MaRS Market Insights

GOING GLOBAL China

Entering China's Emerging Life Sciences Markets: The opportunity for Ontario startups

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To download the original report, please visit
http://www.marsdd.com/news-and-insights/china-emerging-life-sciences-market-opportunity-for-ontario-startups

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About this report

This report examines the market opportunities in China for Ontario life sciences startups, as well as issues around market access. Entering China's market can present numerous challenges for life sciences startups until they become familiar with the market and its related funding opportunities. The report also explores the concerns of Ontario startups about venturing into China's markets, including a look at intellectual property (IP) protection, regulation hurdles and collaboration models.

This publication is the second part of a series produced by MaRS called *Going Global: China.* Download the earlier report, Playing the Long Game: China's market opportunities for Ontario startups.

Note: *In this report, we use the term "life sciences" to refer to the pharmaceutical and medical devices industry. All dollar figures are cited in Canadian dollars, unless otherwise noted.*

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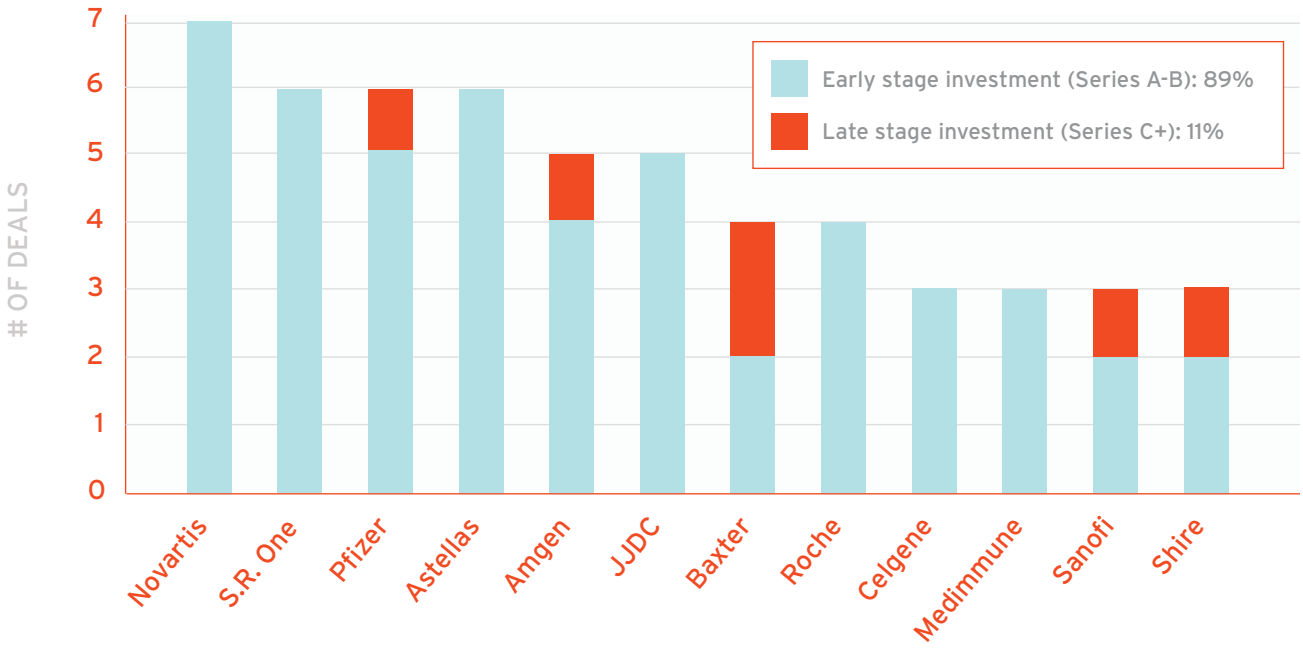
The global life sciences industry: Startups are driving innovation

The innovation landscape in the global life sciences industry has changed dramatically in recent years. More and more multinational companies are seeking new sources of innovation in order to replenish their off-patent pipelines in cost-effective and efficient ways. As noted in JLL's 2014 Global Life Sciences Cluster Report, the life sciences industry is moving from one that was driven by Big Pharma to one where small- and medium-sized enterprises (SMEs) are propelling innovation. One sees this transformation with nearly all major pharmaceutical companies either setting up their own venture capital funds or collaborating with venture partners to invest in life sciences startups. Examples of this funding shift include:

- 2011: Merck establishes the new Merck Research Venture Fund (MRVF) with $250 million to invest in companies around the world. The company also set up a separate Global Health Innovation Fund with another $250 million[1]
- 2013: Eli Lilly establishes a $150 million Montreal-based venture fund called TVM Life Science Ventures VII. Two-thirds of the TVM VII fund is earmarked for investment in "project-focused companies" that are developing a single drug. The other third of the money will be used for traditional investments in small life-science companies[2]

As observed by Silicon Valley Bank, from 2012 to 2013, "nearly 90% of top corporate investment deals in biopharma [were] directed at series A or B rounds. More than half of these new investments were in pre-clinical or phase I companies."[3]

Figure 1: Biopharma top corporate investors: New money investors by stage (2012-2013)



Source: *CB Insights, PitchBook, VentureSource and SVB proprietory data*

Despite the changing focus of corporate funding and increased government funding for life sciences startups, life sciences entrepreneurs still face critical challenges in raising risk capital in Canada. According to Thomson Reuters, "venture capital (VC) investments in the Canadian life sciences sector declined to $250 million in 2013, a decrease of 27% below the $342 million invested the previous year."[4] In particular, life sciences startups in Ontario, recognized for their excellence in research and innovation, are struggling with reaping the commercial benefits of their innovations due to a small domestic market and limited early-stage funding support.

Outside of Canada, life sciences startups that face similar challenges as those here in Canada have widened their search. They have sought ways to overcome the shortage of early-stage funding support, achieve lower research and development (R&D) costs, and access greater market opportunities. Riding the shifting waves of the global economic order, these startups are taking advantage of attractive funding and market access offers from emerging high-growth economies. They are focusing on China.

China is Asia's number one biopharma cluster according to Genetic Engineering & Biotechnology News. China led all other countries in the following areas:

- Biomedical R&D spending ($160 billion out of $243 billion in all of Asia)
- The number of life science companies (7,500 in 2013)
- The total number of industry jobs (over 250,000)
- Active venture capital investment

China came second to Japan in initial public offerings (IPOs), with $2.1 billion raised by 14 companies since 2010, while its 9,302 biotech/pharma patents (from 1970 to the present) were in third place overall.[5]

A quick scan of statistics from ChinaBio shows that

life sciences startups from other countries, especially the US, Europe and Israel, are busy tapping into China's market. There were almost 60 cross-border transactions or collaborations involving startups recorded between April 1 and November 12, 2014: a rate of 10 transactions per month.

This industry perspective is reinforced by a recent 2014 European Business in China Business Confidence Survey, which indicates that

> **"healthcare SME companies, including those dealing in medical devices, were the most optimistic, with 88 percent saying they had a positive outook for growth in 2014.[6]"**

Partnership deals in 2014 between China and foreign startups included:

- **September 10, 2014:** Beike Biotechnology acquires China market rights to a novel cancer immunotherapy from Altor Bioscience in the US. Beike also agrees to a package of over US$200 million in development and sales milestones and will pay a tiered double-digit royalty on sales
- **October 20, 2014:** Fosun Pharma leads $12 million in fundraising for Check-Cap, an Israeli medical device company. Check-Cap has developed an ingestible capsule that performs an endoscopy as its passes through the digestive tract. Check-Cap will use the money to conduct a clinical trial in Europe, followed by trials in the US, China and Japan. In all likelihood, Fosun will distribute the product in China
- **October 16, 2014:** MID Labs Ltd., a California medical device company that develops novel products for vitreoretinal surgery, closes $51 million in funding from Chinese investors. The investment was led by OrbiMed and Frontline BioVentures and it included Softbank China Venture Capital (SBCVC), Allen Chao and Sungent bioVENTURE. The proceeds will be used to continue development of MID Labs' products and increase production capacity in the US and China
- **October 22, 2014:** Enigma (a UK company specializing in developing next-generation rapid molecular diagnostic instrument platforms for decentralized and point-of-care [PoC] settings) forms a joint venture with Beijing's Leadman Biochemistry for the development of Enigma's molecular diagnostic PoC infectious disease test. Enigma will out-license China rights for its technology to the joint venture

The majority of the 60 cross-border deals mentioned above involve small companies in the US and several European countries, such as the UK and Germany. They span the life sciences sector, encompassing new drug development, medical devices and diagnostic kits.

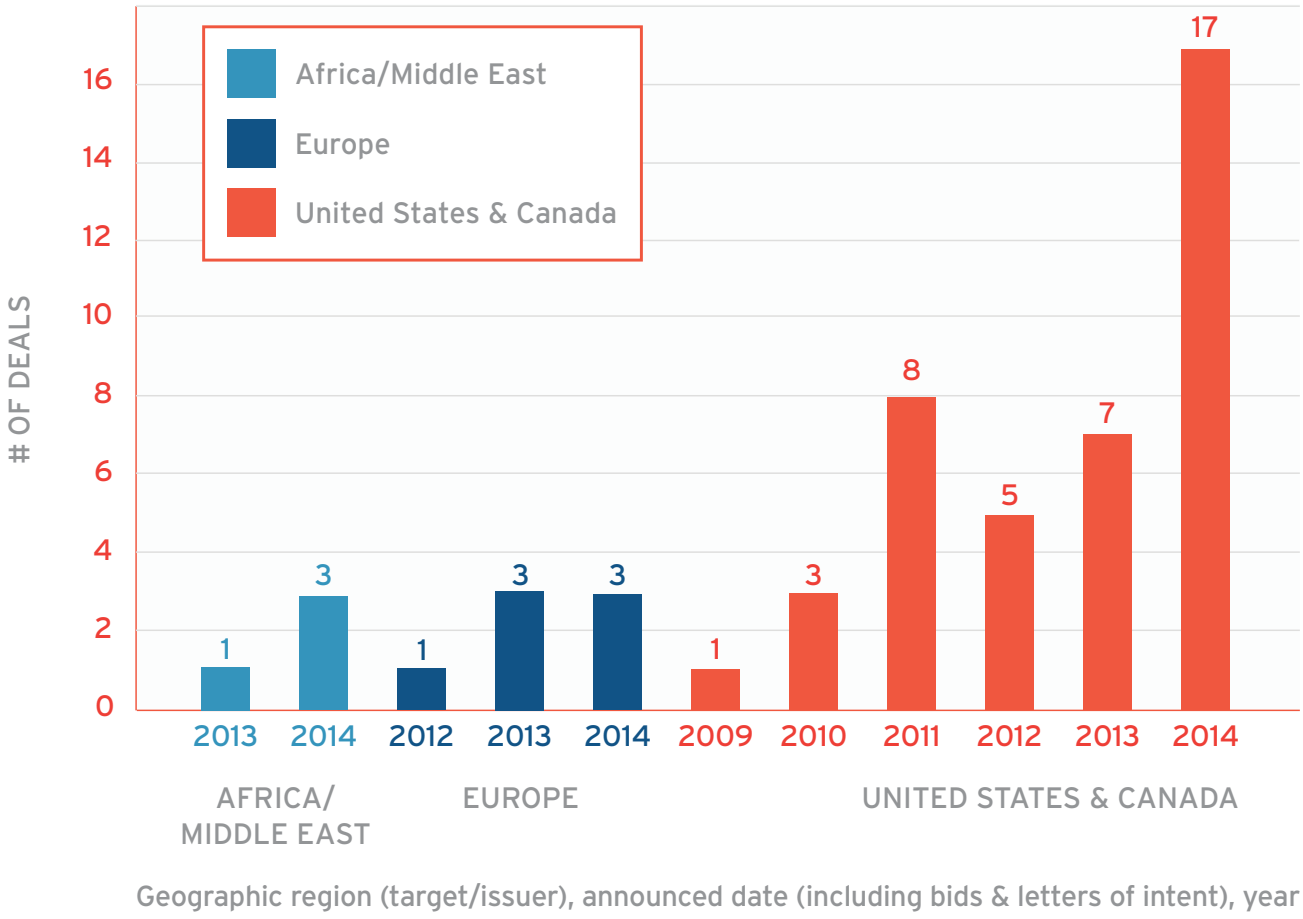
Only four of these 60 deals involved players in Canada. Not one of these is from Ontario, and none is a startup. Canada's numbers are low in terms of its agreements with China, and almost all Canadian deals are restricted to medical devices sector. Table 1 outlines the Canada-China transactions that took place between April 1 and November 12, 2014.

Table 1: List of Canada-China cross-border life sciences transactions from April 1 to November 12, 2014

CANADA	CHINA
RESPONSE BIOMEDICAL OF CANADA	HANGZHOU JOINSTAR BIOMEDICAL TECHNOLOGY
October 16th, 2014: A funded Technology Development Agreement (totaling $8.82 million) that supports the co-development by Response and Joinstar of components and multiple assays that will run on a high throughput rapid immunoassay analyzer developed by Joinstar.	
VERISANTE TECHNOLOGY	N/A
October 3rd, 2014: With an equity investment of $2,150,000 and $1 million development fee, Verisante enters into a Definitive Agreement to sublicense the global rights to develop and commercialize the Core™ Raman technology with the ClearVu™ endoscopic camera system for the detection of lung cancer, and the China marketing rights for other Core™ series products (subject to existing agreements) into an limited liability company (LLC) in China.	
MIRACULINS	CATALYN MEDICAL TECHNOLOGIES LIMITED, CACHET PHARMA
August 14th, 2014: Miraculins reaches an agreement for the China distribution of its Scout DS® Non-Invasive Diabetes Screening Device. The device will be imported by Catalyn Medical Technologies Limited, a private Hong Kong company, and distributed by Cachet Pharma of China.	
DIAGNOCURE	SHUWEN BIOTECH
June 9th, 2014: Under the exclusive license and collaboration agreement, DiagnoCure has granted Shuwen Biotech an exclusive license to commercialize the Previstage™ GCC colorectal cancer staging test in the Greater China Region.	

From China's outbound innovation investment perspective, Canada is not a major player. In 2014, out of 17 of China's venture capital (VC) and growth capital life-sciences investments in North America (January 1 to November 12), only one was made in Canada (in Toronto). The majority of this VC investment capital went to the US. Figure 2 shows the distribution and size of China's overseas life sciences investments from 2012 to 2014.

Figure 2: China's overseas venture capital and growth investment in the life sciences sector, 2012-2014



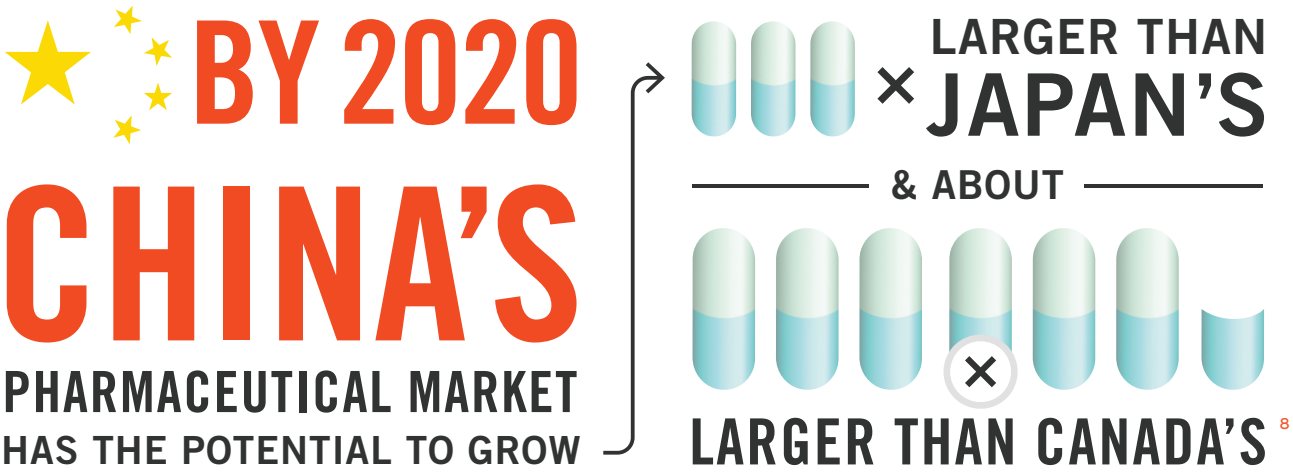
Source: *Capital IQ*

In 2014, Canada's government introduced its **Global Markets Action Plan** (GMAP) and set the ambitious target of growing the export presence of Canadian SMEs in emerging markets from 29% to 50% by 2018. This projected growth means increasing 11,000 companies to 21,000. Given the current landscape in the Canadian life sciences sector, this will involve significant change for startups.

Why does China present a robust opportunity?

Strong market growth and potential

China is leading the pharmerging (emerging pharmaceutical) markets with a projected average market growth of 15% to 18% (2012-2017), and it is growing faster than almost all developed markets including those of the US and Canada.[7]



Source: *Globaldata*

GlobalData estimates China's pharmaceutical market for Western medicines to earn US$76 billion in revenue in 2014 and to reach US$315 billion at a compound annual growth rate (CAGR) of 22.5% by 2020.[9] If the market meets expectations, China's pharmaceutical market would become the second largest in the world, behind the US and ahead of Japan.

Figure 3: Developed markets versus pharmerging markets: Compound annual growth rates (CAGR) of global pharmaceutical markets

Developed Markets CAGR 2012-2017
US: 1-4%
Japan: 2-5%
Germany: 1-4%
France: (-1)-2%
Italy: 0-3%
Canada: 1-4%
Spain: (-4)-(-1)%
UK: 1-4%
Developed 1-4%

Pharmerging Markets CAGR 2012-2017
Tier 1 China: 15-18%
Tier 2: 10 - 13%
Brazil: 11 - 14%
Russia: 9 - 12%
India: 11 - 14%
Tier 3: 7 - 10%
Pharmerging 11 - 14%

Source: *IMS Health Market Prognosis, March 2013*

The market for medical devices is also experiencing significant growth. It is estimated to earn US$25.3 billion by the end of 2014 and this would make China's market for medical devices three times larger than Canada's. By 2020, the market is expected to grow to US$53.5 billion in earnings at 11.3% CAGR. This would place China's market third in the world, behind the United States and Japan and ahead of Germany.

Source: *Globaldata*

Healthcare reform and intensified R&D investment

IMPROVEMENTS TO THE REGULATORY FRAMEWORK

Different levels of governments in China as well as the healthcare regulatory bodies are working to further the country's regulatory framework. They are investing large amounts to develop a strong medical research and clinical trial infrastructure and body of expertise.

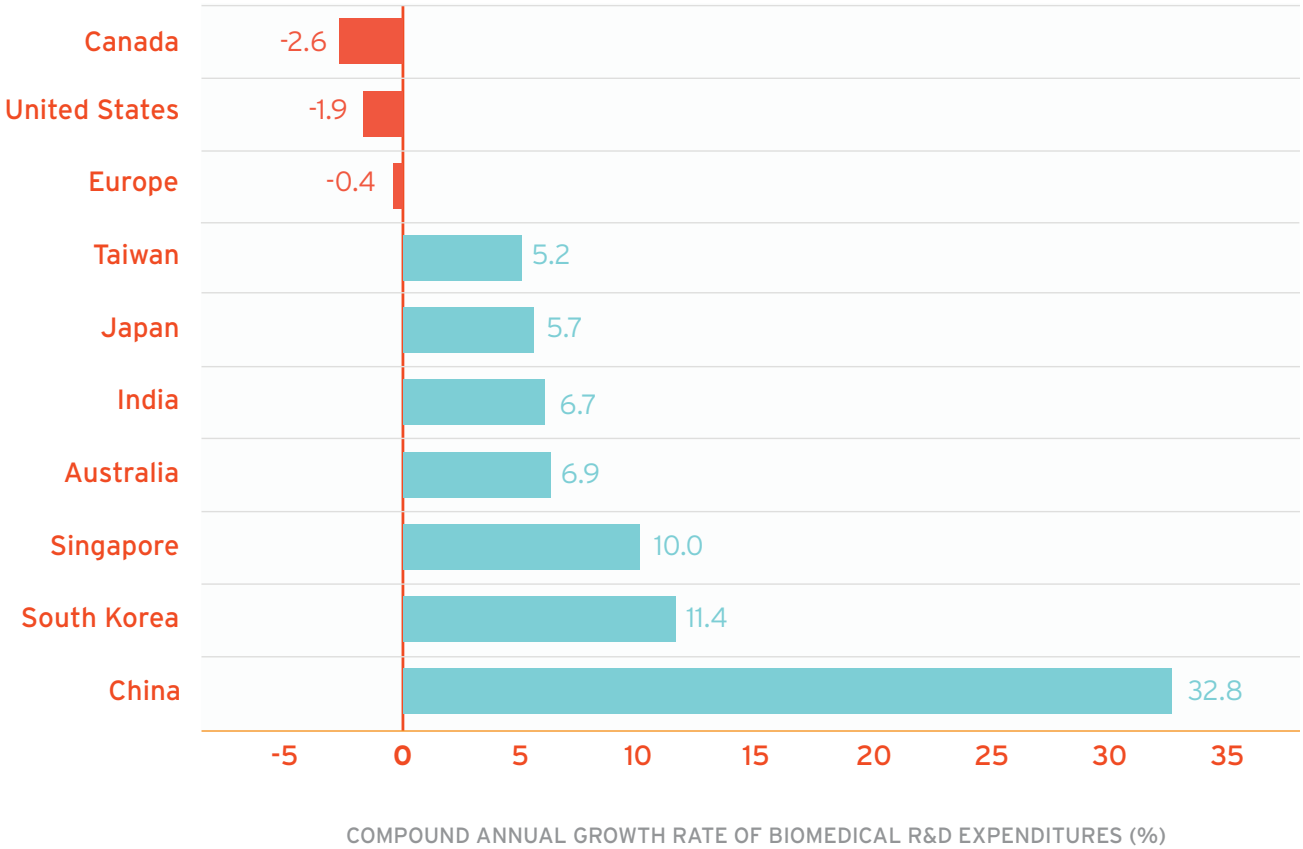
- **In 2010, China's State Food and Drug Administration (SFDA) issued a new version of its Good Manufacturing Practice (GMP) regulations,** which requires manufacturers of sterile drugs (including blood products, vaccines, injections and so on) to receive new GMP certification before December 31, 2013, and all other drug manufacturers to receive new GMP certification before December 31, 2015. The new GMP regulations were introduced in order to raise quality in line with international standards. This framework will eventually squeeze out smaller companies that cannot meet the new regulation and enable healthier industry consolidation
- **In 2013, the SFDA proposed fast-track drug registration for China-based innovation and clinical priorities.** This plan ensures that its Drug Registration rules match international standards, and sets the stage to (eventually) allow data from overseas clinical studies to be submitted during technical reviews and regulatory approvals. As commented by IHS, "The emphasis on supporting local innovation and indigenous intellectual property does not necessarily exclude participation of foreign firms, with the importance of foreign firms having **strong local connections and joint-venture relationships in China likely to be reinforced.** Foreign firms would also stand to benefit directly if the SFDA eventually accepts overseas clinical trial data, with streamlined, more transparent review processes theoretically leading to faster drug development and approvals" [10]
- **In March 2014, the SFDA set up a special office at the Center for Medical Device Evaluation in order to speed up the approval of innovative medical devices.** This division will determine whether a specific medical device qualifies as innovative. If it does, the same group will supervise the approval process under priority-review procedures. Both foreign and domestic companies are eligible for the program. The priority review is expected to shorten the entire approval process to about 160 days (as versus a year or more under the previous system)
- **In July 2014, the Center for Drug Evaluation began outsourcing reviews for generic drug approvals to speed up the process.** Reviews are outsourced to either China's provincial drug agencies or independent third parties. Additionally, the SDFA is being advised to allow new drugs to begin clinical trials if the agency does not approve an investigational new drug (IND) filing within 90 days [11]
- **On October 27, 2014, China lifted caps on retail prices for low-cost medications and is now moving toward free-market pricing for pharmaceuticals.** Free-market pricing allows the market to set its own prices for drugs, and avoids the risk that accompanies government-regulated price caps, which is that the market may see supply shortages and questionable drug quality. **Lifting price controls on innovative patented drugs means that prices will rise and, in turn, spur innovation**

GOVERNMENT INVESTMENT IN INFRASTRUCTURE AND BASIC RESEARCH

Significant funding has been poured into R&D by both the public and corporate sectors with the goal to establish a strong research infrastructure and accelerate innovation. By 2013, China had overtaken Japan in terms of R&D spending, with China's R&D spending having risen from $148 billion in 2012 to $166.5 billion in 2013. Analysts predict that by 2018, the country will surpass the combined R&D spending of Europe's 34 countries. And by 2022, China's R&D spending is expected to match that of the US, when the two countries are likely to each spend about $600 billion on R&D.[12]

Figure 4 illustrates the CAGR for the life sciences R&D expenditures in China, the US, Canada and other key markets during the years 2007 to 2012. China leads with a CAGR of 32.8% per year, compared with the declining growth numbers in the US and Canada, which show -1.9% and -2.6% respectively. Both domestic and foreign players can take advantage of this increase of R&D budget, allocated by the government specifically to acquire novel IP or establish in house R&D.

Figure 4: Compound annual growth rate (CAGR) of biomedical R&D expenditures by country, adjusted for inflation, 2007-2012



Source: *The New England Journal of Medicine, "Asia's Ascent – Global Trends in Biomedical R&D Expenditures", January 2014*[13]

Note: *The compound annual growth rate was calculated on the basis of total inflation-adjusted bio- medical R&D expenditures in U.S. dollars for 2007 and 2012.*

Significant market opportunities for Western life sciences startups

Favourable macroenvironment

The Chinese government values innovation. The life sciences industry has been identified in China's 12th five-year plan as being strategically important for the country's sustainable economic growth. It is expected to receive the same support, if not more, from Beijing in the 13th five-year plan, which is due in March 2016. According to China's state council, the healthcare market (which spans the life sciences, healthcare services and healthcare IT sectors) in China is projected to expand to **$1.5 trillion** by 2020.

Nevertheless, the reality is that the current life sciences industry in China is fragmented and lags far behind the West in terms of innovation capability. With over 5,000 pharmaceutical companies in China, no single blockbuster drug (i.e., with sales exceeding US$500 million) has been delivered from China in the last 30 years. Of this multitude of companies, 97% compete in the crowded, low-profit generics sector.

According to Don Qiu from ChinaBio, "many smaller pharmaceutical companies are earning less than 1.5 cents a pill" and struggling to survive, left with very limited resources to upgrade innovation capability and develop their own IP. Even bigger companies (such as state-owned companies) that have deeper pockets and healthy market growth in China have found themselves facing challenges similar to those of multinational pharmaceutical giants. According to **Sinohealth**, a leading health information provider in China, about 800 to 900 patented drugs in China will expire in 2016 and the Chinese companies who own these drugs will need to undertake the same innovative drug candidates scouting process as larger multinational companies.

In order to address these challenges, life science companies in China are racing to source innovations both within and beyond the border. But "for now, early-stage, innovative life sciences companies are still nascent in China, [with] not many companies doing high-quality innovation, and fewer receiving investment from venture capital."[14] **This environment has opened a significant window of opportunity in China for foreign innovative life science startups.**

The following trends have been observed from recent cross-border transactions involving foreign startups:

- Chinese expat researchers who used to work in the US, Canada or Europe ("returnees," or "sea turtles") are returning to China and setting up their own startups, spurred by the slowing economy in the West and China's lucrative incentive policies and research funding support. As Chakma commented in his blog for "Nature", "These people are becoming involved in copy-cats, improvement of old drugs, and some purely proprietary discovery work. Most of the work is sourced from the proprietary knowledge of returnees who have been educating in leading foreign universities"[15]
- Chinese life-sciences industry giants are setting up subsidiaries in bio-clusters worldwide to scout innovative startups to fill their pipelines. Yangtze—one of China's largest players—opened a San Francisco subsidiary, Pan Pacific BioPharma, and companies like Hengrui, which are all heavily invested in research and development

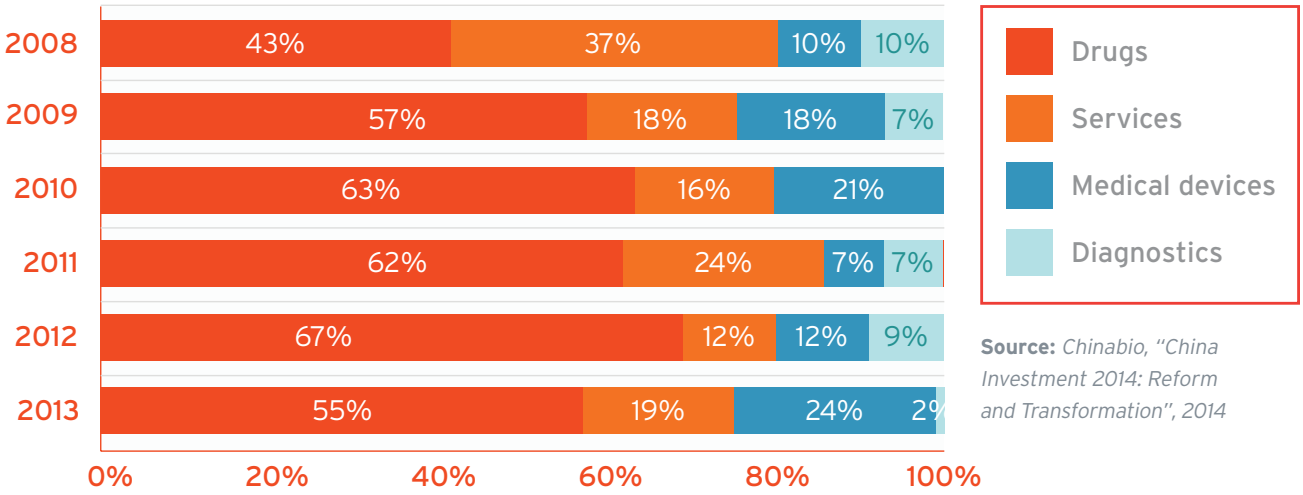
- More cross-border collaborations or transactions are taking place, such as licensing, co-development, mergers and acquisitions (M&As) or joint ventures (JVs), depending on the stage of the technology and the startups' objectives in entering China's market

Active venture capital and private equity investment

In China, there are over 300 VC or private equity (PE) investors focusing on the life sciences, and around $7 billion has been invested since 2009.

Figure 5 shows the breakdown by sub-sector of healthcare VC and PE investment in China from 2008 to 2013. Over half of the deals involve therapeutic drugs and the trend has been steady since 2009. The medical devices sector has been gaining more traction since 2011, with the number of deals doubling from 2012 to 2013.

Figure 5: Venture capital and private equity investment in China's healthcare market by sub-sector, 2008-2013

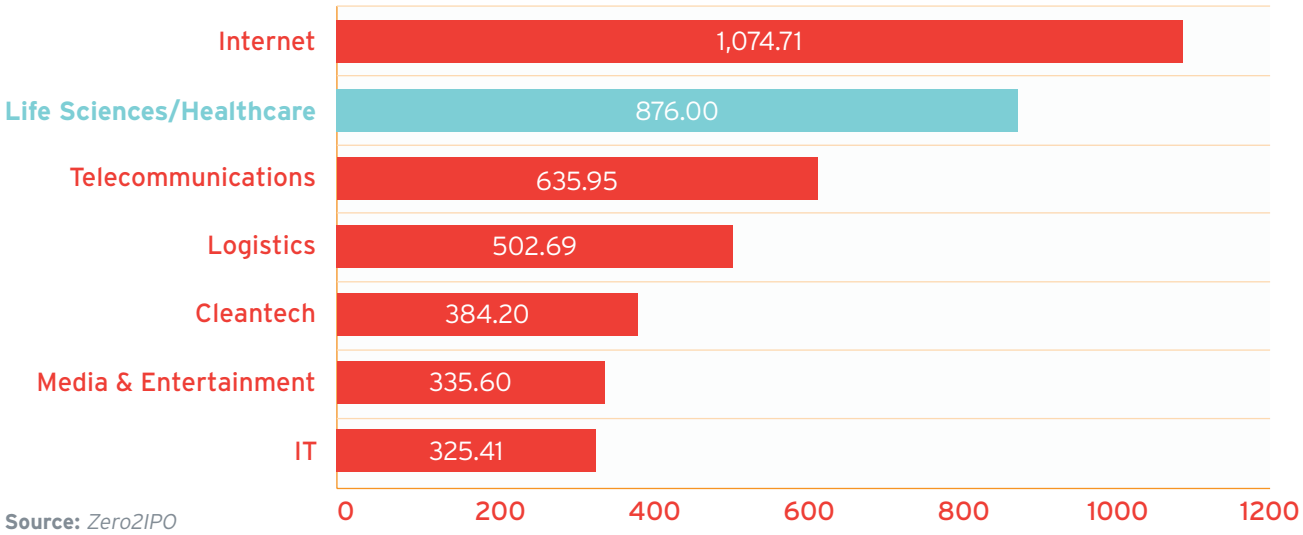


Source: *Chinabio, "China Investment 2014: Reform and Transformation", 2014*

Life sciences startups are finding it easier to access early-stage risk capital in China. Venture capital investment in Chinese life sciences reached the US$1 billion mark in 2014, beating the previous year's total of US$900 million. If that number seems surprisingly small, it might be because investments in China are often kept well under the radar.[16] According to Don Qiu, general manager of consulting in ChinaBio, "If a foreign life sciences startup's technology is truly advanced and demonstrated to have China market potential, it's a norm for a life sciences startup to get early-stage funding support at around $1.5 million from different sources before they settle down in one of the China's high-tech parks. This level of funding could be very critical for startups to survive through 'the valley of death'."

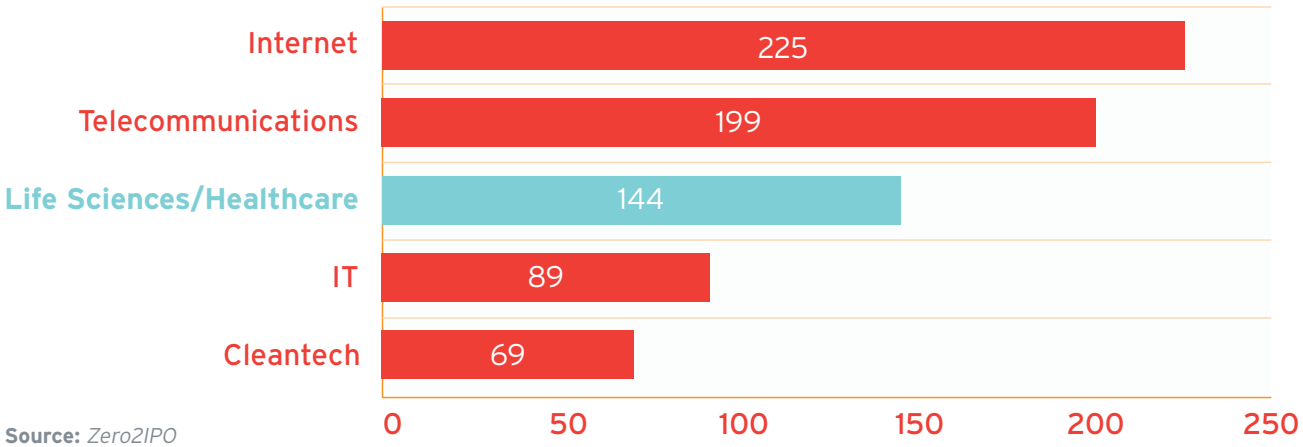
In China, the average VC/PE deal size was US$27 million in 2013, which is much higher than the average investment size in the West.

Figure 6: China's venture capital investment by industry sector (total value, US$ million), 2013



Source: *Zero2IPO*

Figure 7: China's venture capital investment by industry sectors (number of deals), 2013



Source: *Zero2IPO*

CHINA'S PHARMA VENTURE ARMS

Like the multinational pharmaceutical companies, local players are setting up their own venture arms in order to acquire innovations from abroad. Sinopharm, China's largest pharmaceutical company, established Sinopharm Capital in June 2012. By 2014, the fund was already worth roughly US$160 million and is heavily focused on specialty pharma. Roughly ten more local big players, which are all hungry in innovation, are likely to follow the path in order to dominate the research arena amidst foreign entrants.

According to Bioassociate Consulting, "China-focused hedge funds and VCs in the West are also growing in numbers. One of the world's PE leaders—the Israeli China-focused Infinity Group—has sixteen funds, totaling nearly US$1 billion, fourteen of which are located in China. 13 of the 48 companies Infinity is invested in are in the Life Science sector, roughly a third of which are performing R&D—a substantial number, considering the early stage the innovative pharma industry in China is at."[17]

Top 10 China VCs focusing on early-stage investment, 2013 (by number of deals)

1. Legend Capital
2. Gobi Fund
3. Sequoia Capital
4. Govtor Capital
5. Matrix Partners China
6. Qiming Venture Partners
7. SB China Venture Capital
8. Cybernaut (China) Investment
9. Shanghai Zhonglu Group
10. Shenzhen Co-win Venture Capital Investments

Top 10 China life Sciences VCs, 2013

1. CDH Investments
2. Greenwoods Asset Management
3. JD Capital
4. Qiming Venture Partners
5. SB China Venture Capital
6. Shenzhen GTJA Investment Group
7. Shenzhen Co-win Venture Capital Investments
8. Suzhou Oriza Holdings
9. Tianjin Hidea Venture Capital
10. New Horizon

Source: *Zero2IPO, Dec 2013*

Government-backed venture funds

We all know that government is hardly a typical venture-capital investor given the public sector's aversion to risky investments. However, many governments around the world are still committing this type of investment in the life sciences sector in order to "fill a void left by the private sector, which has been pulling back on investing in early-stage biotechnology companies."[18]

For example, in 2013, New York City created a US$-100million venture fund for small New York biotechs. In 2014, the Ontario government proposed a new life sciences seed venture capital fund of up to $30 million to support Ontario's early-stage life sciences firms.

China has also created its version of this type of venture fund in the form of a "Guidance Fund," called the "Fund of Funds" (国有母基金-FoF) in many cases.

The most noteworthy of these is China's national FoF, "Cdb Kai Yuan Capital," with $10 billion in the fund. It was established in 2010 and is mainly focused on leveraging private VC capital into investing in early-stage innovative companies.

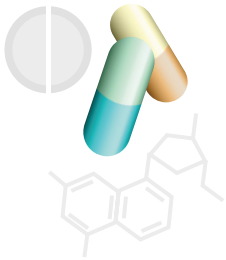
What does China's life sciences market need most?

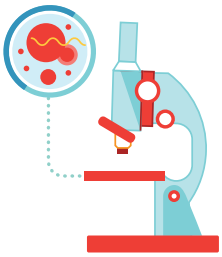
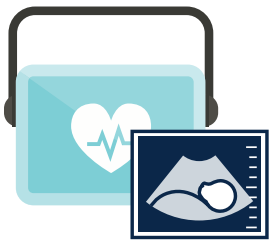
China's five-year plan sets up strategic goals for each of its major industry sectors. These goals are based on China's current stage and structure of economic development as well as consultations with major sector stakeholders. The plan highlights the sector demands in the coming five years and prioritizes the government's support toward these sectors. Governments of different levels and of different ministries in China all have five-year plans with a varying focus. Foreign companies need to keep this in mind when targeting market opportunities for specific disease categories, and think about partnerships in specific regions.

Life sciences market needs

Table 2 shows the technologies and disease categories listed as priorities in China's 12th five-year plan for the pharmaceutical and medical devices sectors.

Table 2: China's 12th five-year plan for the pharmaceutical and medical devices sector

SECTORS	PRODUCT/TECHNOLOGIES	TARGET DISEASES/CORE FEATURES
 **SMALL MOLECULE DRUGS**	**Anti-infective drugs**	Antiviral (hepatitis, flu, AIDS), antifungal, anti-mycobacterium tuberculosis, anti-microorganisms (chlamydia, mycoplasma, malaria, parasites)
	Anti-neoplastic drugs	Lung cancer, liver cancer, breast cancer, gastric cancer, colon cancer
	Drus for cardiovascular diseases	Hypertension, apoplexy, cardiac failure, myocardial infarction, hypertensive pulmonary vascular disease, hyperlipidaemia, thrombosis
	Drugs for endocrine and metabolic diseases	Diabetes, osteoporosis
	Drugs for CNS disease	Depression, anxiety, insomnia, schizophrenia, degenerative diseases (e.g., Alzheimer, Parkinson's disease)

SECTORS	PRODUCT/TECHNOLOGIES	TARGET DISEASES/CORE FEATURES
	Drugs for autoimmune diseases	Rheumatoid arthritis, systemic lupus erythematous, psoriasis, gout
 **BIOLOGICS**	**Humanized monoclonal antibodies**	Cancer; autoimmune, central nervous system (CNS) and infectious diseases - There is strong support for antibody products that have finished clinical research
	Vaccines	Flu, hepatitis, malaria, tuberculosis, AIDS, zoonosis, DPT, varicella, measles, HIV, polio.
	Genetically engineered protein and polypeptide	Low immunogenicity, stable, highly targeted, long-acting, high bioavailability
	Nucleic acid drugs and gene therapy	Antisense drugs, RNAi, Gene therapy
	Cell therapy (stem cell therapy)	Cancer, autoimmune diseases
	Blood products	Factor VIII, cytomegalovirus (CMV)
 **MEDICAL DEVICES**	**Imaging**	Digital radiography systems, multi-slice computer tomography (MSCT), MRI, nuclear medicine, ultrasound, imaging processing and analysis
	In vitro diagnostic (IVD) devices and reagents	Automatic analyzers and corresponding reagents for specimens
	Surgical equipment	High performance anaesthesia stations, non-invasive ventilators, cardiac defibrillators, pacemakers, high-resolution endoscopes, surgical power systems
	Specialized devices	For interventional treatment: chemotherapy, cardiovascular therapy, ophthalmic treatment, haemodialysis, ultrasound therapy
	Consumer medical devices	Focus on safety and reliability in the consumer medical devices sector

SECTORS	PRODUCT/TECHNOLOGIES	TARGET DISEASES/CORE FEATURES
MEDICAL DEVICES	**Rehabilitation medical devices**	Cochlear implants, hearing aids, intelligent assistive devices
	Implants and medical materials	Cardiovascular implants; catheters; adhesives

A funding program has been specifically set up by China's government to support innovative drug discovery activities. Named the "National Major Scientific and Technological Special Project for Significant New Drugs Development"(SNDD), it was built into the five-year plan and it mainly supports pre-commercialization pharmaceutical research.

With this program, funds for SNDD projects have been allocated as follows:

- $1.1 billion for the 11th five-year plan
- $6.5 billion for the 12th five-year plan
- $12.5 billion for the 13th five-year plan

In the newly released SNDD program 13th five-year plan, special funding support will go to:

- Oncology therapeutic drugs
- Innovative generic drugs for chronic obstructive pulmonary disease (COPD)
- Pulmonary hypertension and asthma therapeutic drugs
- Innovative treatment for extensively drug-resistant tuberculosis (XDR-TB)
- The development of China's National Compounds Library

Emerging opportunities in respiratory drugs also stand out in this plan due to China's pressing air pollution issues.

Table 3: China's 13th five-year plan and SNDD: Small molecule drugs

DISEASE CATEGORY	TARGETS
Central nervous system (CNS) diseases	BACE, AMPA
Metabolic Diseases	PCSK9, and others
Targeted cancer therapies and immunotherapy	WNT, PI3K-AKT-mTOR, c-Met, PD1, PD-L1, CTLA4, miRNA, and others
Pulmonary hypertension and COPD	sGC and others
Cardiovascular and cerebrovascular diseases	Aβ, DC20
Neurodegenerative disease	PCSK9, SGLT2
Autoimmune diseases	SYK

Products in other therapeutic areas such as anti-infective drugs, anti-tuberculosis drugs, anti-viral drugs, as well as small molecule compounds that induce cell reprogramming, co-crystallization for enhanced druggability are also mentioned in the plan.

CHINA'S SNDD 13TH FIVE-YEAR PLAN: BIOLOGICS

The SNDD 13th five-year plan supports the following biologics categories:

- New antibody structures
- Bispecific antibodies
- Antibody-drug conjugates (ADC)
- Protein and peptide drugs with new structures
- Biosimilars
- Vaccines with new formulations, combined vaccines and therapeutic vaccines

Through partnerships with companies in China, foreign companies can (indirectly) take advantage of this funding opportunity. In SNDD's 12th five-year period, many funding recipients included foreign in-licensed products in their applications. Examples include:

- GB608 from Globe Biomedical Co. (Beijing): In-licensed BBI608 from Dainippon Sumitomo (Japan)[19]
- BL-8030 from Chia Tai TianQing (Jiangsu): In-licensed from BioLineRx (Israel)
- MESUPRON from Link Health Group (Guangdong): In-licensed from WILEX (Germany)
- Rilotumumab from Beijing Cancer Hospital (Beijing): In-licensed from Amgen (US)

Major market opportunities: Pharmaceutical sector

The biggest pharmaceutical market opportunities lie in the following sectors:

A. **Innovative therapeutics with novel compounds in the disease categories mentioned in the previous section.** China's domestic players are mostly interested in novel compounds that have just started global clinical trials. They then develop same-class compounds—often referred to as "me-too" or "me-better" compounds—and carry the discovery work through to candidate selection. **Betapharma** in Zhejiang and **Chipscreen** in Shenzhen, the hottest innovative biotechnology startups in China, both originate from the US and are focusing in this category.

B. **Differentiated generics (i.e., generics that have some unique feature or attribute, such as a new form of administration).** Differentiated generics are entitled to premium pricing and are sold by companies other than the original developer (it can be a major or niche market in China).

C. **Biologics indicated in the previously mentioned five-year plans that have the potential to become more affordable biopharmaceuticals.** China has strongly focused on monoclonal antibodies, vaccines and biosimilars.[21]

A. Innovative therapeutics with novel compounds in the disease categories mentioned in the previous section.

INVESTORS

- Multinational pharmaceutical company venture arms in China (such as Lilly Asia Ventures)
- Foreign life sciences VC firms who have a presence in China (e.g., OrbiMed Asia, Qiming Ventures). China has five or six dominant VC firms of this type. Most of the firms' investments focus on prevalent diseases in China, such as gastric cancer and hepatitis C
- Public pharmaceutical companies in China

INVESTMENT SCALE

- US$2 million to US$50 million

GOVERNMENT FUNDING PROGRAMS

- The SNDD program, if the collaboration is with innovative drug development companies in China or industry-academic-R&D (IAR) hubs
- 973 (China National Basic Research Program) or 863 (China State High-Tech Development Plan), if the collaboration is with academic research institutions
- Funding programs offered by China's high-tech parks or the life sciences parks concentrated on the east coast of China
- The Regional Government Guidance Fund (or Fund of Funds), which ranges from US$1.5 million to US$150 million
- Talent attraction programs offered by the federal, provincial and municipal governments, which range from US$150K to US$1.5 million

PARTNERS

- Multinational pharmaceutical company R&D centres
- Academic researchers who have access to greater government grant support such as the 973, 863 and national SNDD and regional SNDD programs
- Innovative new drug development companies (see the following list)
- Public life sciences companies in China

COLLABORATION MODELS

- Co-development
- Licensing
- JVs
- M&As

Companies like Roche have a clear mandate that they are not interested in any generic drug development activities in China:

"When we form partnerships, we look for unique differentiators, either first-in-class or best-in-class and they don't do biosimilars, branded generics or generics. We are focused solely on innovation-based medicines." [20]

CHINA'S INNOVATIVE NEW DRUG DEVELOPMENT COMPANIES THAT ACTIVELY PURSUE GLOBAL COLLABORATIONS

Xcovery艾科睿控股公司(Shanghai)

Xcovery was founded in 2006 in the US and established several partnerships with Chinese companies.

Collaboration model: VC+IP+CRO

Therapeutic area: Oncology

Targets: VEGFR, ALK, c-Met, PI3K/mTOR

Bei Gene百济神州生物科技有限公司(Beijing)

BeiGene was established by US researchers in 2010.

Therapeutic area: Oncology

Products: BRAF inhibitor, PARP inhibitor, BTK inhibitor, EG-FRT790M inhibitor, BRD4 inhibitor, anti-PD1MAb and anti-Pdl1 MAb

In 2013, the BRAF inhibitor BGB-283 and PARP inhibitor BGB-290 were licensed to Merck with milestone fees at €170 million.

Centaurus Biopharma 北京赛林泰医药技术有限公司(Beijing)

Centaurus Biopharma was established in 2010 and focused mainly on oncology and diabetes drug development. The company has received equity investments from the Bejing municipal and Beijing Haidian District governments.

Products: ALK/FAK/Pyk2 inhibitor CT- 707and BRAF inhibitor

Targets: Ramatroban, selumetinib, AR-231453, tamoxifen, ibrutinib, ceritinib, fasiglifam and others

Shenogen Pharma北京珅奥基医药科技有限公司(Beijing)

Shenogen Pharma Group was established by US researchers in 2006.

Therapeutic area: Breast cancer

Target: estrogen receptor ER-alpha 36

Ascletis歌礼生物科技有限公司(Hangzhou-Jiangsu Province)

Ascletis is focused mainly on conducting China's clinical trials for in-licensed Western drugs. The company has received US$100 million from investors in China.

Products: In-licensed ALN-VSP from Alnylam Pharmaceuticals, in-licensed danoprevir

from Roche, in-licensed TMC310911 from Janssen

Hutchison MediPharma 和记黄埔医药（上海）有限公司(Shanghai)

Hutchison is a drug development company with pipelines in oncology and autoimmune disease. The company signed license agreements with AstraZeneca and Johnson & Johnson for a total value of US$96.5 million, and has a license agreement with Eli Lilly for a total value US$86.5 million.

ZAI Laboratories- 再鼎医药(Shanghai)

ZAI Laboratory was launched by the previous founder and CEO of Hutchison Medi Pharma and focuses on partnering with global companies to jointly develop innovative drugs. In 2014, the company raised more than US$30 million in series A funding from an international group of healthcare investors that included Qiming, KPCB and Sequoia. ZAI Laboratory in-licensed two pre-clinical compounds from Sanofi (one of them being ZAI1101) for the treatment of COPD, asthma and idiopathic pulmonary fibrosis.

Hansoh Pharmaceutical 江苏豪森药业股份有限公司(Jiangsu province)

In 2014, Hansoh Pharmaceutical developed its first new drug, Morpholine (metronidazole). The company's pipelines also include early-stage developments in a EGFR/HER2 inhibitor, a PLK inhibitor, an ALK inhibitor and potassium-competitive acid blockers.

Hengrui Medicine 江苏恒瑞医药股份有限公司(Jiangsu province)

Established in 1970, Jiangsu's Hengrui Medicine Co. Ltd. is the largest research and manufacturing base of antineoplastics and surgical products in China. Hengrui is especially experienced with technologies such as sustained-release preparations, liposomes, orally disintegrating tablets, inhalation powders and nasal sprays.

Pipelines: Early-stage developments of TPO receptor agonists, an EGFR/HER2 inhibitor, a PI3K/mTOR inhibitor, a CDK4/6 inhibitor, a SGLT2 inhibitor, an androgen receptor antagonist, a GPR40 agonist, a hedgehog inhibitor, a JAK inhibitor and a PPAR inhibitor.

Ascentage Pharma 江苏亚盛医药开发有限公司 (Jiangsu province)

Established by researchers from Ascenta Therapeutics in the US, Ascentage Pharma is dedicated to oncology drug development. The company has a portfolio of apoptosis-triggering small molecules that target protein-protein interactions, including two clinical compounds, AT-101 and AT-406. In June 2010, Ascenta announced a $398 million global collaboration and licensing agreement with Sanofi-Aventis for its third program, targeting the p53-HDM2 (human double minute 2) protein-protein interaction.

Pipelines: IAP inhibitor AT-406, APG-1387 and R-(-)-gossypol acetic acid AT-101, a pre-clinical Bcl-2 inhibitor and an ALK inhibitor.

Advenchen Laboratories 南京爱德程医药科技有限公司 (Jiangsu province)

Advenchen Laboratories is a China-US joint venture based in China. The company is mainly focused on developing tyrosine kinase inhibitors. A well-known molecule that was discovered by the company is aidecheng YN968D1.

Chipscreen BioSciences 深圳微芯生物科技有限责任公司 (Shenzhen)

Chipscreen BioSciences was established as a Sino-Foreign joint venture in 2001 by Chinese returnees from the US. The company is among the most well-known life sciences startups in China, with a reputation of focusing on unique therapeutic targets.

Pipelines: An HDAC inhibitor, sodium pan-PPAR agonist Siegel in phase III clinical trials, and early-stage development of CS994X, CS3158 and CS410.

CSPC Pharmaceutical 石家庄制药集团有限公司 (Hebei province)

CSPC Pharmaceutical Group is probably the most innovative state-owned veteran pharmaceutical company in China. The company in-licensed the DPP-4 inhibitor DBPR108 from Taiwan in 2013.

Simcere Pharmaceutical 先声药业有限公司 (Jiangsu province)

Simcere is China's first pharmaceutical company listed on the New York Stock Exchange. The company partnered with Merck in 2011 in the areas of cardiovascular and metabolic disease. In the cardiovascular disease category, the partnership offers a combined portfolio of selected medication from both companies, including Zocor® (simvastatin), Cozaar® (losartan) and Renitec® (enalapril) by Merck/MSD, and Xinta (levamlodipine) and Shufutan (rosuvastatin) by Simcere. In the metabolic disease area, the partnership will work to maximize access in China to sitagliptin, a DPP-IV inhibitor for the treatment of type 2 diabetes.

Zhao Ke Pharm 兆科药业有限公司 (Anhui province)

Zhao Ke Pharm is a subsidiary of Lee's Pharmaceutical Holdings. The company is well known for focusing on collaborations with foreign life sciences startups. Zhao Ke Pharm in-licensed JX-594 from Jennerex and thymosin beta-4 from Regene Rx Biopharmaceuticals, and, more recently, it licensed the anti-Pdl1 monoclonal antibody STI-A1014 for $46 million from Sorrento Therapeutics.

Betta Pharmaceutical 浙江贝达药业有限公司 (Zhejiang province)

Betta Pharmaceuticals was founded by returnees from the US in 2003, and is one of the leading new drug development companies in China. In 2010, it partnered with Eli Lilly through a strategic investment. In 2013, Betta Pharmaceuticals signed a strategic agreement with Amgen to set up a joint venture, Amgen-Betta Pharmaceuticals, to co-promote Amgen's Vectibix® (panitumumab) in China. In October 2014, the company announced a $20 million investment in Xcovery (see above), a virtual drug developer based in Florida.

Hisun Pharmaceutical 浙江海正药业股份有限公司 (Zhejiang province)

Hisun Pharmaceutical has been very active in in-licensing products from foreign companies. It licensed ThermoDox from Celsion in 2013, and licensed PEG-SN-38 from Enzon Pharmaceuticals in 2012. In the same year, Pfizer and Hisun announced the launch of Hisun-Pfizer Pharmaceuticals, a joint venture formed between the two companies to develop, manufacture and commercialize off-patent generics.

B. Differentiated generics (i.e., generics that have some unique feature or attribute, such as a new form of administration

INVESTORS

- Foreign life sciences VC firms who have a presence in China (e.g., Orbimed Asia, Qiming Ventures). China has five or six dominant VC firms of this type. Most of these firms' investments focus on prevalent diseases in China, such as gastric cancer and hepatitis
- Public pharmaceutical companies in China

INVESTMENT SCALE

- US$2 million to US$50 million

GOVERNMENT FUNDING PROGRAMS

- 973 program or 863 programs, if the collaboration is with academic research institutions in China
- Funding programs offered by China's high-tech parks or the life sciences parks concentrated on the east coast of China
- The Regional Government Guidance Fund (or Fund of Funds), which ranges from US$1.5 million to US$150 million
- Talent attraction programs offered by the federal, provincial and municipal governments, which range from US$150K to US$1.5 million

PARTNERS

- A small portion of multinational pharmaceutical company R&D centres
- Innovative drug development companies that focus on generics (see the following list)
- Public life sciences companies in China

COLLABORATION MODELS

- Contract research organizations (CROs)
- Contract manufacturing organizations (CMOs)
- JVs
- M&As

CHINA'S DRUG DEVELOPMENT COMPANIES IN THE DIFFERENTIATED GENERICS SECTOR THAT ACTIVELY PURSUE GLOBAL COLLABORATIONS

Hansoh Pharmaceutical 江苏豪森药业股份有限公司 (Jiangsu province)

In 2014, the company developed its first new drug, Morpholine (metronidazole). Its pipelines also include early-stage developments in an EGFR/HER2 inhibitor, a PLK inhibitor, an ALK inhibitor and potassium-competitive acid blockers. In recent years, the company has focused on off-patent generics categories.

Qilu Pharmaceutical 齐鲁制药有限公司 (Shandong province)

Qilu Pharmaceutical is one of the largest pharmaceutical companies focusing its R&D on generic drugs. In recent years, the company has focused on biologics.

Pipelines: The anti-EGFR monoclonal antibody and anti-RANKL monoclonal antibody, the anti-TNF-alpha monoclonal antibody,

the anti-VEGF monoclonal antibody, the anti-HER2 monoclonal antibodies and thrombopoietin proposed peptide-FC fusion protein, albumin interferon alpha-2A, fusion protein, TNF receptor-FC fusion protein, PEG-GCSF, follicle stimulating hormone, and keratinocyte growth factor.

Luye Pharma 山东绿叶制药有限公司
(Shangdong province)

Luye Pharma is a leading generic drug company in China. The company recently in-licensed the pan-HER inhibitor poziotinib for US$20 million from Korea.

Chia-tai Tianqing Pharmaceutical
正大天晴药业集团股份有限公司
(Jiangsu province)

Chia-tai Tianqing is among the few companies in China with highly efficient R&D facilities for off-patent generics. In 2013, the company in-licensed BL-8030, an oral treatment for hepatitis C, from BioLineRx, an Israeli clinical-stage pharmaceutical company for up to $30 million in upfront and milestone payments.

C. Biologics indicated in the previously mentioned five-year plans that have the potential to become more affordable biopharmaceuticals

INVESTORS

- The venture arms of China's local big pharma players
- Foreign life sciences VC firms who have a presence in China (e.g., Orbimed Asia, Qiming Ventures). China has five or six dominant VC firms of this type. Most of the firms' investments focus on prevalent diseases in China, such as gastric cancer and hepatitis C
- Public biologics companies in China

INVESTMENT SCALE

- US$2 million to US$50 million

GOVERNMENT FUNDING PROGRAMS

- 973 program or 863 program, if the collaboration is with academic research institutions in China
- Funding programs offered by China's high-tech parks or the life sciences parks concentrated on the east coast of China
- The Regional Government Guidance Fund (or Fund of Funds), which ranges from US$1.5 million to US$150 million
- Talent attraction programs offered by the federal, provincial and municipal governments, which range from US$150K to US$1.5 million

PARTNERS

- Multinational pharmaceutical company R&D centres
- Innovative biologics development companies (see the following list)
- Leading biologics companies in China

COLLABORATION MODELS

- Licensing
- Co-development
- M&As

CHINA'S BIOLOGIC DRUG DEVELOPMENT COMPANIES WITH INTENSIVE GLOBAL COLLABORATION ACTIVITIES

Hengrui Medicine 江苏恒瑞医药股份有限公司 (Jiangsu province)

Established in 1970, Jiangsu Hengrui Medicine Co. Ltd. is the largest research and manufacturing base of antineoplastics and surgical products in China. Hengrui's biological products include a long-acting insulin antibody coupled with SHR0302 and the drug SHR-A1201.

Biotech Pharma 百泰生物药业有限公司 (Beijing)

Biotech Pharma, a joint venture between China and Cuba, was established in 2000. The company developed the China's first humanized antibody technology platform. Biotech Pharma's other biologics products include EGF cancer vaccines, monoclonal antibodies anti-CD6 (psoriasis) and an exendin-4 Fc fusion protein (long GLP-1).

Genor Biopharma 嘉和生物药业有限公司 (Shanghai)

Genor Biopharma was founded by researchers from Amgen in the US in 2007. The company mainly develops biosimilars and early-stage innovative monoclonal antibodies. In 2013, it in-licensed the ARGX-109 anti-IL6 monoclonal antibody (RYI-008, GB224) from Anaphor in US for the treatment of autoimmune diseases.

Pipelines: Anti-HER2 monoclonal antibodies, the chimeric α monoclonal antibody anti-TNF, and the humanized anti-TNF-α monoclonal antibody. In May 2013, and from the RuiYi (now part of Anaphore) introduced the ARGX-109 anti-IL6 monoclonal antibody (RYI-008, GB224) for the treatment of autoimmune diseases.

Fosun Pharmaceutical 上海复星医药股份有限公司 (Shanghai)

Fosun Pharmaceutical is well known in China for its active M&A activities in the life sciences sector. The company has a wholly owned subsidiary, Henlius Pharmaceuticals, which focuses on generics. Its pipelines include an anti-CD20 monoclonal antibody, an anti-HER2 monoclonal antibody, and an anti-TNF-α monoclonal antibody. In 2010, Fosun formed a joint venture with Grupo Chemo of Spain for US$73.8 million to develop four anti-cancer monoclonal antibody drugs. Fosun Pharma owns 70% of this joint venture, with Grupo Chemo owning the remaining 30%.

Fudan Zhangjiang BioPharmaceutical 上海复旦张江生物医药股份有限公司 (Shanghai)

Fudan Zhangjiang was established through a public private partnership in 1996.

Pipelines: An early-stage peptide/protein class drug such as a lymphotoxin α derivatives (phase II), fiber dissolved enzyme originated kinase derivatives, the parathyroid hormone 1-34, and an IL-1 receptor antagonistic anti-agent.

Lansheng Guojian Pharmaceutical 上海兰生国健药业有限公司 (Shanghai)

Lansheng Guojian is the leading company in antibody research in China and has billed itself as "the Genentech in China." The company developed China's first TNF receptor-Fc fusion protein (etanercept) and the first anti-CD25 monoclonal antibody.

3SBioInc 沈阳三生制药股份有限公司 (Liaoning province)

3SBio focuses on collaborations with foreign biologics companies. In November 2014, the company in-licensed tanibirumab, a cancer antibody developed by PharmAbcine, a Korean biotech. Tanibirumab is a VEGFR2/KDR antibody with an anti-angiogenesis mechanism.

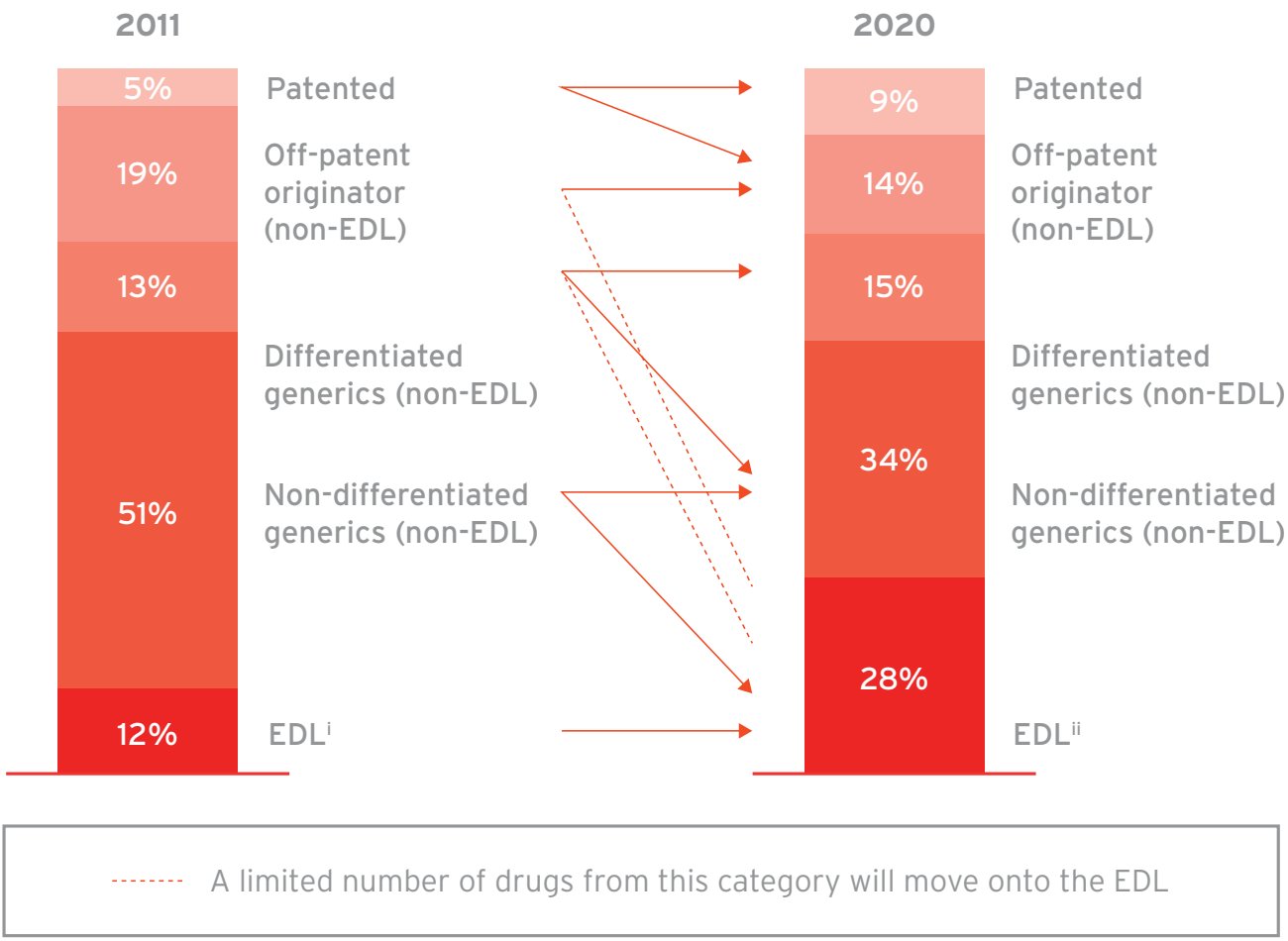
HENGRUI'S ME-TOO, ME BETTER APPROACH

As indicated by Boston Consulting Group,

> **"If the original compound achieves proof of concept, Hengrui proceeds with clinical trials of its own versions, confident in the outcome. Throughout the process—and especially during the trials—Hengrui emphasizes efficiency and streamlined decision making. This approach could allow the company to narrow the gap between the launch of a novel compound and the release of its own follow-on product to about one to two years. Strategies like Hengrui's have two major implications for the Chinese biopharma market. First, they will change the marketability of new medicines in China, as lower-price competition will arise very quickly, even for first-in-class drugs. Second, by allowing local companies to become more familiar with the process of developing drugs, they will eventually lead to a more competitive industry. The former is clearly a threat to multinationals, while the latter is a mixed blessing. Multinationals will face stiffer competition, but they will also find new options for partnering with or acquiring local companies."[22]**

Boston Consulting Group has published a breakdown of China's pharmaceutical market (see Figure 8). It shows the shifting pharmaceutical landscape in China, with the main battlefield for foreign startups being the growing markets for "patented drugs" and "differentiated generics drugs." Even with the predicted market share at only 9% for patented drugs and 15% for "differentiated generics," the market value for these two sectors will stand at US$28 billion and US$47 billion respectively, considering the China's total pharmaceutical market size is expected to reach to US$315 billion by 2020.

Figure 8: Breakdown of China's pharmaceutical market by segment based on sales value



Source: *China's Health Statistics Yearbook 2012; National Health and Family Planning Commission; China Food and Drug Administration; EvaluatePharma; literature search; BCG modeling and analysis.*

Note: EDL = essential-drug list.

[i] Excludes the retail channel and traditional Chinese medicines.
[ii] The EDL consists mostly of nondifferentiated, generic drugs.

Major market opportunities: Medical devices sector

Compared to the long lifespan of pharmaceutical drug discovery, the relatively short product lifecycle of medical devices—normally a few weeks to a few years, depending on whether the product is a predicate device—is very attractive to both industry and investors in China. Medical devices present a huge market opportunity, as well as a lower entrance hurdle for medical device startups looking to enter China. Currently 92% of China's medical device technologies hail from foreign companies. China is hungry for high-quality IP in the medical devices sector, which Canada and Ontario are well-positioned to provide.

The biggest market opportunities lie in the following sectors:

- Ophthalmic devices
- In vitro diagnostic (IVD) devices
- Diagnostic imaging

These sectors are currently driving growth in China's medical devices market.

According to Globaldata, ophthalmic devices accounted for 21.3% of the revenue earned by the overall medical devices market in 2012, with growth fueled by the vision care segment.

The current market size of IVD devices in China is around $2 billion and is expected to grow at an average 16% per year, leading all other countries. The gross profit margin of leading IVD reagents companies is valued at around 70% to 75%. Future growth in the IVD market will be motivated by patients' increasing awareness of the possibilities of early detection and diagnosis, as well as the availability of cost-effective diagnostic tests.

Demand for ultrasound and computed tomography (CT) technologies are responsible for growth in the diagnostic imaging market. The ophthalmic, cardiovascular and orthopedic device markets are all influenced by China's growing elderly population. As the prevalence of diseases associated with aging increases, so will the demand for new medical treatments and devices.

INVESTORS

- China's local specialized life sciences VC firms
- Foreign life sciences VC firms who have a presence in China (e.g., Orbimed Asia, Qiming Ventures). China has five or six dominant VC firms of this type). Most of these firms' investments are focused on prevalent diseases in China, such as gastric cancer, liver cancer and hepatitis C
- Public medical devices companies in China

INVESTMENT SCALE

- US$2 million to US$50 million

GOVERNMENT FUNDING PROGRAMS

- 973 program or 863 program, if the collaboration is with academic research institutions in China
- Funding programs offered by China's high-tech parks or life sciences parks concentrated on the east coast of China
- The Regional Government Guidance Fund (or Fund of Funds), which ranges from US$1.5 million to US$150 million
- Talent attraction programs offered by the federal, provincial and municipal governments, which range from US$150K to US$1.5 million

PARTNERS

- Academic research institutions (mostly interested in diagnostics platform technologies)
- Leading medical devices companies in China

COLLABORATION MODELS

- Licensing
- Co-development and co-marketing
- JV
- M&As

Advantages for accessing China life sciences market

The first report of MaRS' Going Global: China series, entitled Playing the Long Game: China's market opportunities for Ontario startups (June 2014) highlighted the many advantages of entering China's market, including new market opportunities, sustainable R&D investment and reduced commercialization costs. Certain benefits specific to the life sciences sector also stand out as valuable to foreign early-stage companies:

- **Partnerships:** Partnerships with local Chinese players can appeal to both sides. Such deals typically enable the foreign startup to access capital and reduce risk, opening the opportunity to develop multiple life sciences products at one time. In return, the company signs over the marketing rights for China, but retains the rights to most of the global market. For the Chinese partner, it is a chance to gain access to key R&D and an opportunity to secure its own product [23]
- **Research services:** Direct investment in R&D via the research labs of multinational pharmaceutical companies has contributed to the sharp growth of life sciences R&D expenditure in China and it also supports the development of a contract research services (CRS) sector in China. The CRS offerings are expanding on the whole R&D value chain. And the current concentration of global R&D resources would provide relatively low-cost and high-quality research services and could potentially fit as good development partners for research-focused life sciences startups
- **New markets:** China has many unique disease mechanisms. Gastric and liver cancers, for example, are prevalent, which presents an area for R&D innovation to pursue. New therapies against those diseases are desperately needed for the market. This opens up new markets for foreign companies [24]
- **Laboratory space:** Beyond R&D, real-estate and facility costs are among some of the biggest expenses for life sciences companies. Incubator-style buildings that offer flexible space options and access to shared laboratory services are in high demand and are emerging in many life sciences parks across China. Most of them offer the space at no cost for three to six months on general terms. When a company reaches the manufacturing stage, it is common to receive government approval to rent the factory facilities free of charge for about three to five years

Regional life sciences market opportunities in China

China's major life sciences clusters

Similar to the life sciences clusters we see in Ontario (such as Toronto's Discovery District), life sciences clusters in China are also the result of an organic concentration of key elements for the sector. These include universities and research institutions, key players along industry value chains, investors and excellent research talent. But one major difference exists. Unlike innovation hubs in the West where the private sector fuels innovation, clusters in China are mainly designated by the government in a "top-down" manner.

In accordance with China's 12th five-year plan, many provinces and cities recently moved toward establishing biotech parks and life sciences parks. The government created 22 national life sciences parks (along the lines of Silicon Valley), within which the majority of China's multinational life sciences companies set up their global/Asia research centres or labs. The industry production value from these 22 hubs accounts for two-thirds of China's total life sciences industry production.

Most of these clusters are situated along the east coast of China. All are experienced in working with foreign companies, and each hub has its own industry expertise and incentive packages to attract prospective companies. Most foreign life sciences startups opt to set up shop in one of these clusters due to the proximity of low-cost, high-quality research facilities, accessibility to both public and private funding, and being able to easily meet with other companies or institutions in the sector.

In some regions such as Shanghai and Shenzhen, a special zone (Shanghai Free Trade Zone and Qianhai Special Economic Zone, respectively) has been set up to provide more convenience and policy and funding support to foreign companies.

Among these life sciences clusters in China, three regions are leading the others in terms of innovation capability, R&D intensity, talent pool and expertise in commercialization.

These regions are:

- Beijing and Tianjin
- Yangtze River Delta (including Shanghai, Jiangsu Province and Zhejiang
- Guangdong Province (including Shenzhen and Guangzhou)

Off the 22 life sciences parks across the country, eight of them (36%) are located within these three regions. The national market share of medical devices from these three regions is over 80%.

The Yangtze River Delta Region holds China's two wealthiest regions, Jiangsu Province and Shanghai, which are home to the largest number of life sciences companies and account for more than 30% of the total investment in the industry. Shenzhen, called "the capital of the VC industry in China," has one-third of all the VC firms in China.

Most of China's VC funds and government-backed Guidance Funds (Fund of Funds) are concentrated in these regions as well. Greatly varied from common commercial FOFs world-wide, all of the existing FOFs in China are regional government guidance funds with funding support from local governments. They focus on supporting the local economy.

Major Government Guide Funds in the region

FUND NAME	ESTABLISHMENT DATE	LOCATION
Shanghai Chengtou Fund of Funds	2011-11-01	Shanghai
Guochuang Kaiyuan Fund of Funds	2010-12-28	Suzhou (Jiangsu)
Oriza Capital	2010-09-01	Suzhou (Jiangsu)
Dothink Fund of Funds	2013-01-22	Shenzhen
Beijing Private Equity Growth Fund	2009-09-29	Beijing
Shenzhen VC Fund of Funds	2012-01-01	Shenzhen
BECC	2010-11-01	Beijing
Guangdong Strategy Emerging Industry VC Guidance Fund	2013-08-01	Guangdong
Guangdong Yueke Innovation Fund of Funds	2014-06-20	Guangdong

Quick facts: Beijing and Tianjin, Yangtze River Delta and Guangdong Province

BEIJING & TIANJIN

CHINA REGIONAL INNOVATION CAPABILITY:

BEIJING 3RD

2 NATIONAL LIFE SCIENCES **PARKS**

19 LIFE SCIENCES **STATE KEY LABORATORIES**

TOTAL VC INVESTMENT IN BEIJING, 2013:

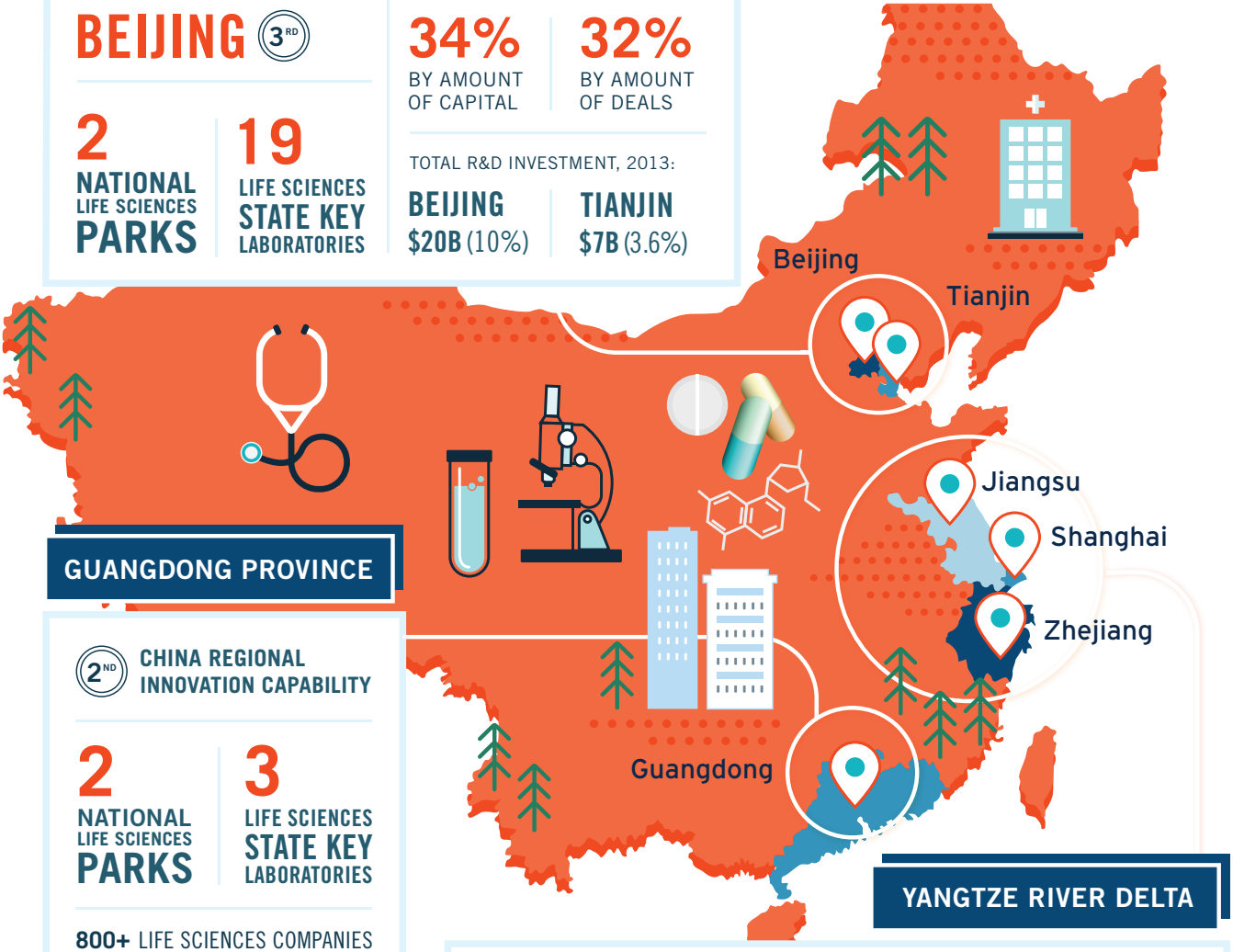
34% BY AMOUNT OF CAPITAL

32% BY AMOUNT OF DEALS

TOTAL R&D INVESTMENT, 2013:

BEIJING $20B (10%)

TIANJIN $7B (3.6%)



GUANGDONG PROVINCE

2ND CHINA REGIONAL INNOVATION CAPABILITY

2 NATIONAL LIFE SCIENCES **PARKS**

3 LIFE SCIENCES **STATE KEY LABORATORIES**

800+ LIFE SCIENCES COMPANIES

TOTAL VC INVESTMENT IN SHENZHEN, 2013:

12% BY AMOUNT OF CAPITAL

8% BY AMOUNT OF DEALS

TOTAL R&D INVESTMENT IN THE REGION, 2013:

$24B (12.2%)

YANGTZE RIVER DELTA

CHINA REGIONAL INNOVATION CAPABILITY:

JIANGSU 1ST / **SHANGHAI** 4TH

3 NATIONAL LIFE SCIENCES **PARKS**

9 (Shanghai) LIFE SCIENCES STATE KEY **LABORATORIES**

3,000+ LIFE SCIENCES COMPANIES

LIFE SCIENCES MARKET SHARE **27%**

TOTAL VC INVESTMENT IN THE REGION, 2013:

25% BY AMOUNT OF CAPITAL

33% BY AMOUNT OF DEALS

(Shanghai, Jiangsu and Zhejiang combined)

TOTAL R&D INVESTMENT, 2013[25]:

SHANGHAI	JIANGSU	ZHEJIANG
$13B (6.6%)	$25B (12.6%)	$14B (6.9%)

Source: *China Regional Innovation Capability Report, 2013*

A closer look at China's top clusters: Beijing, Shanghai, Jiangsu and Guangdong

In this section, we examine the two cities and two provinces that form the most prominent life science clusters in these regions. We also look at the strength of each cluster, as well as their research and clinical resources.

Beijing Life Sciences Cluster

Population: 21 million **Industry Revenue:** $ 20 billion

Research resources: Beijing is home to around 40 colleges and universities, including Peking University and Tsinghua University. It also houses numerous national scientific institutions, state-level laboratories, national engineering research centres and national technological research centres.

Clinical resources: Beijing has very rich clinical resources compared to other cities in China due to its high concentration of hospitals and healthcare institutions.

Mainly therapeutic target areas:
Cardiovascular, diabetes and oncology

Main target areas for medical devices: Digital imaging devices, new radiation therapy devices

Funding initiatives: China's first Life Sciences Technology Transfer Fund, "Hong De Chong Xin Fund," was established in Beijing in 2013 with raised capital equivalent to $45 million. Another fund also established in Beijing is called the "Beijing Life Sciences Investment Consortium." It has raised capital equivalent to over $850 million, collectively through 12 investment companies in Beijing. It is mainly focused on providing funding support for life sciences startups settled in Beijing.

Major regional life sciences parks: There are three major life sciences parks in Beijing, including Z-park Daxing Bio-medicine Industry Park (ZDBIP), Z-park Life Science Park (ZLISP) and Beijing Economic Technological Development Area (BETDA).

Compared to other science parks, ZDBIP's most competitive advantages are its level of industrialization and its efficient public service platform for the industry. BETDA is the only area that enjoys the preferential policies of both state economic and technological development areas as well as state high-tech industrial parks. Known as "medical valley," BETDA is one of China's three national biological pharmaceutical innovation incubator bases.[26]

Shanghai Life Sciences Cluster

Population: 19 million **Industry revenue:** $65 billion

R&D talent pool
70,000—Shanghai ranked number one in a 2014 list published by GEN of hot spots for biotech jobs outside the US[27]

Clinical resources
150 hospitals (as of 2011)

Research resources
Shanghai has the highest concentration of medical R&D resources in China. It has five medical universities and medical schools and is also home to over 30 high-level medical research institutions. Shanghai also houses intensive multinational pharmaceutical industry R&D centres from multinational companies such as Pfizer, GlaxoSmithKline, AstraZeneca, Novartis, Roche and Thermo Fisher Scientific.

Main therapeutic target areas
Development of anti-tumour antibodies, drugs for rheumatoid arthritis, vaccines for viral hepatitis and cervical cancer, nucleic acid drugs, stem cells, recombinant cytokines such as anticancer drugs, and other biotech innovations

Main target areas for medical devices
High-end medical imaging, as well as diagnostics, minimally invasive implants, and precision therapy and rehabilitation devices

Funding initiatives
Shanghai created a unique incubation model for life sciences startups, named "VIC," short for venture capital + IP + CRO. For innovative life sciences startups, after receiving VC injection from the public and private sectors, the company can deploy low-cost and high-quality research services offered by CROs in life sciences parks.

Major life sciences parks
There are six major life sciences parks in Shanghai, including ZJ Innopark, Minhang District R&D base, Xuhui District CRO base, Fengxian District Industrial base, Jinshan District Industrial base and Qingpu Industrial base. According to statistics from Shanghai S&T Committee, this cluster's six industrial parks achieved a life sciences industrial production value of nearly $10 billion in 2011, accounting for 75% of Shanghai's total industry production value.

Jiangsu Life Sciences Cluster

Population: 79 million **Industry revenue:** $53 billion

Jiangsu province is the leader of China's life sciences industry. Among China's 13 pharmaceutical companies listed in the Fortune 500 global pharmaceutical ranking, 10 of them are located in Jiangsu. In the medical devices sector, the disposable medical devices and supplies market in Jiangsu accounts for more than half of the domestic market share. This cluster specializes in:

- **Wuxi:** Ophthalmic equipment, ultrasound
- **Nanjing:** Microwave and radio-frequency tumour hyperthermia
- **Ningbo:** Magnetic resonance imaging

Main therapeutic target areas
Development of vaccines, diagnostic reagents, nucleic acid drugs, therapeutic antibodies, gene and protein and peptide drugs

Main target areas for medical devices
High-end medical equipment, and the acceleration of the development of diagnostics imaging such as PET-CT and MRI

Major life sciences parks
The most well-known life science parks in Jiangsu are bioBAY in Suzhou and Taizhou National Medicine Hi-tech Industry Development Zone (China Medical City).

Since it opened in June 2007, bioBAY has been awarded titles, including "China International Nano-tech Innovation Cluster," "Chinese Service Outsourcing Pilot Base," "High Level Overseas Talent Innovation and Venture Base," "Jiangsu Bio-medical Industrial Park," and "Jiangsu Nano Technology Industrial Park." The region has developed capabilities for gene technology and nanotechnology with the most complete industrial chain and the highest industrial agglomeration level in China. Its gene technology cluster covers the complete industrial value chain consisting of gene reagent development, gene detection services, gene diagnostics, gene therapeutic drug R&D, and gene engineering drug and vaccine R&D.[28]

Based in Taizhou, China Medical City provides one-stop R&D services to research-intense life sciences companies through public service platforms that include pharmacology, toxicology evaluation, and more.

Funding initiatives
In 2011, Avenue Capital Group, a global asset management company, signed an agreement with Taizhou Medical City for the establishment of China's Medical City-Avenue Bio-Pharmaceutics Equity investment Fund, with a projected size is RMB2 billion ($330 million). The aim of the fund is to invest in bio-pharmaceutics, drug distribution, medical devices and hospital construction in China Medical City.

bioBAY, in addition to regular rent relief, provides capital matching with certain conditions. On aver-

age, drug development companies receive around
$10 million after several rounds of financing (including grants, VCs and others).

Jiangsu is the sister province of Ontario and in 2015 the two provinces will mark the 30th anniversary of being twinned. During Ontario Premier Kathleen Wynne's October 2014 delegation visit to China, Jiangsu Huayi Technology, a company that specializes in R&D for medical imaging technologies, said it is considering a $40 million investment in Ontario's medical sector.

Guangdong Life Sciences Cluster

Population: 22 million (Guangzhou and Shenzhen combined)
Industry revenue: $15 billion

In general, the life sciences industry in Guangdong province lags behind the other clusters. This gap is especially apparent in innovative drug development.

But Shenzhen is very well known in China as the leader in the medical devices sector and the gene sequencing industry. For the medical devices sector, the main products include monitoring equipment, ultrasound equipment, MRI and other imaging devices, and Gamma Knife and XKnife Stereotactic radiotherapy equipment for large, thermotherapy equipment. Shenzhen is also a frontrunner in electronics, computers, telecommunications, mechatronics and other areas, which sheds light on why Shenzhen also excels in the medical devices sector.

BGI in Shenzhen, founded in 1999, is now the biggest genomics organization in the world. BGI's national gene bank is China's first (and the world's fourth) national gene bank.

Research resources

Shenzhen is home to the Chinese Academy of Sciences key laboratory of biomedical information engineering and health, Peking University Shenzhen Graduate School and the State Key Laboratory of Chemical Genomics.

Major life sciences parks

There are four main life sciences parks in Guangdong province, including:

- National Bio-industry base Guangzhou Science City
- Guangzhou International biological Island
- Shenzhen Biomedicine Innovations Industry Park
- Zhongshan national health technology industry base

Funding initiatives

This cluster has two key funding programs:

- **Pearl River Talents Program** (珠江人才计划)
  Special focus on stem cell and tissue engineering
  Funding support: $1.5 million – $150 million
- **Peacock Program** (孔雀计划)
  Funding support: One time award of CAN$150K
  Project grant: $1.5 million – $150 million

Addressing concerns and challenges

Intellectual property protection

When considering entering China's markets, many startups are apprehensive about the Chinese government's ability to protect their intellectual property (IP). In the life sciences sector, this concern is especially unfounded.

As discussed in "Get your intellectual property ready for the Chinese market," 80% or more of the IP trials and lawsuits in China relate to copyright (such as movies, music and publishing). Less than 10% are related to patents, which is the category for IP in the life sciences. And among these patent-related legal challenges, the number of cases won by foreign companies is growing. This shows that China is making strong progress in patent protection. This view is reinforced by the Asia Pacific Foundation of Canada's "Canadian Businesses in China" survey (September 2014), which indicated that "only 11% of respondents reported experiencing a violation of IPR [IP rights] in the last five years."

Supporting the indications that the country is emphasizing IP protection, China passed legislation on August 31, 2014, to establish specialized IP courts in Beijing, Shanghai and Guangzhou. This measure is to help the legal system cope with the rapid growth of the number of IP court cases.

China has been revising and improving its IPR policies in the hope of encouraging innovation and facilitating better patent oversight. Patent protection has been strengthened and is moving toward the structures used in Japan, Europe and the United States. This restructuring includes a commitment to data exclusivity and the implementation of a patent linkage system.

The view that China is firming up IP protection is echoed by Yang Shao, CEO of Geneseeq Technology Inc., a Toronto cancer diagnostic company and a MaRS client. In 2014, Geneseeq Technology received a $5-million VC investment from China. In Shao's experience, both industries and investors in China are very alert and cautious about patent protection and will not start any business discussion if a company does not have technology patent protection in place.

Regulatory hurdles

To successfully enter China's markets, startups must recognize and prepare for the regulatory process and environment. Major features of this include:

- Foreign manufacturers in China cannot directly sell medical devices. They must work with their own registered distribution company or a local third party. Similarly, drug manufacturers cannot sell directly to hospitals and must also go through a local distributor. Foreign companies should seek

partnerships or joint ventures with local leading players

- Foreign companies must stay up to date on political affairs. China's government will continue to play a major role in the purchasing decisions of public medical institutions
- The regulatory process to apply for either clinical trials or new drugs is much longer than in the West, despite China's efforts to shorten it. For instance, an application for a clinical trial for a biologic drug will take approximately 19 to 22 months, and for a small molecule drug, 10 to 18 months. In the US or South Korea, in comparison, this can sometimes be done within 30 days, if certain conditions are met
- Registration trials must be driven by statistics and prove that the efficacy is as similar for the Chinese population as it was for the population that participated in the phase III trials. Part of the registration trial is also an additional safety test—and that applies even if a trial is as small as 50 people. The SFDA generally requires that for small molecule drugs, the study involve 100 people. For biologics, the study may need to involve 300 people, and for biosimilars, up to 600 people.

Startups must take into account the required investment of both time and money to reach regulatory approval.

Deal negotiation and government relationships

As discussed, the Chinese government plays a key role in connecting startups to potential partners in China and in providing funding support. It's critical to be able to access that voice from the government and their knowledge and network. Startups should not lose sight of this in any deal discussion with China.

But while building close "guanxi" (relationships) with the government is important, foreign companies should be cautious about being too keen on connecting to certain circles in order to gain a business advantage, as this may carry risk. As frequently commented by Jack Ma, the CEO of Alibaba, about doing business in China, "be in love with government, but never marry them."

Ontario startups should remember too that the decision-making process unfolds differently in China. As commented by Charkma in his "Nature" article,

"In the United States or Canada, deals are clean, and you don't have to worry about the government, assets or hand-hold the company as much. In China, it requires more involved decision-making, because they focus more on the local market needs and low cost, as opposed to being innovation-focused. Third, developing a strong brand is key in order to attract the right deal flow." [29]

Life sciences collaboration models

Knowing which collaboration model to pursue in China is not straightforward. Different companies will require different collaboration models as different partnerships present different advantages. The precise needs will depend on a startup's technology, its objectives and its expectations of the partnership. To help streamline the process, startups should consider whether they need their partner to help with developing or commercializing the product, and whether their product is a generic or a biosimilar, or is innovative.

Technology transfer through in-licensing has been increasingly adopted by companies in China when dealing with foreign startups. In 2014, among cross-border life sciences deals, licensing deals were on the rise and accounted for more than half of all partnerships.

It is also very common to see deals in the form of one-time buy-outs, due to the lack of financial transparency by local companies.

Earlier-stage partnering is growing. According to ChinaBio, "more deals are moving away from phase I/II and going toward pre-clinical. Oncology dominates—making up about half of all deals—while diabetes and infectious diseases each make up 13 percent, although the number of infectious disease agreements has declined significantly over the last several years, partially due to government's new move of promoting rational use of antibiotics. The commitment-heavy joint venture approach is typically a less popular deal structure in China. And looking at the numbers reveals an eye-catching decline in joint venture partnerships, with only 3 percent of partnering deals going this route compared to a more robust 15 percent in 2013."[30]

Co-development agreements make up a quarter of all deals and the partners in China are mostly academia or research institutes. For research-intense life sciences startups, this type of partnership offers greater benefits in terms of accessing Chinese government funding support. The major funding programs in China such as 973 (National Basic Research Program) or 863 (National High-tech R&D Program) can offer up to $7 million per project, depending on the technology.

Due diligence must be conducted before approaching a potential partner in China. Startups can benefit substantially if they have a clear understanding about potential partners' strengths and capabilities. Some innovative life sciences companies in China are very active in scouting foreign technology and are quite experienced with technology commercialization in their sector. For example, with an innovative drug, if a potential Chinese partner had the capability to adopt a "first in China" strategy (meaning that the first in-human trial [FIH] would take place in China) and the FIH used materials manufactured locally and the drug manufacturing also happened in China, a key market benefit would follow. The drug would be able to take advantage of a certain period of market exclusivity that is offered by regulatory bodies.

Lastly—and obviously—working successfully with China's health regulators is crucial to a startup's success in the market. China has substantial and complex regulatory guidelines, and the details of how to satisfy these guidelines are not always clear. Being able to communicate with the SFDA on a regular basis to obtain its feedback is critical. Having local partners with this capability enables greater opportunities for foreign startups.

Help for startups: Ontario organizations

Startups going global need a lot of guidance during the process due to their inherent limited financial resources and uncertainty about markets abroad. Many Ontario start-ups build their first China connections through conferences, trade shows or personal relationships. This approach can be a bit random and, despite the best efforts of entrepreneurs, can unfortunately be in vain if due diligence and partnership screening are not properly carried out.

Yang Shao, CEO of Geneseeq Technology Inc., believes startups would benefit if they could tap into global markets through an "organizational approach." To Shao, this would be a system of partnerships between high-level organizations in both countries. Such an approach would give startups a leg up when dealing with investors or partners in the global market and, to some extent, would provide an endorsement to startups when a collaboration discussion is started.

In response to this need, several Ontario organizations are stepping forward to explore China's market opportunities for Ontario startups, with the aim to help them advance their technologies. The efforts of these organizations, such as the ones listed below, are in addition to those of the Canada's federal and provincial governments.

MaRS Discovery District

MaRS Discovery District is one of the biggest innovation hubs in Canada. In 2014, MaRS signed a collaboration agreement with Shanghai Technology Innovation Center (STIC), one of the biggest incubators in China. (See the related MaRS blog for details). The main goal of the partnership is to enhance supportive environments for startups in Ontario and to help them bring their innovative technologies to China's market.

Under this agreement, MaRS will work together with STIC to:

- Advise companies on how to grow from the early stages to global market success, particularly in the health, ICT (information and communications technology) and cleantech sectors
- Aid companies with market due diligence and analysis
- Help companies develop talent through entrepreneur education, training and mentorship
- Assist companies in connecting with investors, including seed and venture funds, licensing, R&D and manufacturing partners
- Create "soft-landing" programs that facilitate the settlement of Ontario-based small- and medium-sized enterprises (SMEs) in Shanghai, and of Shanghai-based SMEs in Ontario. Program services include help with:
  - Validating innovative technologies
  - Connecting to incubators, service providers, investors, regulators and government
  - Developing local and overseas marketing

MaRS market intelligence services

The MaRS market intelligence team has dedicated research analysts and resources for entrepreneurs who are considering entering global emerging markets such as China, India and countries in South America. It offers due diligence about industries, competitors, markets, transactions, intellectual property and best business practices.

MaRS workshops

MaRS also offers the Entrepreneur's Toolkit Workshops, a collection of experiential, hands-on workshops facilitated by experienced entrepreneurs. These sessions are designed for a maximum of 30 participants and allow time for exercises and peer-to-peer feedback on participants' own ventures. Sessions on reaching out to global markets will soon join this suite of workshops.

Health Technology Exchange (HTX)

Health Technology Exchange (HTX) is an Ontario non-profit venture financing company created to accelerate the growth of Ontario's medtech ecosystem. The company has made China a focus of its future foreign market access assistance programs for Ontario SMEs.

HTX has established a strategic partnership with WORLDiscoveries, a not-for-profit agency spun out of the University of Western Ontario, and has developed soft-landing services for Ontario SMEs in the medical devices sector. Under the partnership
agreement, HTX and its companies have access to three WORLDiscoveries offices in Tianjin, Nanjing and Sha Tin (Kowloon/Hong Kong), as well as to support staff.

Additionally, as part of an international soft-landing effort, HTX has identified a number of highly qualified consultants who specialize in Chinese market access and to whom interested companies can be connected.

University of Western Ontario

Launched in 2009, WORLDiscoveries Asia is an initiative aimed at promoting international research collaboration and IP commercialization in China and Asia. WORLDiscoveries maintains close ties with many Chinese industry players, including, but not limited to, Taizhou Medical City, Changzhou biomedical industrial park, and Suzhou high-tech park.

Canada China Business Council

The Canada China Business Council (CCBC)'s Business Incubation Platform is a suite of services that addresses the infrastructure needs of Canadian SMEs entering China and those of Chinese investors entering Canada. The services include:

- Business incubation centres in Shanghai: This provides SMEs with an affordable, low-risk way of building a presence in China
- Virtual office space in Beijing and Shanghai:

This type of service is available for SMEs that do not require a permanent presence in China. It includes a mailing address, telephone answering service, WiFi, website translation (into Mandarin) and the occasional use of a conference room

The next 10 years: A wealth of opportunity

The life sciences industry in China is unique and uncharted. Although the success of reaching this high-growth market may seem uncertain to startups, China's rising incomes, improving healthcare infrastructure and increasing medical needs, coupled with the backing of substantial government and private capital, are generating much greater opportunities than those of unmet niches in other countries.

In 2013, Qibin, an official from the China Securities Regulatory Commission, commented about the rise of Chinese mobile phone company, Xiaomi. Xiaomi's sales had reached US$2 billion in just two years (compared to 10 years for Apple, seven years for Facebook and six years for Google). Qibin pointed out that "Xiaomi's success can only happen during this historical window in China—provided with the China's current stage of development, huge internal market demand and 1.3 billion gradually progressing into middle-class. For technology-based companies, even with a small competitive advantage, which can meet even a tiny niche market need in China, even if you are ranked 100th or 200th in that niche market, they will still have great opportunities in China's market."

China is rapidly becoming a dominant force in the global life sciences industry. It is currently the third-largest global pharmaceutical market and it is prioritizing innovation. Western life science companies need to zero in on this emerging market in their strategic R&D and commercialization plans as China is currently outpacing the growth of global and Western life sciences markets.[31] For Ontario startups, the coming decade offers a wealth of opportunity.

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