different partner group types.

Local Chinese pharmas

Established Chinese pharma companies have been operating in the market for decades, building up extensive clinical, commercial and regulatory experiences and networks. Many are transitioning now from their traditional generics business to

Figure 6
International pharma out-licensing deals in China (2016-2021, number of deals)



Source: Cortellis, L.E.K. analysis

innovation, and from developing internal pipelines to actively seeking in-licensing opportunities. Although the decision-making process is usually efficient, in many cases there is a trade-off: potential concerns over regulatory, commercial, IP protection and other types of compliance, especially among licensors less familiar with the Chinese market.

Furthermore, a considerable number of newly established Chinese biotech companies are focusing on innovation. In addition to developing their own pipelines, they are aggressively licensing international assets in order to jump-start their clinical development and commercial presence. Despite not having much of a track record in successful registration or commercialization of innovative drugs, these companies are typically led by experienced industry veterans from established international or Chinese pharmas, and are backed by financial investors that provide the funding needed for clinical development and commercialization.

International pharmas

There are significant advantages associated with having international pharmas as partners in China as well, especially in terms of safety perceptions. The top reasons for partnering with an MNC are related to safety and risk reduction: key merits include extensive regional or global experience, more robust IP protection, a strong corporate reputation, and stringent compliance practices. China-only or Asia-only development and commercialization deals are usually part of global or regional pharmas' business development considerations — or even a key element of portfolio expansion in the region. The trade-off here, however, depends on the organization's business development functions: transactions with MNC pharmas likely require decision-making at the regional and global level, potentially resulting in lengthier timelines and increased transaction costs. In most cases, when considering China-only deals, MNC pharmas also have a much stronger preference for late-stage pipelines or commercialized products and are reluctant to commit major clinical development investments for China-only in-licensing deals.

6. Conclusion

The Chinese pharmaceutical market, at US$300 billion, is the world's second-largest pharma market and continues to enjoy expectations of the highest potential growth among major economies. Underlying drivers for healthcare demand, including the country's aging population, rising living standards and improving healthcare infrastructure, will sustain strong growth in the foreseeable future.

For international pharma companies, when it comes to serving the unmet healthcare needs of the 1.4 billion population as well as participating in an increasingly important hub for global pharmaceutical, life sciences and digital innovation, China is too important a market to neglect. Understanding how to interpret policy directions and navigate the complexities of this market is critical for companies looking to seize these opportunities.

The objectives of policymakers and regulators in China are clear: they are making every effort to cultivate high-quality innovation and provide affordable healthcare to the world's largest population, who are pursuing a new level of happiness and well-being. The NMPA is among the most open-minded Chinese government institutions and is working relentlessly to catch up with the highest global standards. In the Chinese pharmaceutical market, international companies are granted the same rights of access as their domestic counterparts'. What's more, neither the origin of innovation nor the location of production is a limiting criterion for procurement decisions.

After all, China is a developing market, and participants should expect policies to keep evolving. Some changes may seem abrupt, and regulations may appear vague, as policymakers persist in adapting to the rapidly evolving technologies and market dynamics — but their objectives remain consistent. In a market as unique as China, established global institutions cannot simply be replicated domestically. For these reasons, "crossing the river by feeling the stone" has been (and likely will continue to be) the best approach to ensure continued advancement.

China's grand vision is to "build a community for mankind with a shared future" — a solemn commitment to openness and inclusiveness. The pharmaceutical industry, with both Chinese and international participants complementing each other, will contribute to and benefit from this journey.

Endnotes

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[8] A variety is defined as a specific dosage form of a molecule (e.g., immediate-release oral form of rivaroxaban)

[9] Success rate is defined as number VBP winners divided by total number of VBP participants; data excludes Batch 6 for insulins where different rules were applied

[10] 100doc, Digital Marketing Insights of Oncology Pharmas, March 2021

[11] ChinaBio, State of China Life Science - 2021

[12] Adapted and updated from Heading East – Biopharma International Expansion to China and Asia, L.E.K. Consulting, 2018

[13] Adapted and updated from Heading East – Biopharma International Expansion to China and Asia, L.E.K. Consulting, 2018

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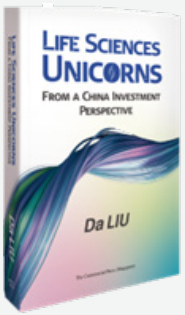
About the Book, in which the report was originally published



Life Sciences Unicorns: From a China Investment Perspective by Da Liu
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